INFORMATION TO USERS

This material was produced from a microfilm copy of the original document. While the most advanced technological means to photograph and reproduce this document have been used, the quality is heavily dependent upon the quality of the original submitted.

The following explanation of techniques is provided to help you understand markings or patterns which may appear on this reproduction.

1. The sign or “target” for pages apparently lacking from the document photographed is “Missing Page(s)”. If it was possible to obtain the missing page(s) or section, they are spliced into the film along with adjacent pages. This may have necessitated cutting thru an image and duplicating adjacent pages to insure you complete continuity.

2. When an image on the film is obliterated with a large round black mark, it is an indication that the photographer suspected that the copy may have moved during exposure and thus cause a blurred image. You will find a good image of the page in the adjacent frame.

3. When a map, drawing or chart, etc., was part of the material being photographed the photographer followed a definite method in “sectioning” the material. It is customary to begin photoing at the upper left hand corner of a large sheet and to continue photoing from left to right in equal sections with a small overlap. If necessary, sectioning is continued again — beginning below the first row and continuing on until complete.

4. The majority of users indicate that the textual content is of greatest value, however, a somewhat higher quality reproduction could be made from “photographs” if essential to the understanding of the dissertation. Silver prints of “photographs” may be ordered at additional charge by writing the Order Department, giving the catalog number, title, author and specific pages you wish reproduced.

5. PLEASE NOTE: Some pages may have indistinct print. Filmed as received.

Xerox University Microfilms
300 North Zeib Road
Ann Arbor, Michigan 48106
LEE, Len Fang, 1945-
I. ATTEMPTED SYNTHESIS OF ROTAXANES. II. A NEW SYNTHESIS OF 6-SUBSTITUTED BENZO[a]PYRENES INVOLVING 5a,6-DIHYDRO-5a,6-EPOXYBENZO[a]PYRENE.

The Ohio State University, Ph.D., 1974
Chemistry, organic

Xerox University Microfilms, Ann Arbor, Michigan 48106
I. ATTEMPTED SYNTHESIS OF ROTAXANES

II. A NEW SYNTHESIS OF 6-SUBSTITUTED BENZO[a]PYRENES INVOLVING 5a,6-DIHYDRO-5a,6-EPOXYBENZO[a]PYRENE

DISSERTATION

Presented in Partial Fulfillment of the Requirements for the Degree Doctor of Philosophy in the Graduate School of The Ohio State University

by

Len Fang Lee, B.S.

* * * * *

The Ohio State University

1974

Reading Committee:  
Professor Jack Hine  
Professor Melvin S. Newman  
Professor John S. Swenton

Approved By

Melvin S. Newman  
Adviser  
Department of Chemistry
The research described in this dissertation is present in two parts. Part I deals with attempted synthesis of rotaxanes. Part II is devoted to a new synthesis of 6-substituted benzo[a]pyrenes involving 5a,6-dihydro-5a,6-epoxybenzo[a]pyrene.
ACKNOWLEDGMENTS

I wish to express my great appreciation to Professor Melvin S. Newman for his constructive criticism, guidance, encouragement, and generous assistance in the preparation of this manuscript.

I also wish to thank my wife, Peggy, for her untiring patience and unlimited assistance.
VITA

May 14, 1945 .......................... Born - Taipei, Taiwan, Republic of China

1967 ...................................... B.S., National Taiwan University, Taipei, Taiwan

1967-1968 .............................. Second Lieutenant, Army, Republic of China

1968-1970 .............................. Teaching Assistant, Department of Chemistry, State University of New York at Binghamton, Binghamton, New York

1970-1974 .............................. Teaching Associate, Research Associate, Department of Chemistry, The Ohio State University, Columbus, Ohio

PUBLICATIONS


### TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>PREFACE</td>
<td>ii</td>
</tr>
<tr>
<td>ACKNOWLEDGMENTS</td>
<td>iii</td>
</tr>
<tr>
<td>VITA</td>
<td>iv</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>vi</td>
</tr>
<tr>
<td>LIST OF SCHEMES</td>
<td>vii</td>
</tr>
</tbody>
</table>

**PART I. ATTEMPTED SYNTHESIS OF ROTAXANES**

- Introduction .................................................................................. 1
- Historical Background ................................................................... 2
- Results and Discussion ................................................................ 14
- Experimental Section .................................................................. 23

**PART II. A NEW SYNTHESIS OF 6-SUBSTITUTED BENZO[a]PYRENES INVOLVING 5a,6-DIHYDRO-5a,6-EPOXYBENZO[a]PYRENE**

- Introduction .................................................................................. 37
- Historical Background ................................................................... 39
- Results and Discussion ................................................................ 58
- Conclusion .................................................................................... 78
- Suggestions for Future Experimentations .................................... 82
- Experimental Section .................................................................. 88

**BIBLIOGRAPHY** ............................................................................ 120
LIST OF TABLES

Part I

Table 1. Yield of 1,9-bis-[(3,5-di-t-butyl)phenyl]-1-nonyne, \( \frac{42}{42} \) ......................................................... 20

Part II

Table 1. Yields of 19 (isolated as 19a), 19b, and 19c obtained by treatment of 30 with various bases in various solvents.............................................. 70
# LIST OF SCHEMES

## Part I

<table>
<thead>
<tr>
<th>Scheme</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>7</td>
<td>18</td>
</tr>
</tbody>
</table>

## Part II

<table>
<thead>
<tr>
<th>Scheme</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>44</td>
</tr>
<tr>
<td>2</td>
<td>45</td>
</tr>
<tr>
<td>3</td>
<td>46</td>
</tr>
<tr>
<td>4</td>
<td>47</td>
</tr>
<tr>
<td>5</td>
<td>51</td>
</tr>
<tr>
<td>6</td>
<td>52</td>
</tr>
<tr>
<td>7</td>
<td>57</td>
</tr>
<tr>
<td>8</td>
<td>60</td>
</tr>
<tr>
<td>9</td>
<td>64</td>
</tr>
<tr>
<td>10</td>
<td>65</td>
</tr>
<tr>
<td>Scheme</td>
<td>Page</td>
</tr>
<tr>
<td>--------</td>
<td>------</td>
</tr>
<tr>
<td>11</td>
<td>67</td>
</tr>
<tr>
<td>12</td>
<td>72</td>
</tr>
<tr>
<td>13</td>
<td>74</td>
</tr>
<tr>
<td>14</td>
<td>79</td>
</tr>
<tr>
<td>15</td>
<td>83</td>
</tr>
</tbody>
</table>
PART I

THE ATTEMPTED SYNTHESIS OF ROTAXANES
INTRODUCTION

Rotaxanes are compounds which consist of ring and threaded chain portions as shown in 1. No chemical bond connects the ring and the chain in this class of compounds. The bulky end groups prevent the extrusion of the threaded chain from the macrocyclic ring. The compounds of this type may possess the interesting physical properties different from those of the mixture of separated ring and chain portions.

In this work attempted synthesis of various rotaxanes was described.

HISTORICAL BACKGROUND

Synthesis of Rotaxanes

Rotaxanes have been prepared by statistical and direct synthesis.

(1) Statistical Synthesis

Reaction of 2-hydroxycyclotriacontane, 2a, with succinic anhydride in pyridine gave the hemisuccinate ester, 2b, which was coupled via the sodium salt with Merrifield's peptide resin to form adduct, 2c. The resin bonded macrocycle, 2c, was treated 70 times with 1,10-decanediol and triphenylmethylchloride in a mixture of pyridine, dimethylformamide, and toluene. After hydrolysis and chromatography of crude product 6% of rotaxane, 2, was obtained as crude oil which was stable up to 200°. The yield in each reaction was therefore only 0.09%.

When a macrocycle mixture, 4a, containing all size rings from C_{14} through C_{42} was heated with 1,10-bis(triphenylmethoxy)decane, 5, at 120°, a small equilibrium concentration of only rotaxane, 6a, containing C_{29} ring, was obtained as shown in Scheme 1. Heating 6a to 120° caused the expected extrusion of the threaded chain, 5. If reaction of the macrocycle mixture, 4a, with 5 was catalyzed with trichloroacetic acid at 120°, a small amount of mixture of rotaxanes, 6b, containing C_{25} to C_{29} rings were obtained. None of the yield of rotaxanes 6a and 6b was mentioned in this communication.

In later work Harrison reported that heating a mixture of cyclo- dotriacontane, 4b, with 1,13-di-(tris-4-t-butylphenylmethoxy)tridecane, 7, in the presence of β-naphthalenesulfonic acid, a crystalline rotaxane, 8b, was isolated in 1.1% yield. When a mixture of macrocycles, 4a, con-
Scheme 1
taining all size rings from C\textsubscript{14} through C\textsubscript{42} and ether, \textit{J}, was heated in the presence of acid, a mixture of rotaxanes, \textit{8a}, containing C\textsubscript{23} to C\textsubscript{33} size rings was obtained. The mixture was then treated with acid, which cleaved the ether function and released the macrocycles. GLC of released macrocycles allowed a determination of yield of rotaxanes, \textit{8a}, for each ring size (Scheme 2). The yield of rotaxanes, \textit{8a}, increased with ring size from C\textsubscript{24} (0.0013\%) to C\textsubscript{33} (1.6\%) and dropped to zero for larger ring sizes. The author also reported heating a mixture of macrocycles, \textit{4a}, containing all size rings from C\textsubscript{14} through C\textsubscript{42}, with diester, \textit{5b}, instead of ether, \textit{5a}, in the absence of acid, a small amount of 28 membered ring rotaxane, \textit{6c}, was obtained (see Scheme 1).

Schill et al have synthesized the rotaxane, \textit{1\textsubscript{4}}, by the statistical method as shown in Scheme 3. The macrocyclic diol, \textit{2}, was ketalized with ketone, \textit{10}, in the presence of p-toluenesulfonic acid to give the ketal, \textit{11a}, which existed in an extra-intraannular conformational equilibrium with \textit{11b}. The mixture obtained was converted to a mixture of \textit{12a} and the prerotaxane \textit{12b} by reaction with triphenylmethylolithium. After hydrolysis with acid, rotaxane, \textit{1\textsubscript{4}}, was obtained in 0.12\% yield.

In summary, the yield of rotaxanes obtained by using the statistical method depended on statistical principles and therefore were generally low.
\[
\begin{align*}
\text{Scheme 2} & \\
\text{Ar}_3C - O - (\text{CH}_2)_n - O - \text{Ar}_3 & + \text{Ar}_3C - O - (\text{CH}_2)_{13} - O - \text{Ar}_3 \\
\text{4a, } n = 14-42 & \\
\text{4b, } n = 32 & \\
\hline
\text{8a, } n = 24-33 & \\
\text{8b, } n = 32 & \\
\hline
\text{4b, } n = 32 & \\
\text{4c, } n = 24-33 & \\
\text{Ar = } & \\
\text{CH}_3 & \\
\text{CH}_3 & \\
\text{CH}_3 & \\
\end{align*}
\]
Scheme 3

R = C(C₆H₅)₃
(2) Direct Synthesis

The first directed synthesis of rotaxanes was reported in 1969.

The synthetic route is shown in Scheme 4.

Veratrole diacid, \(15a\), was demethylated with hydrobromic acid to catechol derivative \(15b\) which was reduced with lithium aluminum hydride to the catechol diol, \(16\). The catechol diol, \(16\), was ketalized with 1,21-dichloroheneicosan-11-one to compound, \(17a\). The diacetate, \(17b\), of \(17a\) was nitrated to \(17c\) which was saponified to diol \(17d\) followed by catalytic hydrogenation to \(17e\). The compound \(17e\) was cyclized by potassium carbonate to \(18a\) using high dilution method. Treatment of diol, \(18a\), with triphenylphosphine dibromide in benzene gave dibromide, \(18b\), which reacted with sodium salt of N-acetyl-2,4,6-tri-p-tolylaniline to yield \(18c\). Ketal cleavage of \(18c\) with hydrobromic acid gave \(19a\). Oxidation of \(19a\) with ferric sulfate yielded an amino-o-benzoquinone, \(20a\), which was hydrolyzed to rotaxane, \(21a\). The rotaxane, \(21a\), was acetylated to its tetraacetate, \(21b\), which was converted to hexaacetate, \(22a\), by reductive acetylation.

Recently dibromide, \(18b\), was reacted with triphenylmethyllithium to give \(18d\) which was converted to rotaxane, \(22b\), using the pathway similar to that for preparation of \(22a\).

To date the rotaxanes were prepared either in low yield (by statistical synthesis) or via lengthy construction of the prerotaxanes such as \(19a\) and \(19b\). The directed synthesis of rotaxanes mentioned above is limited to the rotaxanes containing benzene rings and nitrogen atoms.

Scheme 4
Scheme 4 (Continued)
Several years ago an idea for directed synthesis of rotaxanes was developed in these laboratories as follows.

If a metal acetylide having a bulky end group such as that of 3,5-di-t-butylphenylacetylene, 23, could be solvated by a macrocyclic polyether in such a way that the anion would lie in the vicinity of a macrocyclic polyether, the anion could react with an alkyl halide having a bulky end group such as 7-(3,5-di-t-butyl)phenylheptyl bromide, 24a, by threading through the macrocyclic ring to give rotaxane, 25, as shown in Scheme 5.

[Chemical structures and reactions as shown in the image]
The concept was based on the reports that several macrocyclic polyethers form stable complexes with alkali or other metal cations. The most effective complexing reagents were those macrocyclic polyethers containing five to ten oxygen atoms each separated from the next by two carbon atoms. If complexation between cation and macrocyclic polyether were too strong, no threading process would be expected to occur because the anion would lie far away from the cation due to the complexation.

In this investigation 24 membered ring polycyclic ether, 7,10,13,-16,19-pentaoxacyclotetracosane-1-one ethylene ketal, 26, was used

![Chemical structure](attachment:image)


because models showed that the diameter in the ring is large enough for an acetylide anion to thread through and small enough to prevent the extrusion of the threaded chain once the rotaxane, \( \textsuperscript{28} \), formed. In \( \textsuperscript{26} \), the cation, \( M \), could be solvated in such a way that it would lie at the left side of the ring between oxygen atoms at positions 7, 10, 13, 16, and 19, while the acetylide anion, \( A \), would be at the right side of the ring between oxygen atoms at positions 7 and 19 and carbon atom at position 1. Therefore the reaction between acetylide anion \( A \) and bromide would occur by threading through the ring to form the rotaxane, \( \textsuperscript{28} \).
RESULTS AND DISCUSSION

Synthesis of 3,5-di-t-butylphenylacetylene, \( \text{23} \).

The successful synthesis of \( \text{23} \) is illustrated in Scheme 6. The 3,5-di-t-butyltoluene, \( \text{30} \), was prepared in 61.7% yield by treatment of toluene with 2 equivalents of \( \text{t}- \)butyl chloride in the presence of a catalytic amount of aluminum chloride. \(^{14}\) Bromination of \( \text{30} \) with N-bromosuccinimide followed by a Sommelet reaction \(^{15}\) of the intermediate bromide with hexamethylenetetramine gave 3,5-di-t-butylbenzaldehyde, \( \text{31} \), in 63% yield. Conversion of aldehyde, \( \text{31} \), to 3,5-di-t-butylphenylacetylene, \( \text{23} \), was accomplished by the published reaction sequence. \(^{17}\)

Reaction of \( \text{31} \) with zinc and methyl bromoacetate gave the crude hydroxy ester, \( \text{32} \), which was converted to the hydroxy hydrazide, \( \text{33} \), in 82.5% yield (from \( \text{31} \)). The hydroxy hydrazide, \( \text{33} \), was diazotized with nitrous acid and the resulting azide heated to effect a Curtius rearrangement to 5-(3,5-di-t-butylphenyl)oxazolidone, \( \text{34} \), in 90% yield.


Scheme 6

1. ArCH₃ → ArCH

2. 1) Zn, BrCH₂COOMe → ArCHOHCOOMe
   2) NH₄OH → ArCHOHCOOMe

3. 1) H⁺ → ArCH⁻

4. ArCH⁻N⁻NO → ArCH⁻NH⁻NH⁻NH₂

5. Ar-C≡CH
Nitrosation of 34 with nitrosyl chloride in pyridine gave 5-(3,5-di-t-butylphenyl)-3-nitrosooxazolidone, 35, in 93.5% yield. Treatment of 35 with butylamine in refluxing chloroform gave 23 in 95% yield. If 35 was treated with sodium hydroxide as in earlier work a substantial amount of 3,5-di-t-butylphenylethananal was produced in addition to 23.

The formation of 23 by decomposition of 35 with butylamine can be explained by the intermediacy of either a vinyl cation, 36, or an unsaturated carbene, 37. The good overall yield of 23 (67.5% from

\[
\begin{align*}
36 & \quad \text{R} \quad \text{C} = \text{C} : \\
\text{H} & \quad \text{H}
\end{align*}
\]

R = \begin{align*}
\text{(X)}
\end{align*}


indicates that this route deserves serious consideration for the synthesis of arylacetylenes. Other synthesis of arylacetylenes from arylaldehydes ranging from 29% to 80% yield have been published. The method, involving the reaction of the aldehyde with carbon tetra-bromide-triphenylphosphine followed by reaction of dibromoolefin formed with 2 equivalents of butyllithium (eq. 1), was published after this work was completed. In one run using this method, 31 was converted to 23 in 39% yield.

\[
\begin{align*}
\text{CHO} & \xrightarrow{\text{CBr}_4-(\text{C}_6\text{H}_5)_3\text{P}} R \underbrace{\begin{array}{c}
\text{Br} \\
\text{H} \\
\text{Br}
\end{array}}_{2 \text{ eq BuLi}} \rightarrow R-\text{C}≡\text{CH}
\end{align*}
\]

Synthesis of 7-(3,5-di-t-butyl)phenylheptyl bromide, 24a, and 7-(3,5-di-t-butyl)phenylheptyl iodide, 24b.

The successful route to 24a and 24b is shown in Scheme 7. Tetrahydropyranoxyhexyl chloride, 39, was prepared by reaction of 6-chloro-1-hexanol with dihydropyran and a catalytic amount of hydrochloric acid. The Grignard reagent of 39 was prepared in tetrahydro-
Scheme 7
furan and reacted with 3,5-di-t-butylbenzaldehyde, 31, to give crude 1-(3,5-di-t-butyl)phenyl-1,7-heptandiol, 40, in 80% yield. The diol, 40, was converted to 7-(3,5-di-t-butyl)phenyl-1-heptanol, 41, in 95% yield by hydrogenolysis. Reaction of 41 with aqueous sodium bromide or sodium iodide in the presence of a phase-transfer catalyst afforded 7-(3,5-di-t-butyl)phenylethyl bromide, 24a, or 7-(3,5-di-t-butyl)phenylethyl iodide, 24b, in 91% and 82% yield, respectively.

Preparation of 1,9-bis[(3,5-di-t-butyl)phenyl]-1-nonyne, 42.

It was necessary to react the metal acetylide of 23 with bromide, 24a, or iodide, 24b, in the absence of a macrocyclic polyether to see whether the nucleophilic displacement reaction could be carried out in a reasonable yield. The results are shown in Table 1. Besides the expected product, 42, alcohol, 41, and its ether, 43, were also detected by mass spectral analysis. The structure of 42 was supported by hydrogenation to 46. The sodium acetylide was prepared by reaction of 23 with either sodium hexamethyldisilylamide, 44, or dimethylsodium, 45, as recommended. 28 The lithium acetylide was prepared by reaction of 23 with butyllithium. Hexamethylphosphoric triamide (HMPT) has been

Table 1
Yield of 1,9-bis-[(3,5-di-t-butyl)phenyl]-1-nonyne, 42.

<table>
<thead>
<tr>
<th>Metal</th>
<th>Solvent</th>
<th>Halide</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na</td>
<td>DMSO</td>
<td>-Br</td>
<td>50</td>
</tr>
<tr>
<td>Na</td>
<td>diglyme</td>
<td>-Br</td>
<td>32</td>
</tr>
<tr>
<td>Na</td>
<td>DMSO</td>
<td>-I</td>
<td>50</td>
</tr>
<tr>
<td>Li</td>
<td>HMPT-THF</td>
<td>-Br</td>
<td>72</td>
</tr>
</tbody>
</table>

recommended as solvent for alkylation reactions. 30

\[
\text{Na}^+ \text{CH}_2\text{SOCH}_3 \quad \text{Na}^+ \text{N}^\ominus [\text{Si(CH}_3)_3]_2
\]

\[
\begin{align*}
\text{R-(CH}_2)_7\text{-O-(CH}_2)_7\text{R} & \quad \text{RC}^\equiv\text{C-(CH}_2)_7\text{R} \\
43 & \quad 42
\end{align*}
\]

Attempted Synthesis of rotaxan, \(28\).

Reaction of lithium acetylide of \(23\) with bromide, \(24a\), in the presence of 1.2 equivalent of 7,10,13,16,19-pentaoxacyclotetracosane-1-one ethylene ketal, \(26\), using hexamethylphosphoronic triamide as solvent gave \(42\) in 68% yield. No rotaxane was detected by mass spectral analysis of every chromatographic fraction. Reaction of sodium acetylide of \(23\) with iodide, \(24b\), in the presence of 2 equivalents of di-cyclohexyl-18-crown-6, \(47\), using dimethyl sulfoxide as solvent yielded \(42\) in 50% yield. No rotaxane was detected by mass spectral analysis.

31. Prepared by Dr. V. K. Khanna in these laboratories.
Since the molecular ion of rotaxane is detectable by mass spectroscopy, the failure to detect the molecular ion in our case indicated that no rotaxane was obtained.

Other reactions performed in these laboratories involving reactions of sodium and lithium acetylide of 23 with 3-(3,5-di-t-butyl)-phenylpropyl bromide, 48, using 3 equivalents of 26 as the only solvent, yielded a mixture of products which showed a molecular ion, m/e = 849 (p+1), expected for the rotaxane, 49. Since efforts to purify this heterogeneous fraction failed, the yield of 49 could not be determined.

Since the original purpose of the project was to synthesize rotaxanes in reasonable yields, the failure to isolate a pure rotaxane demonstrated that continuation of the project would be unjustified.

\[
\begin{align*}
R-(CH_2)_3Br & \quad \text{(48)} \\
R & = \begin{array}{c}
\text{x}
\end{array}
\end{align*}
\]

32. Performed by Dr. R. L. Robey.
EXPERIMENTAL SECTION

Generalizations

1. All melting and boiling points are uncorrected. Melting points were taken with a Thomas-Hoover capillary melting apparatus.

2. Microanalyses were performed by the M-H-W Laboratories, Garden City, Michigan.

3. Infrared (ir) absorption spectra were recorded on a Perkin-Elmer Infracord Spectrophotometer.

4. Nuclear magnetic resonance (nmr) spectra were recorded on an A-60 nmr spectrophotometer, Varian Associates, Palo Alto, California.

5. A Varian Aerograph A90-P3 was used for gas liquid chromatographic (GLC) analyses.

6. Silica gel, 100-200 mesh, purchased from Matheson, Coleman, and Bell Chemical Company and Woelm activity grade I alumina were used for column chromatography.

7. The phrase 'worked up as usual' means that the reaction mixture was extracted with ether-benzene, and the organic solution was washed successively with water, saturated sodium chloride solution, dried by filtering through a bed of anhydrous magnesium sulfate, and the solvent removed in vacuo on a rotary evaporator.
3,5-Di-t-butyltoluene, 30.

A mixture of 1000 g (10.9 mole) of toluene, 2000 g (21.7 mole) of t-butyl chloride and 32 g of aluminum chloride was stirred for three days at room temperature. The reaction mixture was poured onto a mixture of concentrated hydrochloric acid and ice, then worked up as usual. After fractionation with column A the residue yielded 1.388 g (62.7%) of 30, bp 97-99° at 5 mm (lit bp 98° at 5.7 mm); nmr (CCl₄): δ 1.35 (s, 18, t-Bu), 2.32 (s, 3, -CH₃), 6.90 (d, J = 1 Hz, 2, Ar-H), and 7.15 (t, 1, J = 1 Hz, ArH).

3,5-Di-t-butylbenzaldehyde, 31.

A mixture of 228 g of 1, 300 g of N-bromosuccinimid, 1 g of benzoyl peroxide, and 600 ml of carbon tetrachloride was heated at reflux for 4 hr. After cooling to room temperature succinimid was removed by filtration. The filtrate was concentrated on a rotary evaporator. The residue (320 g) was then added to a solution of 430 g of hexamethylenetetramine in 300 ml of water and 300 ml of ethanol. The solution was refluxed for 4 hr, 200 ml of concentrated hydrochloric acid was added during 20 min, and refluxing was continued for 30 min. The reaction mixture was worked up as usual to yield 253 g of crude product which after crystallization from Skelly solve B, gave 153 g (63% from 1) of 31, mp

33. Column A is a 24 in x 1 in column packed with 5 mm glass beads and coated with a heating jacket. On top of the column was placed a total reflux partial take-off condenser.

34. Skellysolve B is essentially petroleum ether of bp 60-68°.
84-85° (lit mp 84.2-84.3°); ir (KBr): 1670 cm⁻¹ (s, C=O); nmr (CDCl₃):
δ 1.35 (s, 18, t-Bu), 7.3 (s, 3, ArH), and 10.0 (s, 1, -CHO).

About 3% more of 31 could be obtained by distillation of the material in filtrate followed by crystallization as above.

Methyl β-(3,5-di-t-butylphenyl)-β-hydroxypropionate, 32.

A mixture of 136 g (0.65 mole) of 31, 400 ml of benzene, and 44 g (0.705 atom) of activated zinc was heated until 200 ml of benzene had distilled. After 200 ml of dry ether was added, 96 g (0.634 mole) of methyl bromoacetate was added during 5 hr to the refluxing mixture. After refluxing for 10 hr more, the cooled reaction mixture was treated with 1 ℥ of concentrated ammonium hydroxide and worked up as usual.

A small amount of crude residue was crystallized from Skellysolve B to yield the analytical sample of 32, mp 66-67°; ir (KBr): 1720 cm⁻¹; nmr (CDCl₃): δ 1.35 (s, 18, t-Bu), 2.65 (d, 2, J = 6 Hz, -CH₂-), 2.05 (d, 1, J = 3 Hz, -OH), 3.70 (s, 3, -CO₂CH₃), 4.05 (m, 1, -CHОН), 7.15 (d, 2, J = 2 Hz, ArH), and 7.30 (t, 1, J = 2 Hz, ArH).

 Anal. Calcd for C₁₀H₂₀O₃: C, 73.9; H, 9.7.
 Found: C, 73.9; H, 9.7.

The remainder was treated as described below to yield 33.

37. Attempted purification by distillation caused decomposition of 32 indicated by the appearance of C=O stretching of aldehyde in IR spectrum.
**8-(3,5-Di-t-butylphenyl)-β-hydroxypropionic acid hydrazide, 33.**

To a solution of crude 32, obtained as above, in 60 ml of ethanol was added 10.0 g of 95% hydrazine hydrate. The mixture was heated until a clear solution resulted. After cooling, the resulting crystalline hydrazide was recrystallized from benzene-ethanol to yield 66.7 g (82.5% from 2) of 33, mp 143-145°; ir (KBr): 3300 (NH), 1670 cm⁻¹ (C=O); nmr (CD₃OD): δ 1.30 (s, 18, t-Bu), 2.55 (d, 2, J = 6 Hz, -CH₂-), 3.90 (s, 4, -OH, and -NHNH₂), 4.10 (t, 1, J = 6 Hz, -CHOH-), 7.20 (d, 2, J = 2 Hz, ArH), and 7.35 (t, 1, J = 2 Hz, ArH).

**Anal.** Calcd for C₁₇H₂₈N₂O₂: C, 69.8; H, 9.6; N, 9.6.

Found: C, 69.5; H, 9.4; N, 9.8.

**5-(3,5-Di-t-butylphenyl)oxazolidone, 34.**

To a stirred mixture of 32.0 g of 33, 200 ml of 6N hydrochloric acid, and 50 ml of chloroform at 0-5° was added 12.0 g of sodium nitrite during 30 min. After stirring for 30 min, the excess nitrous acid was destroyed with sodium sulfite. The organic product was taken into three 100 ml benzene extracts, which were washed with saturated salt solution and dried by pouring through magnesium sulfate. The benzene solution was added dropwise to refluxing benzene. After nitrogen evolution had ceased, the solvent was distilled and the residue was crystallized from Skellysolve B-ether to yield 27.1 g (90%) of 34, mp 167.5-168.5°; ir (KBr): 3300 (NH), 1730, 1700 cm⁻¹ (C=O); nmr (CDCl₃): δ 1.33 (s, 18, t-Bu), 3.45-4.17 (m, 2, -CH₂-), 5.65 (t, 1, J = 8 Hz, -CH-0), 6.92 (s, 1, br, NH), 7.23 (d, 2, J = 2 Hz, ArH), and 7.45 (t, 1, J = 2 Hz, ArH).
5-(3,5-Di-t-butyl)-3-nitrosooxazolidone, 35.

To an ice cooled solution of 10.5 g of \( \frac{3}{4} \) in 50 ml of pyridine was added dropwise a cooled solution of 5.9 g of nitrosyl chloride in 30 ml of acetic anhydride in such a way that the reaction temperature was maintained below 6°. After complete addition of nitrosyl chloride, the mixture was poured onto ice water. The yellow precipitate was filtered and washed with water followed by Skellysolve B to give 11.4 g of crude product, mp 186-189°, which after recrystallization from acetone yielded 10.8 g (95.5%) of \( \frac{3}{5} \), mp 193-195° (dec); ir (KBr): 1800 (C=O), 1600, 1500 cm\(^{-1}\) (N=O); nmr (CDCl\(_3\)): \( \delta \) 1.33 (s, 18, t-Bu), 3.53-4.70 (m, 2, -CH\(_2\)-), 5.90 (t, 1, \( J = 8 \) Hz, -CH-0-), 7.35 (d, 2, \( J = 2 \) Hz, ArH), and 7.50 (t, 1, \( J = 2 \) Hz, ArH).

Anal. Calcd for C\(_{17}\)H\(_{25}\)N\(_2\)O\(_3\): C, 67.1; H, 8.0; N, 9.2.

Found: C, 67.1; H, 7.9; N, 8.9.

3,5-Di-t-butylphenylacetylene, \( \underline{23} \).

Method A: To a refluxing solution of 4.90 g (0.066 mole) of butylamine in 100 ml of chloroform was added 20.0 g (0.066 mole) of \( \underline{6} \) in portions during 30 min. About 95% of the theoretical nitrogen was evolved. After removal of solvent, distillation yielded 13.4 g (95%) of \( \underline{23} \), bp 106° at 2 mm, mp 87.0-87.5°; ir (KBr): 3300 cm\(^{-1}\) (-C=C-H); nmr (CDCl\(_3\)): \( \delta \) 1.33 (s, 18, t-Bu), 2.85 (s, 1, -C=CH), and 7.30 (s, 3, ArH).
Anal. Calcd for C₁₆H₂₂: C, 89.7; H, 10.4.

Found: C, 89.7; H, 10.4.

In another run, 9.23 g of 35 was added to a refluxing solution of 3.0 g of butylamine in 100 ml ether. After working up as usual, 5.1 g (78%) of 23 was obtained.

Method B: To a mixture of 10.5 g triphenylphosphine and 6.6 g of carbon tetrabromide in 50 ml of dry methylene chloride was added at 0° 2.2 g of 3,5-di-t-butylbenzaldehyde. The mixture was stirred for 30 min, and worked up as usual. The residue was extracted with hexane. The triphenylphosphine oxide was removed by filtration. The filtrate was concentrated and distilled to yield 3.7 g (86%) of 3,5-di-t-butylstyrene dibromide, 38, bp 181-186° at 1 mm.

To a solution of 2.6 g of 38 in 30 ml of THF was added 8.0 ml of 2 M n-butyllithium at -78° under nitrogen. After stirring at -78° for 1 hr and room temperature for another hr, the mixture was hydrolyzed with dilute hydrochloric acid and worked up as usual. After distillation, the crude product yielded 1.0 g (45.5%) of 23.

6-Tetrahydropyranyl-oxy-hexyl chloride, 39.

To a mixture of 100.0 g (0.74 mole) of 6-chlorohexanol 38 and 0.5 ml of concentrated hydrochloric acid at 5° was added 92.4 g (1.10 mole) of dihydropyran in 2 hr. After stirring for 1 hr, the mixture was diluted with 200 ml benzene and neutralized with 100 ml sodium bicar-

38. Obtained from the Chemical Samples Company and distilled before use.
bonate. The benzene solution was worked up as usual. The residue was fractionally distilled using column A to yield 138 g (85%) of 39, bp 125-128° at 4.5 mm (lit bp 107° at 0.25 mm).

1-(3,5-Di-t-butyl)phenyl-1,7-heptandiol, 40.

To 6.8 g of magnesium in 150 ml dry THF was added dropwise 2.0 g of 1,2-dibromoethane followed by 45 g (0.25 mole) of 39 in 1 hr. After being refluxed for 2 hr and cooled, 25 g (0.12 mole) of 3,5-di-t-butylbenzaldehyde in 50 ml of THF was added to the Grignard reagent. The reaction mixture was heated at reflux for 2 hr, cooled, and hydrolyzed with 45 ml of saturated ammonium chloride. After removal of inorganic salt by filtration, the filtrate was concentrated on a rotary evaporator. The residue was distilled to yield 30 g (80%) of 40 as viscous liquid, bp 204-206° at 0.5 mm. This material is suitable for the next reaction. After standing for 2 weeks the viscous liquid solidified. An analytical sample (mp 79-80°) was obtained by recrystallization of the solid from Skellysolve B; ir (KBr): 3300-3100 cm⁻¹ (-OH); nmr (CDCl₃): δ 1.37 (s, 28, t-Bu and -(CH₂)₅-), 2.99 (br, 2, -OH), 3.48 (br, 2, -CH₂OH), 4.62 (br, 1, -CHOH-), 7.15 (d, 2, J = 2 Hz, ArH), and 7.32 (t, 1, J = 2 Hz, ArH).

Anal. Calcd for C₂₁H₃₈O₂: C, 78.7; H, 11.3.

Found: C, 78.9; H, 11.6.

7-(3,5-Di-t-butyl)phenylheptanol, 41.

A mixture of 62 g of 40, 200 ml of methanol, 1 ml of concentrated sulfuric acid, and 0.5 g of 5% palladium on charcoal was hydrogenated
under 50 psi of hydrogen for 10 hr. After filtration, solid sodium carbonate was added to the filtrate to neutralize the acid. Methanol was removed on a rotary evaporator. The residue was worked up as usual to yield 56 g (95%) of 41, bp 158-160° at 0.9 mm; ir (neat): 3300 cm⁻¹ (OH); nmr (CDCl₃): δ 1.33 (s, 28, t-Bu and -(CH₂)₅-), 2.55 (br, 2, Ar-CH₂-), 3.50 (t, 2, J = 6 Hz, -CH₂-OH), 6.91 (d, 2, J = 2 Hz, ArH), and 7.15 (t, 1, J = 2 Hz, ArH).

Anal. Calcd for C₂₁H₃₅O: C, 82.8; H, 11.9.

Found: C, 82.6; H, 12.2.

7-(3,5-Di-t-butyl)phenylheptyl bromide, 2₄₄a.

To a solution of 30 g (0.10 mole) of 41 and 15 g of triethylamine in 30 ml of benzene at 0° was added dropwise 15 g of methanesulfonyl chloride. After stirring at 0-10° for 3 hr, the reaction mixture was diluted with 30 ml of ether, washed with dilute hydrochloric acid, and worked up as usual. The crude product was added to a mixture of 50 ml of benzene, 100 g of sodium bromide, 100 ml of water, and 1.0 g of Aliquat 336.³⁹ The mixture was heated at reflux for 36 hr, cooled, and worked up as usual. The residue was distilled to afford 32 g (91%) of 2₄₄a, bp 160-162° at 0.5 mm; ir (neat): 1600, 710 cm⁻¹; nmr (CDCl₃): δ 1.29 (s, 28, t-Bu and -(CH₂)₅-), 2.50 (t, 2, J = 7 Hz, Ar-CH₂-), 3.25 (t, 2, J = 7 Hz, -CH₂br), 6.68 (d, 2, J = 2 Hz, ArH), and 7.12 (t, 1, J = 2 Hz, ArH). Because 2₄₄a was not stable to prolong heating no further purification was made, and was used as such.

³⁹. Aliquat 336, obtained from General Mills Co., is a mixture of straight chain C₈ to C₁₂ trialkylammonium chlorides.
7-(3,5-Di-t-butyl)phenylheptyl iodide, 24b.

To a solution of 14.6 g (0.048 mole) of 41 and 8.0 g of triethylamine and 300 ml of benzene at 0° was added dropwise 8.0 g of methane sulfoxyl chloride in 1 hr. The mixture was stirred at 0-10° for 3 hr. After removal of triethylamine hydrochloride by filtration, the filtrate was washed with dilute hydrochloric acid and worked up as usual. The residue was added to a mixture for 24 hr, cooled, and worked up as usual. The crude product was rapidly distilled to yield 16.2 g (82%) of 24b, bp 188-184° at 1.5 mm; ir (liquid): 1600, 710 cm⁻¹; nmr (CDCl₃): δ 1.29 (s, 28, t-Bu and -(CH₂)₅-), 2.50 (t, 2, J = 7 Hz, ArCH₂-), 3.10 (t, 2, J = 7 Hz, -CH₂I), 6.85 (d, 2, J = 2 Hz, ArH), and 7.12 (t, 1, J = 2 Hz, ArH). Because 24b discolored on heating no further purification was made.

1,9-Bis[(3,5-di-t-butyl)phenyl]non-1-yne, 42.

Method A: Reaction of sodium 3,5-di-t-butylphenylacetylide, A, with 24a in dimethyl sulfoxide.

To a 100 ml three neck flask was added 0.50 g of sodium hydride (57% dispersion in mineral oil). Sodium hydride was washed three times with light petroleum by swirling and decanting the liquid portion in order to remove the mineral oil. The flask was flushed with nitrogen to remove the last trace of petroleum ether then 20 ml of dimethyl sulfoxide was added. The mixture was heated at 70-75° for 1 hr until hydrogen evolution had ceased, cooled to room temperature, and a solution of 2.14 g (0.01 mole) of 3,5-di-t-butylphenylacetylene, 23, in 10
ml ether was added at room temperature. The solution was stirred for 30 min at room temperature, transferred by a syringe under nitrogen to a pressure equalizing dropping funnel and added dropwise to a solution of 3.67 g of 24a in 10 ml dry ether. Vigorous reaction occurred with precipitation of white sodium bromide. After distilling the ether, the reaction mixture was kept at 70-75° for 24 hr, cooled to room temperature, poured onto dilute hydrochloric acid, and worked up as usual. The residue was chromatographed over 150 g silica gel to give the following.

<table>
<thead>
<tr>
<th>Fraction</th>
<th>Eluant</th>
<th>Weight</th>
<th>Character</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>400 ml Skellysolve B</td>
<td>0.4 g</td>
<td>oil</td>
</tr>
<tr>
<td>2</td>
<td>900 ml Skellysolve B</td>
<td>1.33 g</td>
<td>a mixture of oil and solid</td>
</tr>
<tr>
<td>3</td>
<td>600 ml Skellysolve B</td>
<td>0.7 g</td>
<td>oil</td>
</tr>
<tr>
<td>4</td>
<td>600 ml ether-Skellysolve B (1:20)</td>
<td>2.5 g</td>
<td>oil</td>
</tr>
<tr>
<td>5</td>
<td>1 &amp; ether</td>
<td>0.5 g</td>
<td>an oily mixture</td>
</tr>
</tbody>
</table>

Fraction 1, was a mixture of an olefinic compound and recovered 23 as indicated by ir spectrum. Fraction 2, after washing with petroleum ether, gave recovered 23. Fraction 3 was mainly recovered bromide 24a as indicated by GIC. Fraction 4 was desired 1,9-bis[(3,5-di-t-buty)]-
phenyl\textsubscript{1}-1-nonyne, \textsuperscript{42}; nmr (CDCl\textsubscript{3}): \delta 1.33 (s, 46, t-Bu and -(CH\textsubscript{2})\textsubscript{5}-), 2.3-2.8 (br 4, -C=CH\textsubscript{2} and ArCH\textsubscript{2}-), 7.02 (d, 2, J = 2 Hz, ArH), and 7.20-7.40 (m, 4, ArH); mass spectrum, m/e = 500 (p).

\textbf{Anal.} Calcd for C\textsubscript{37}H\textsubscript{56}: C, 88.7; H, 11.3.

Found: C, 88.6; H, 11.2.

Fraction 5 was a mixture of 7-(3,5-di-t-butyl)phenylheptanol, \textsuperscript{41}, and di-[7-(3,5-di-t-butyl)phenylheptyl]ether, \textsuperscript{43}, as indicated by ir (0-H absorption at 3300 cm\textsuperscript{-1}) and mass spectra (m/e = 590, p, for \textsuperscript{43}).

\textbf{Method B: Reaction of A with 24a in diglyme.} To a solution of 2.0 g of sodium hexamethyldisilylamide \textsuperscript{27} in 10 ml of dry diglyme \textsuperscript{40} was added under nitrogen a solution of 2.14 g (0.01 mole) of 23 in 5 ml diglyme. After stirring for 30 min, a solution of 3.67 g of 24a in 5 ml of diglyme was added in one portion, the reaction mixture was stirred and heated at 50\textdegree for 36 hr. The reaction mixture was hydrolyzed with dilute hydrochloric acid and worked up as usual. The crude product was chromatographed on 150 g silica gel as described above to yield 1.6 g (32\%) of \textsuperscript{42}.

\textbf{Method C: Reaction of A with iodide 24b in dimethyl sulfoxide.} As described in Method A, 2.07 g (50\%) of \textsuperscript{42} was obtained from 2.14 g of 23 and 4.14 g of 24b in 20 ml dimethylsulfoxide.

\textsuperscript{40} Distilled from sodium before use.
Method D: Reaction of lithium 3,5-di-t-butylphenylacetylide B with bromide, 24a, in hexamethylphosphoric triamide (HMPT).

To a solution of 2.14 g (0.01 mole) of 23 in 10 ml of hexane was added at 0° 5.3 ml of 1.9 M n-butyllithium in hexane. The white precipitate formed was dissolved after adding 10 ml tetrahydrofuran. To this solution was added a solution of 3.67 g (0.01 mole) of bromide, 24a, in 20 ml HMPT at 0°. The mixture was stirred overnight at room temperature, hydrolyzed with dilute hydrochloric acid, and worked up as usual. The crude product was chromatographed as described in Method A to yield 3.6 g (72%) of 42.

Reaction of Sodium acetylide A with 24b in the presence of dicyclohexyl-18-crown-6, 46.

To a dimsylsodium solution prepared as described in Method A from 0.50 g of 57% sodium hydride and 20 ml of dimethyl sulfoxide was added a solution of 2.14 g (0.01 mole) of 23 in 10 ml of dry ether under nitrogen, followed by 7.50 g of 46. After stirring for 0.5 hr, this reaction mixture was added a solution of 4.14 g (0.01 mole) of iodide 24b in 10 ml of dry ether. The mixture was stirred overnight, hydrolyzed with dilute hydrochloric acid, and worked up as usual. The crude product was chromatographed over 360 g silica gel. The first fraction, obtained by using 4 l of Skellysolve B, yielded 1.18 g of crude oil.

41. Distilled over calcium hydride before use.

42. Obtained from Dupont Chemical Company.
The second fraction, obtained by using 2 L of Skellysolve B-benzene (9:1), yielded 2.5 g (50%) of 42. The third fraction, obtained by using 2 L of benzene-ethyl acetate (7:3), yielded 0.6 g of a mixture which contained alcohol 41 and its ether 43 as indicated by the mass spectra analysis. The fourth fraction, obtained by using 4 L of ethyl acetate, yielded 7.5 g of recovered crown ether, 46. No desired rotaxane was detectable in the mass spectra of each fraction.

Reaction of lithium acetylide B with bromide, 24a, in the presence of 7,10,13,16,19-pentaaclyclotetraicosan-1-one ethylene ketal, 26.

To a solution of 2.14 g (0.01 mole) of 23 in 10 ml of hexane was added 5.3 ml of 1.9 M butyllithium in hexane at 0°, followed by 10 ml of THF and 5.0 g of 26. After stirring for 1 hr, a solution of 3.67 g (0.01 mole) of 24a in 20 ml of hexamethylphosphoric triamide was added to this mixture. The reaction mixture was stirred at room temperature overnight, hydrolyzed with dilute hydrochloric acid, and worked up as usual. The crude product was chromatographed over 300 g of silica gel.

The first fraction, obtained by using 3 L of Skellysolve B, yielded 0.42 g of oil. The second fraction, obtained by using 3 L of benzene-Skellysolve B (1:9), yielded 3.4 g (68%) of 42. The third fraction, obtained by using 3 L of benzene, yielded 0.3 g of a mixture which contained alcohol 41 and the ether 43 as indicated by the mass spectra analysis. The fourth fraction, obtained by using 6 L of ethyl acetate, yielded 5.0 g of recovered 26. No rotaxane was detectable in the mass spectra in every fraction.
1,9-Bis[(3,5-di-tert-butyl)phenyl]nonane, 46.

A mixture of 3.7 g of 42, 50 ml of ethyl acetate, and 0.5 g of 5% palladium on charcoal was hydrogenated under 50 psi of hydrogen for 1 hr. After removal of palladium on charcoal by filtration, the solvent was removed on a rotary evaporator. The residue was distilled to yield 2.5 g (68%) of 46, bp 233-238°C at 0.3 mm, mp 45-46°C; nmr (CDCl₃): δ 1.33 (s, 50, -C(CH₃)₅ and -(CH₂)₇-), 2.60 (t, 4, J = 8 Hz, Ar-CH₂-), 7.65 (d, 4, J = 2 Hz, ArH), and 7.25 (t, 2, J = 2 Hz, Ar-H).

Anal. Calcd for C₃₇H₆₆O: C, 89.1; H, 10.9.

Found: C, 89.1; H, 10.8.
PART II

A NEW SYNTHESIS OF 6-SUBSTITUTED BENZO[a]PYRENES

INVOLVING 5a,6-DIHYDRO-5a,6-EPOXYBENZO[a]PYRENE
INTRODUCTION

Ever since Boyland postulated that arene oxides might be intermediates in the oxidative metabolism of aromatic substrates, much attention has been focused on the synthesis of various arene oxides especially those of the two most potent carcinogens, namely 7,12-dimethylbenz[a]anthracene, 1, and benzo[a]pyrene, 2. Three benzo[a]pyrene epoxides have been prepared. 3,4

![Image](image.png)

In this work efforts to synthesize a new type of arene epoxide namely 5a,6-dihydro-5a,6-epoxybenzo[a]pyrene, 3, are described. Although

2. For review on arene oxides, see D. M. Jerina, H. Yagi, and J. W. Daly, Heterocycles, 1, 267 (1973).
was not isolated, a new synthesis of 6-substituted benzo[a]pyrenes was developed which may have proceeded through the intermediacy of \( \text{3} \).
HISTORICAL BACKGROUND

Boyland and Levi observed that anthracene was metabolically converted to trans-1,2-dihydroxy-1,2-dihydroanthracene in mammals. The metabolic formation of dihydrodiols has been demonstrated with naphthalene, phenanthrene, and other aromatic hydrocarbons. Boyland suggested that the dihydrodiols arose from epoxides or arene oxides. In 1968 Jerina et al identified naphthalene-1,2-oxide, as the obligatory intermediate in the hepatic metabolism of naphthalene. Naphthalene can be converted to naphthalene-1,2-oxide which can either isomerize to 1-naphthol spontaneously, hydrolyze to trans dihydrodiol enzymatically or conjugate both chemically or enzymic catalysis with glutathione. Other arene epoxides shown to be formed in the metabolism

of polycyclic aromatic hydrocarbons include 9,10-dihydro-9,10-epoxyphenanthrene, \(5\), 5,6-dihydro-5,6-epoxybenz[a]anthracene, \(6\), and 5,6-dihydro-5,6-epoxydibenzo[a,h]anthracene, \(7\), \(8,9\), 4,5-dihydro-4,5-epoxybenzo-a]pyrene, \(11\), \(12\) and 5,6-dihydro-5,6-epoxy-7,12-dimethylbenz[a]anthracene, \(10\).


One hypothesis concerning the carcinogenicity of polycyclic aromatic hydrocarbons is that the hydrocarbons are converted to active intermediates which might be the arene epoxides. In one test 5,6-dihydro-5,6-epoxybenz[a]anthracene, \( \text{6} \), and 5,6-dihydro-5,6-epoxydibenzo[a,h]-anthracene, \( \text{7} \), were found to be more active in the production of malignant transformation in hamster embryo cells than the hydrocarbons or the corresponding K-region phenols. In other tests epoxides are less active carcinogens than the corresponding hydrocarbons.

Synthesis of arene oxides

Three general methods for the synthesis of arene oxides have been developed. One stems from cis dihydrodiols obtained by hydroxylation of a phenanthrene-type bond with osmium tetroxide, the second from trans dihydrodiols obtained by reduction of quinones, and the third by dehydrobromination of polybromoepoxide precursors.

The first preparation of an arene oxide namely, 11,12-epoxy-11,12-dimethylchrythene, reported in 1940, involved dehydration of diol

\[ \text{O} \quad \text{CH}_3 \text{MgI} \quad \text{HCl, CH}_3 \text{OH} \]

28. C. L. Hewett, J. Chem. Soc., 293 (1940). This work was checked in our laboratories by Dr. V. Sankaran.
arising from reaction between chrysaquinone and methylmagnesium chloride as shown above.

Newman and Blum prepared 9,10-dihydro-9,10-epoxyphenanthrene, 5, 5,6-dihydro-5,6-epoxybenz[a]anthracene, 6, and 5,6-dihydro-5,6-epoxy-7-methylbenz[a]anthracene, 2, by closure of the corresponding o,o-biphenyldialdehyde with Mark's reagent (trisdimethylaminophosphine).

\[ P(N(CH_3)_2)_3 \]

This method has been applied to synthesis of K-region epoxides of carcinogenic hydrocarbons such as 5,6-dihydro-5,6-epoxy-7,12-dimethylbenz[a]anthracene, 10, and 4,5-dihydro-4,5-epoxybenzo[a]pyrene, 11.

Arene oxides have been prepared by the method of Neumann\textsuperscript{30} for conversion of trans-diols to epoxides with the dimethyl acetal of dimethylformamide (DMA-DMF) as shown in Scheme 1.

\[
\begin{align*}
\text{SO}_3\text{-pyridine} & \quad \rightarrow \\
\text{LiAlH}_4 & \quad \rightarrow \\
\text{DMA-DMF} & \quad \rightarrow 
\end{align*}
\]

\textbf{Scheme I}

This method involves a tedious transformation of the cis-diols to the trans-diols, by oxidation of cis-diols with $\text{SO}_3$-pyridine to o-quinones, reduction of o-quinones to mixture of cis- and trans-diols and separation of the undesired cis-diols from trans-diols. The overall yields are substantially lower than those obtained using Mark's reagent.

Recently arene oxides have been prepared using the method developed in these laboratories which involves conversion of orthoesters of cis-diols into halohydrin acetates followed by cyclization with base into epoxides as shown in Scheme 2. This method is the most facile synthesis of K-region epoxides now known.

\[ \text{Scheme 2} \]

The third general route was first developed by Vogel\textsuperscript{28} for synthesis of 1,2-dihydro-1,2-epoxynaphthalene, \textsuperscript{4}, as shown in Scheme 3. Bromination of 1,2-epoxy-1,2,3,4-tetrahydronaphthalene, \textsuperscript{12}, yields a bromide, \textsuperscript{13}, which on dehydrobromination with tertiary amine yields the epoxide. Several arene epoxides have been prepared by Vogel's route.\textsuperscript{4,32,33} The yield of the desired arene oxides were generally low using this method because the dihydroepoxide precursors such as \textsuperscript{12} are unstable under the reaction condition.

The problem was solved\textsuperscript{27} by using halohydrin esters which are stable to the bromination conditions. The bromohydrins were converted to trifluoroacetates which were brominated with N-bromosuccinimide (NBS).

\textsuperscript{32} N. Kaubisch, J. W. Daly, and D. M. Jerina, Biochemistry, 11, 3080 (1972).

\textsuperscript{33} P. Sims, Biochem. J., 125, 159 (1971); ibid., 130, 27 (1972).
The resulting dibromoesters were hydrolyzed to dibromo alcohols which were treated with base to give arene oxides in 60-70% overall yield as shown in Scheme 4.

These three general routes complement each other. The first two routes can only be applied to prepare the K-region epoxides while the third one has only been applied to prepare the non-K-region epoxides.
Benzo[a]pyrene epoxides.

To date three of benzo[a]pyrene epoxides have been prepared. Benzo[a]pyrene-4,5-oxide, 11, was obtained from cyclization of the corresponding dialdehyde with trisdimethylaminophosphine, while benzo-[a]pyrene-7,8-oxide, 14, and benzo[a]pyrene-9,10-oxide, 15, were prepared by Vogel's route. 4,27

Benzo[a]pyrene metabolism.

Of the many metabolites of benzo[a]pyrene (BP) that have been identified only 4,5-dihydro-4,5-dihydroxy-BP, 16, 7,8-dihydro-7,8-dihydroxy-BP, 17, and 9,10-dihydro-9,10-dihydroxy-BP, 18, supposedly 4,34

34. N. Kinoshita, B. Shears, and H. V. Gelboin, Cancer Research, 33, 1937 (1973) and references cited within.
arise from the corresponding epoxide 11, 14, and 15. However there is no good explanation for the detection of 6-hydroxy-BP, 19, as major metabolite in vivo and BP-1,6-quinone, 20, BP-3,6-quinone, 21, and 3,6-dihydroxy-BP, 22, in vitro.


Cavalieri and Calvin suggested one possible mode of metabolism or carcinogenic action of benz[a]pyrene as the following. Benzo[a]-pyrene is activated by electrophilic attack at the 6-position by positive oxygen produced by the action of hydroxylating enzymes. The activated intermediate is then further attacked by nucleophilic cellular components at position 1 and 3 as shown in Scheme 5.

The suggestion is based on their observation that proton exchange at position 6 of benzo[a]pyrene was most rapidly followed by exchange at positions 1 and 3. These results indicated that position 6 is the most nucleophilic position in benzo[a]pyrene. On protonation at position 6, benzo[a]pyrene forms a stable cationic system, \(^{23a}\). These results also showed that positive charge would localize mainly at positions 1 and 3 as in \(^{23b}\) and \(^{23c}\) (Scheme 5). These data agreed with the molecular orbital (M.O.) calculation, \(^{40}\) which indicated that positions 6, 1, and 3 have the lowest carbon localization energy, and the fact that ozonation and oxidation of benzo[a]pyrene produces

---

Scheme 5

R = O
   = H
Scheme 6
Scheme 6 (Continued)
only the 1,6 and 3,6-derivatives.

However, we suggested formation of 5a,6-dihydro-5a,6-epoxybenzo-[a]pyrene, \( \mathcal{Z} \), as metabolic intermediate would also explain the formation of 6-hydroxy-BP, 1\( \mathcal{Z} \), 3-hydroxy-BP, 24, 1-hydroxy-BP, 25, 1,6-dihydroxy-BP, 26, 3,6-dihydroxy-BP, 22, BP-1,6-quinone, 21, and BP-3,6-quinone, 20, as metabolites as shown in Scheme 6.

Benzo[a]pyrene could spontaneously rearrange \(^{46}\) to 1\( \mathcal{Z} \) or ring open by protonation to give 27a and other localized forms 27b and 27c as described above. Hydration and deprotonation of 27b and 27c would lead to 1,6-dihydro-1,6-dihydroxy-BP, 28b, and 3,6-dihydro-3,6-dihydroxy-BP, 28c. After losing water 28b and 28c could give 25 and 24. Oxidation of 28b and 28c would give 26 and 22 which could be further oxidized to 21 and 20, respectively.

With the above concepts in mind, a synthesis of \( \mathcal{Z} \) was desired.

The immediate precursor for formation of \( \mathcal{Z} \) was to be 0-(9-phenalenonyl)benzaldehyde, 29, or dimethyl-[0-(9-phenalenonyl)benzyl]sulfonium salt, 30.

---

\(^{46}\) For spontaneous rearrangement of 1,2-dihydro-1,2-epoxy naphthalene see G. J. Kasperek and T. C. Bruce, J. Amer. Chem. Soc., 94, 198 (1972).
Cyclization of 29 with Mark's reagent or treatment of 30 with base would theoretically lead to epoxide 31. Reaction of phenalenone 31 with phenylmagnesium bromide was known to yield an intermediate presumably 32 which after distillation gave 9-phenylphenalenone, 33.

Similarly reaction of o-[2-(1,3-dioxolanyl)phenyl]magnesium bromide, 34 with 31 followed by hydrolysis and oxidation was expected to yield 29 while reaction of 31 with o-(methyliothiomethyl)phenyllithium, 35, followed by oxidation would give o-[9-(methyliothiomethyl)phenyl]phenalenone, 36, which after treatment of methyl iodide would give 30.

Further application of the same type of synthesis to 7-H-benz-[d,e]anthracen-7-one, 37, and tropolone, 38, might afford epoxide 41 and 42 as shown in Scheme 7 since 37 and 38 were known to react with phenyl magnesium bromide or phenyllithium to give 6-phenyl-7H-benz[d,e]-anthracene-7-one, 39a, 52,53 and 2-phenyltropone, 40a, 54 respectively.


Scheme 7
RESULTS AND DISCUSSION

It was required to prepare o-(9-phenalenonyl)benzaldehyde, 29, hoping reaction of 29 with trisdimethylaminophosphine (TDP) will produce the desired 5a,6-dihydro-5a,6-epoxybenzo[a]pyrene, 3.

Synthesis of o-(9-phenalenonyl)benzaldehyde, 29.

The first attempt to prepare aldehyde, 29, involved the preparation of 9-(o-tolyl)phenalenone, 44, from o-tolyl magnesium bromide and phenalenone, 31. It was hoped that the methyl group could be converted to an aldehyde group by N-bromosuccinimide (NBS) bromination followed by a Sommelet reaction. However, the 9-(o-tolyl)phenalenone, 44, failed to react with NBS. Accordingly, o-bromobenzaldehyde ethylene acetal, 46, was prepared and the Grignard reagent of 46 reacted with phenalenone to yield o-(9-phenalenononyl)benzaldehyde, 29, in 63% overall yield after a hydrolysis and an oxidative work up. The steps are shown in Scheme 8. The o-bromotoluene was converted to o-bromobenzaldehyde, 45, by NBS bromination followed by a Sommelet reaction. The aldehyde, 45, was converted to its ethylene acetal, 46. Phenalenone, 31, prepared from 6-naphthol, was reacted with Grignard reagent, 34.


of 46 at -30 to -10° to give 70% of o-(1H-9-hydroxyphenalen-1-yl)-
benzaldehyde ethylene acetal, 47, which was hydrolyzed to o-(1H-9-
hydroxyphenalen-1-yl)benzaldehyde, 48. On oxidation with benzoquinone,
48 was converted to the desired o-(9-phenalenonyl)benzaldehyde, 29.
When phenalenone was reacted with 34 in refluxing tetrahydrofuran,
8% of benzo[a]pyrene, 2, and 3% of a compound assumed to be 6-(2-
hydroxyethoxy)benzo[a]pyrene, 49, were obtained. The structure assign-
ment of 49 was based on ir absorption at 3200 cm⁻¹ (-O-H), nmr absorp-
tion at δ 4.50 (4H, multiplet), a uv spectrum similar to that of benzo-
[a]pyrene and an observed molecular ion, m/e = 312.1154. (Anal. Calcd.
for C₂₀H₁₆O₂: m/e = 312.1150.)

\[ \text{Chemical structures} \]

\[ 44 \]

\[ 49 \]
Scheme 8
$31 + 34 \rightarrow \text{reaction at } -30^\circ \text{ to } -10^\circ \rightarrow \text{compound 47}$

$\rightarrow \text{compound 48} \rightarrow \text{compound 29}$

Scheme 8 (Continued)
Since a small amount of benzo[a]pyrene 2 had been obtained in the Grignard reaction, 47 was treated with excess phenylmagnesium bromide to see whether the benzo[a]pyrene production was the result of reaction of the Grignard reagent with 47. However an 11% yield of a phenyl benzo[a]pyrene, 50, of unknown structure was obtained. No attempt was made to determine its structure.

Reactivity of o-(9-phenalenonyl)benzaldehyde, 29, with trisdimethylamino-phosphine (TDP).

The only nonpolar material isolated from reaction of 29 with excess TDP in refluxing benzene was benzo[a]pyrene (6%). When an equimolar mixture of 29 and TDP in benzene was stirring for one week at room temperature only starting material 29 and some polar material were detected by TLC. However when the same mixture was heated to reflux in dichlorobenzene for 24 hr, a yellow nonfluorescent substance beside benzo[a]-pyrene was detected by TLC. The substance had a higher Rf value than that of benzo[a]pyrene when eluted with benzene on a silica gel plate. The yellow substance, mp 140-142°, was isolated in 16% yield via the formation of a picrate. This substance showed a singlet at δ 3.30 (6H) in nmr spectrum, a molecular ion of m/e = 295 (P, calcd for C22H17N) and a uv spectrum similar to that of benzo[a]pyrene. Based on this data, the structure, 51, was assigned to this material. When 29 was reacted with excess TDP in refluxing dichlorobenzene, a 32% yield of benzo[a]pyrene (isolated as picrate) was obtained.
The mechanism of reaction between aldehydes and TDP has been suggested to involve a first step in which the phosphorus of TDP attacks the carbonyl carbon as shown in Scheme 9. However by using o-, m-, and p-nitrobenzaldehydes and a cyclic trisdialkylaminophosphine, an alternate mechanism involving the attack of phosphorus on the carbonyl oxygen was suggested as shown in Scheme 10.

Although simple ketones did not react with TDP, fluorenone yielded fluorenylidine. The exact mechanism is not known. The formation of benzo[a]pyrene in our case provides an intramolecular example of double bond formation.

The reaction of with TDP deserves further investigation in order to afford a new benzo[a]pyrene synthesis and to clarify the mechanism of the formation of 51.


Scheme 9
Scheme 10
Since reaction of 29 with TDP did not provide the desired 5a,6-dihydro-5a,6-epoxybenzo[a]pyrene, 3, the alternative route involving reaction of dimethyl[o-(9-phenalenonyl)benzyl]sulfonium tetrafluoroborate, 30, with base was considered. Therefore a synthesis of 30 was required.


The successful synthetic route to 30 is shown in Scheme 11.

o-Bromobenzyl methyl sulfide, 55, was prepared by bromination of o-bromotoluene with N-bromosuccinimide followed by reaction of the resulting o-bromobenzyl bromide, 54, with sodium methylmercaptide.

When phenalenone was added in portions to the lithio derivative of 55 at 0° followed by refluxing in ether, 15% of 1-[o-(methylthiomethyl)phenyl]-1H-phenalene-9-ol, 56, 17% of 9-[o-(methylthiomethyl)phenyl]phenalenone, 36, and 25% of a compound which appeared to be a phenalenone dimer, 57, were obtained. However if a benzene solution of phenalenone was added initially at 0° to an ether solution of o-(methylthiomethyl)phenyllithium during 24 hr while the reaction mixture was allowed to warm up to room temperature, only 7% of 36 was obtained. About 50% of unreacted phenalenone was recovered. The low yield of 56 and 26 was due to the difficulty of isolation (see Experimental Section). The low temperature reaction may prove to be a better procedure as in case of other reactions involving phenalenone and organo lithium or magnesium reagents in this work.
Scheme 11
Heating a benzene solution of 56 with benzoquinone converted 56 to 36 in 86% yield.

Quaternization of 36 with methyl iodide followed by treatment with silver tetrafluoroborate gave dimethyl-[o-(9-phenalenonyl)benzyl]-sulfonium tetrafluoroborate, 30, in 90% yield. The nmr spectrum of 30 in dimethyl sulfoxide-d6 showed two S-methyl groups at δ 2.70 and 2.80 and an AB quartet at δ 4.46 and 4.62 for two benzylic protons. However when trifluoroacetic acid was used as the solvent, the two S-methyl absorption coalesced to a singlet (6H) at δ 2.80 while the two benzylic protons appeared as an AB quartet at δ 4.50 and 4.73. We interpret this result in the following way. In dimethyl sulfoxide the sulfonium salt, 30, exists as a cyclic complex form 30a. Therefore the two methyl groups become nonequivalent. In trifluoroacetic acid, 30 is protonated to rotameric cations, 30b and 30c. The bulky dimethyl-
thiomethyl group on benzene and the medium hydroxy group on phenalenyl ring prevent conversion of $30b$ and $30c$ to each other. Therefore the two benzylic protons are nonequivalent. The two S-methyl groups are coincidentally equivalent.

Reactions of $30$ with bases.

Reaction of $30$ with different bases in different solvents gave various yields of 6-substituted benzo[a]pyrene derivatives, namely 6-hydroxybenzo[a]pyrene, $19$ (isolated as 6-acetoxybenzo[a]pyrene, $19a$), 6-methoxybenzo[a]pyrene, $19b$, and 6-methylthiobenzo[a]pyrene, $19c$. The results are listed in Table I. No 5a,6-dihydro-5a,6-epoxybenzo-[a]pyrene, $3$, was detected by TLC. The compounds, $19a$ and $19b$, were identified by comparison with authentic samples. While the structure of $19c$ was based on the similarity of uv spectrum with that of benzo-[a]pyrene, a S-methyl absorption at $\delta 2.34$ in nmr spectrum, a molecular ion at m/e = 298 (calcd for C$_{21}$H$_{14}$S), a satisfactory elementary analysis and the comparison of mp (168.5-169°) to the mp (169-170°) reported.

We interpret the results in the following way:

The sulfur ylide formed by treatment of the sulfonium salt, $30$, with the methoxide (or hydroxide) ion attacks the carbonyl group in two


Table 1

Yields of 19 (isolated as 19a), 19b, and 19c obtained by treatment of 30 with various bases in various solvents.

<table>
<thead>
<tr>
<th>Base and Solvent</th>
<th>19 (as 19a)</th>
<th>19b</th>
<th>19c</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaOCH₃/CH₃OH, CH₃CN, benzene</td>
<td>66</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>NaOCH₃/(CH₃)₂SO, benzene</td>
<td>43</td>
<td>13</td>
<td>trace</td>
</tr>
<tr>
<td>NaOH/H₂O, CH₃CN, benzene</td>
<td>22</td>
<td>2.0</td>
<td>2.3</td>
</tr>
<tr>
<td>LiOCH₃/CH₃OH, CH₃CN, benzene</td>
<td>68</td>
<td>0</td>
<td>14</td>
</tr>
</tbody>
</table>
ways to yield the trans intermediate, 58a, and the cis intermediate, 58b, as shown in Scheme 12. The predominant isomer, 58a, rapidly cyclizes to the epoxide, 3, which rearranges spontaneously to 19. The cis isomer, 58b, is protonated to an unstable intermediate, 59a, which is either converted to a dimethyl-6-benzo[a]pyrenylsulfonium salt, 19d, by losing water or displacement of dimethyl sulfide by methoxide (or hydroxide) ion to give 60 which can eliminate water to yield 19b (or 19). The sulfonium salt 19d as an alkylating agent can alkylate methoxide (or hydroxide) ion and be thereby converted to 19c. An alternative intramolecular alkylation of 58b to form 5a,6-dihydro-5a-methoxy-6-methylthiobenzo[a]pyrene, 59b, is unlikely because the transition state for converting 58b to 59b can not obtain a 180° angle between attacking and leaving groups required for a $S_N^2$ reaction to occur.

When the reaction is transferred from a protic solvent such as methanol to a dipolar aprotic solvent such as dimethyl sulfoxide, the nucleophilicity of methoxide is enhanced. Therefore the displacement of dimethyl sulfide by methoxide ion in 19a is faster than loss of water.

---


Scheme 12

19, X=OH
19a, X=OAc
19b, X=OCH₃
19c, X=SCH₃
19d, X=S²(CH₃)₂
As a result, only a trace of 6-methylthiobenzo[a]pyrene, $19_c$, was detected. When a poorer nucleophile such as lithium methoxide was used in place of sodium methoxide, the dehydration process (step 4) became predominant and no 6-methoxybenzo[a]pyrene, $19_b$, was detected.

**Attempted Synthesis of 5a, 6-epoxy-6-methylbenzo[a]pyrene, 61.**

Since alkyl substitution of the oxirane ring generally stabilizes arene oxides, we then attempted to synthesize the epoxide 61 hoping the methyl group would reduce the rearrangement of the epoxide and allow isolation of 61.

The attempted synthetic route of 61 is shown in Scheme 13.

_o-Ethylaniline was converted by a Sandmeyer reaction to o-bromoethylbenzene, 62, which was brominated with N-bromosuccinimide followed by reaction of the crude bromide with sodium methylmercaptide to give o-bromo-1-(methylthioethyl)benzene, 63. The o-(1-methylthioethyl)-phenyllithium, 64, prepared by an exchange reaction between butyllithium and slight excess of bromide, 63, was reacted with phenalenone at -60 to -50° to yield 17% of 1H-1[o-(1-methylthioethyl)phenyl]phenalen-9-ol, 65, and 42% of 9-[o-(1-methylthioethylphenyl)phenalenone, 66, mp 129-133°. On oxidation with benzoquinone, 65 yielded 66 in 90% yield. When 66, mp 129-133°, was recrystallized four times from benzene-ethanol, pure 66, mp 146-147°, was obtained. The lower melting material

Scheme 13

1) NaNO₂, HBr
2) Cu

1) NBS
2) NaSCH₃

BuLi

-60 to -50 °

CH₃-C-H
SCH₃

H-C-CH₃
SCH₃

CH₃-C-H
SCH₃

H-C-CH₃
SCH₃

1) CH₃I
2) AgBF₄


showed only one doublet at $\delta$ 1.37 for C-methyl group in nmr spectrum. When the higher melting material was melted and the mp was taken again, the mp dropped to 131-135°. The once melted material again showed two C-methyl absorptions.

We interpret this phenomenon by assuming that the material, mp 129-133°, contains four diastereomers which are RR, SR, SS, and

![RR diastereomer](image)

![SR diastereomer](image)

![SS diastereomer](image)

![RS diastereomer](image)
RS as shown above. The highest melting material contains two of the diastereomers which are magnetically equivalent, therefore only one C-methyl absorption was observed. When the highest melting material was melted, the energy required for overcoming the rotational barrier is provided. Consequently the other C-methyl absorption for the other two magnetically equivalent diastereomers was observed.

Reaction of phenalenone with o-(1-methylthioethyl)phenyllithium, 64, prepared by exchange of bromide, 63, and a slight excess of butyllithium, at room temperature, gave 1.8% of 6-methylbenzo[a]pyrene, 67, 0.5% of a benzo[a]pyrene derivative, tentatively assigned as di-butyl-t-methylbenzo[a]pyrene, 68, and an unidentified substance which was fluorescent under uv light. However, when the aryllithium, 64, prepared

![Chemical structure](image)


by exchange of excess bromide, 63, and butyllithium, was reacted with phenalenone at room temperature, 6-methylbenzo[a]pyrene was obtained in better yield (5.4%).

Quaternization of 66 with methyl iodide followed by treatment with silver tetrafluoroborate gave dimethyl[α-methyl-α-(9-phenalenonyl)-benzyl]sulfonium tetrafluoroborate, 69, in 80% yield. The nmr spectrum of 69 showed two S-methyl absorptions in either dimethyl sulfoxide-d6 or trifluoroacetic acid. The nonequivalence of the two S-methyl groups is due to asymmetric center at the benzylic carbon.

When sulfonium salt 69 was reacted with sodium methoxide in methanol, an unstable amorphous material was obtained. The spectra data did not show conclusively the identity of the material obtained. Further work should be done in this reaction.
CONCLUSION

Although treatment of dimethyl[o-(9-phenalenonyl)benzyl]sulfonium tetrafluoroborate, 30, with base did not give the desired 5a,6-dihydro-5a,6-epoxybenzo[a]pyrene, 2, the formation of 6-hydroxybenzo[a]pyrene as a major product undoubtedly involved the intermediacy of 2.

Same chemistry mentioned above could be applied to 7H-benz[d,e]-anthracene-7-one, 27, and tropolone, 28, as shown in Scheme 14 to give the not yet known compounds, 8-hydroxynaphtho[1,2,3,4-def]chrysene, 70, and 10-hydroxybenz[a]azulene, 71.

Attempted Synthesis of 6-[o-(methylthiomethyl)phenyl]-7H-benz[d,e]-anthracen-7-one, 39b.

Reaction of o-(methylthiomethyl)phenyllithium, 35, with 7H-benz-[d,e]anthracen-7-one, 27, in refluxing tetrahydrofuran gave a mixture of products. Among the product a small quantity (0.5%) of a hydrocarbon, mp 238-241°, was obtained. The hydrocarbon was tentatively assigned as naphtho[1,2,3,4-def]chrysene, *72, based on the molecular ion, m/e = 302, and comparison to the reported uv spectrum and

67. E. Clar, Chem. Ber., 78, B, 609 (1943). The author reported a mp of 225°. The material reported probably was not pure.

*Old name was dibenzo[a,e]pyrene.
Scheme 14
When \( \text{mp.} \) was reacted with \( 3\) at \(-60^\circ \text{C} \) to \(-50^\circ \text{C} \), a 58\% yield of 7-[\( \alpha \)-(methylthiomethyl)phenyl]-7H-benz[\( d,e \)]anthracen-7-ol, \( \text{72} \), was obtained. The structure assignment of \( \text{72} \) is based on the ir spectrum 3350 cm\(^{-1}\) for OH stretching and the absence of a benzylic proton and olefinic protons in the nmr spectrum.

Preparation of dimethyl[\( \alpha \)-(2-troponyl)benzyl]sulfonium tetrafluoroborate, \( \text{40c} \), and its reaction with base.

Tropolone, \( 3\), was reacted with \( \alpha \)-(methylthiomethyl)phenyllithium, \( 3\), to give an unstable intermediate tentatively assigned as 7-[\( \alpha \)-(methylthiomethyl)phenyl]cycloheptatriene-1,7-diol, \( \text{74} \). The intermediate was treated with 30\% sulfuric acid to give 2-[\( \alpha \)-(methylthiomethyl)phenyl]tropane, \( \text{40b} \), in 35\% overall yield. Reaction of \( \text{40b} \) with methyl

68. N. P. Grechkin and A. E. Arbuzov, Compt. Rend. Acad. Sci., USSR, 32, 50 (1941). These authors reported a mp of 238-239\(^{\circ} \text{C} \).

69. A. Zinke and W. Zimmer, Monatsh., 81, 783 (1950). These authors reported a mp of 241-242\(^{\circ} \text{C} \).
iodide followed by treatment of silver tetrafluoroborate yielded a crude sulfonium salt, \( \text{HOCR}_2 \), which after reaction with sodium methoxide gave a mixture of many products. No attempt was made to isolate the pure products.
SUGGESTIONS FOR FUTURE EXPERIMENTATIONS


Various methoxyphenalenones have been prepared. 70-72 Reaction of 3-ethoxyphenalenone with phenylmagnesium bromide followed by oxidation of the primary product gave 9-phenyl-3-ethoxyphenalenone. 73 Application of chemistry to methoxyphenalenones as shown in Scheme 15, followed by demethylation, can be expected to yield dihydroxybenzo[a]-pyrene which has as yet only been postulated as benzo[a]pyrene metabolites using rat liver enzymes.


The benzylic proton of benzaldehyde diethylmercaptal is known to be much more acidic than that of benzaldehyde diethylacetal. 74 This principle has been applied to dithiane as a tool to synthesize aldehydes

Scheme 13

Scheme 15
and ketones as shown.

benzaldehyde diethylmercaptal  

benzaldehyde diethylacetal

\[
\begin{align*}
\text{1) BuLi (1 eq)} \\
\text{2) RX} \\
\text{R-C-H} & \text{H} \\
\text{R-C-R'} & \text{H}
\end{align*}
\]

\[
\begin{align*}
\text{1) BuLi (1 eq)} \\
\text{2) R'X} \\
\text{R-C-R'} & \text{H}
\end{align*}
\]

---


In our experiment, we found that o-(1H-9-hydroxy-1-phenalenyl)-benzaldehyde ethylene acetal, \(47\), or its keto form, \(47b\), reacted with Grignard reagents to give benzo[a]pyrene and derivatives in low yield. The low yield may be due to the difficulty of abstracting a benzylic proton of \(47b\) with base or formation of side products such as benzoic acid or ketone as observed in case of reaction of benzaldehyde ethylene acetal with butyllithium.

\[ \text{Grignard reagent} \]

\[
\begin{array}{c}
\text{H} \\
\text{H} \\
\text{O} \\
\text{O} \\
\text{C}_3 \\
\end{array}
\]

\(47b\)

\[
\begin{array}{c}
\text{R} \\
\end{array}
\]

\(R=\text{H, } \text{O-CH}_2\text{CH}_2\text{OH}\)

---

The problem might be solved by replacing the dioxolanyl group with the dithianyl group to give $\mathbf{75}$ which can be prepared from aldehyde, with propanedithiol. Reaction of $\mathbf{75}$ with strong base such as potassium hydride or sodium hydride in suitable solvents, may give benzo-[a]pyrene and derivatives in better yield than that obtained in case of $\mathbf{47}$ (page 62).

$\text{c m o j o OT}$$^a$ H = H, \text{SCH}_2\text{CH}_2\text{SH}$

$\xrightarrow{\text{a}}$

$\text{OH}$

$\xleftarrow{\text{a}}$
EXPERIMENTAL SECTION

Generalizations

1. All melting and boiling points are uncorrected. Melting points were taken with a Thomas-Hoover capillary melting apparatus.

2. Microanalyses were performed by the M-H-W Laboratories, Garden City, Michigan.

3. Infrared (ir) absorption spectra were recorded on a Perkin-Elmer Infracord Spectrophotometer.

4. Nuclear magnetic resonance (nmr) spectra were recorded on an A-60 nmr spectrophotometer, Varian Associates, Palo Alto, California.

5. A Varian Aerograph A90-P3 was used for gas liquid chromatographic (GLC) analyses.

6. Silica gel, 100-200 mesh, purchased from Matheson, Coleman, and Bell Chemical Company, and Woelm activity grade I alumina were used for column chromatography. Silica gel plates with fluorescent indicator (Eastman 6060) were used for the thin layer chromatographic (TLC) analyses.

7. The phrase 'worked up as usual' means that the reaction mixture was extracted with ether-benzene, and the organic solution was washed successively with water, saturated sodium chloride solution, dried by filtering through a bed of anhydrous magnesium sulfate, and the solvent removed in vacuo on a rotary evaporator.
Phenalenone 31.

To a three-neck flask provided with a short condenser and a mechanical stirrer was added 360 ml of water than 675 ml of concentrated sulfuric acid. To this hot sulfuric acid solution was added 250 g of technical sodium nitrobenzoate, 500 g of glycerol, 200 g of β-naphthol in the order described. The mixture was stirred and heated cautiously with a burner to maintain a temperature of 130-140° for 1 hr, then worked up while hot as described. The tar obtained was combined with those obtained from the second run using the same amount of reagents and the third run using one-fourth the amount of reagents. The total tar was extracted with six 1-l portions of benzene by heating the mixture on a hot plate. The decanted extracts were filtered, combined, clarified with decolorizing carbon (Norite) and concentrated on a rotary evaporator. The residual solid was distilled to give 150 g of crude yellow solid which, after recrystallization from benzene-ligroin (bp 60-100°), yielded 125 g (22.0%) of yellow prisms of 31, mp 152-154° (lit mp 154-155°); nmr (CDCl₃): δ 6.61 (d, 1, J = 10 Hz, H₂), 7.25-8.12 (m, 6, H₃ and ArH), and 8.47 (d of d, J = 7 and 1 Hz, H₃).

1H-1-(o-Toluyl)phenalen-9-ol, 45.

To 2.5 g of magnesium in 200 ml of dry ether was added 17 g (10.01 mole) of o-bromotoluene during 30 min. The mixture was held at reflux

for 30 min, cooled to room temperature and 9.0 g (0.050 mole) of phenalenone \(31\) was added in portions. The reaction mixture was refluxed overnight, cooled, and hydrolyzed with 7 ml of saturated ammonium chloride solution. After removal of inorganic salt by filtration, the solvent was removed on a rotary evaporator. The residual solid was crystallized from benzene-ligroin to yield 9.3 g (69%) of yellow prisms of \(43\), mp 157-158° (lit mp 156-157°); ir (KBr): 3500 (O-H), 1650 cm\(^{-1}\) (C=C); nmr (CDCl\(_3\)): \(\delta\) 2.80 (s, 3, -CH\(_3\)), 9.73 (s, 1, -OH), 5.40 (br, 1, C=CH\(_2\)), 5.83 (d of d, 1, \(J=10\) and 5 Hz, -CH=CH\(_2\)), 6.51 (d of d, 1, \(J=10\) and 2 Hz, -CH=CH-CH), and 6.93-7.66 (m, 9, Ar-H).

\(9-(o-Tolyl)phenalenon, 44.\)

A mixture of 7.3 g (0.027 mole) of \(43\), 5.4 g of benzoquinone, and 30 ml of ethanol was heated on a steam bath for 30 min. After evaporation of ethanol, a benzene solution of the residue was washed with saturated sodium dithionate solution followed by 10% sodium hydroxide, and worked up as usual. The crude product was crystallized from benzene-Skellysolve B (petroleum ether, bp 60-68°) to yield 6.5 g (90%) of yellow prisms of \(44\), mp 133-134°; ir (KBr): 1630 (C=0), 1620 cm\(^{-1}\) (C=C); nmr (CDCl\(_3\)): \(\delta\) 2.80 (s, 3, -CH\(_3\)), 6.65 (d, 1, \(J=10\) Hz, -CH=CH-C=O), and 6.97-8.12 (m, 10, -CH=CH-C=O and Ar-H); mass spectrum, \(m/e=280\) (p).

Anal. Calcd for C$_{20}$H$_{14}$O: C, 88.9; H, 5.2.

Found: C, 88.6; H, 5.1.

Attempted preparation of o-(9-phenalenonyl)benzyl bromide.

A mixture of 2.7 g of 44, 2.0 g of N-bromosuccinimide, few crystals of benzoyl peroxide, and 50 ml of carbon tetrachloride was held at reflux for 4 hr. After working up as usual, only recovered starting material was obtained. When benzene was used as solvent, no reaction occurred after 5 hr of refluxing.

o-Bromobenzaldehyde, 45.

A mixture of 172 g (1.00 mole) of o-bromotoluene, 222 g (1.25 mole) of N-bromosuccinimide, and 1.0 g of benzoyl peroxide in 1.5 l of carbon tetrachloride was refluxed for 6 hr. After cooling and filtration carbon tetrachloride was removed on a rotary evaporator and the residue was added to a solution of 360 g of hexamethylenetetramine in 400 ml of water and 400 ml of ethanol. The solution was refluxed for 4 hr, 200 ml of concentrated hydrochloric acid was added during 20 min, and the refluxing was continued for 30 min. The organic product was isolated as usual to yield a crude product which afforded 86.0 g (46.5%) of 45, bp 133-134$^\circ$ at 4 mm (lit bp 63.5-77$^\circ$ at 0.13-0.28 mm).

o-Bromobenzaldehyde ethylene acetal, \( \text{46} \).

A solution of 86.0 g (0.467 mole) of \( \text{45} \), 80 g of ethylene glycol, and 1.0 g of toluenesulfonic acid in 200 ml of benzene was held at reflux for 18 hr, during which time, the water formed was removed by azeotropically distillation. The reaction mixture was made basic with 10 g of sodium carbonate and worked up as usual. Fractionation on column A yielded 74.0 g (81\%) of \( \text{46} \), bp 102-106° at 0.5 mm (lit bp 126-127° at 5 mm); nmr (CCl\(_4\)): \( \delta 3.80 \) (m, \( -\text{CH}_2\text{CH}_2- \)), \( 6.10 \) (s, 1, \( -\text{OCH}_2- \)), and \( 7.00-7.70 \) (m, 4, \( \text{Ar-H} \)).

Reaction of o-[2-(1,3-dioxolanyl)]phenylmagnesium bromide with phenalenone in refluxing tetrahydrofuran (THF).

To a Grignard reagent prepared from 1.3 g of magnesium, 0.5 ml of 1,2-dibromoethane, and 11 g (0.05 mole) of \( \text{46} \) in 100 ml of THF was added a solution of 7.0 g (0.039 mole) of phenalenone in 25 ml of THF. After being held at reflux overnight, the reaction mixture was hydrolyzed with 7.5 ml of saturated ammonium chloride solution. After removal of inorganic salt by filtration, THF was removed on rotary evaporator and the residue was chromatographed over 500 g of silica gel to give the following.

---

85. Column A is a 24 in x 1 in column packed with 5 mm glass beads and coated with a heating jacket. On the top of the column was placed a total reflux partial take-off condenser.


87. THF was used instead of ether because in ether the magnesium became coated with an insoluble substance.
Fraction 1 showed strong fluorescent under uv light. To this mixture was added a solution of 2.0 g picric acid in 5 ml each of benzene and ethanol. The picrate obtained was recrystallized from benzene-ethanol to yield 1.5 g of purple needles, mp 197.5-199°. The pure picrate was chromatographed over basic alumina to give 0.8 g (8%) of light yellow plates, mp 178-179°, not depressed by authentic benzo[a]pyrene, 2, (mp 176-177°). The UV spectrum was the same as that recorded. Fraction 2 showed a mixture of compounds by TLC. No attempt was made to isolate crystalline material from this fraction. Fraction 3 was recrystallized several times from benzene-ligroin to give 0.3 g of tan prisms, mp 170-173°. The UV, ir, nmr, and mass spec-

88. Obtained from Aldrich Chemical Company.
tral data agreed with the structure of 6-(2-hydroxyethyl)benzo[a]-pyrene, \( \text{IR (KBr):} \ 3200 \text{ cm}^{-1} (\text{O-H}); \text{NMR (CDCl}_3) : \ \delta 2.13 (s, 1, -\text{OH}), 4.50 (m, 4, -\text{CH}_2\text{CH}_2-), \text{and 7.75-9.25 (m, 11, Ar-H}); \text{mass spectrum: anal. calcd for C}_{22}\text{H}_{18}\text{O}_2, 312.1150, \text{found 312.1154.}

No attempt was made to purify the tar in fraction 4.

\( \alpha-(1\text{H}-9\text{-Hydroxy-phenalen-1-yl})\text{benzaldehyde ethylene acetal, 47.} \)

A Grignard reagent prepared from 2.90 g of magnesium, 7.6 g of 1,2-dibromoethane, and 19.0 g (0.080 mole) of \( \text{C}_6 \) in 150 ml of THF was cooled to \(-30^\circ\) and treated with a solution of 9.0 g (0.050 mole) of phenalenone in 50 ml of THF during 5 min. The mixture was stirred at \(-30\) to \(-10^\circ\) for 1 hr and hydrolyzed with excess saturated ammonium chloride solution. The organic product was isolated as usual and crystallized from ether-hexane to yield 12.0 g of light yellow prisms, mp 163-168\(^\circ\), which after recrystallization from benzene-hexane gave 11.5 g (70%) of light yellow prisms of \( \text{47, mp 173-175^\circ, suitable for further use. Further recrystallization from benzene-hexane gave the analytical sample, mp 176-177^\circ, \text{IR (KBr):} \ 3280 (\text{O-H}), 1640 \text{ cm}^{-1} (\text{C=C}); \text{NMR (DMSO-d}_6): \ \delta 4.05 (s, 4, -\text{CH}_2\text{CH}_2-), 5.52 (br, 1, -\text{CH=CH-CH-}), 6.06 (d of d, 1, J = 10 and 5 Hz, -\text{CH=CH-CH-}), 6.47 (s, 1, -\text{O-CH-CH-}), 6.50-7.58 (m, 10, -\text{CH=CH-CH- and Ar-H}), \text{and 9.60 (s, 1, -OH).}

\text{Anal. Calcd for C}_{22}\text{H}_{18}\text{O}_3: C, 80.0; H, 5.5.}

\text{Found: C, 80.2; H, 5.5.}
o-[(1H-9-Hydroxyphenalen-1-yl)benzaldehyde, 48.

To a Grignard reagent, prepared from 0.72 g of magnesium, 2.8 g of 1,2-dibromoethane, 3.4 g of 46 and 30 ml of THF, at -30°, was added a solution of 0.85 g (4.7 mole) of phenalenone in 5 ml of THF. After stirring at -30 to -10° for 1 hr, the mixture was poured onto dilute hydrochloric acid and worked up as usual. After crystallization from benzene-hexane, the crude product yielded 0.75 g (55%) of light yellow prisms of 48, mp 171-174°. One recrystallization from benzene-hexane afforded an analytical sample, mp 173-174°; ir (KBr): 3340 (O-H), 1670 (C=O), 1610 cm⁻¹ (C=C); nmr (DMSO-d₆): δ 5.97-6.49 (m, 2, CH=CH-CH-), 6.70 (d of d, 1, J = 10 and 1 Hz, -CH=CH-CH), 9.77 (s, 1, OH), and 10.67 (s, 1, -CHO).

Anal. Calcd for C₂₀H₁₄O₂: C, 83.9; H, 4.9.

Found: C, 84.2; H, 5.1.

o-(9-Phenalenonyl)benzaldehyde, 29.

A mixture of 200 mg of 48, 400 mg of benzoquinone, and 10 ml of benzene was heated on a steam bath for 30 min. The benzene solution was washed with saturated sodium dithionate followed by 10% sodium hydroxide and worked up as usual. The crude product was crystallized from benzene-ligroin to yield 180 mg (90%) of yellow prisms of 29, mp 125-126°. One recrystallization from benzene-ethanol gave the analytical sample, mp 125.5-126.5°; ir (KBr): 1680 (HC=O), 1630 (-C=O), 1618 cm⁻¹ (C=C); nmr (CDCl₃): δ 6.45 (d, 1, J = 10 Hz, CH=CH-C=O), 7.10-8.18 (m, 10, CH=CH-C=O and Ar-H), and 9.79 (s, 1, -CHO).
Reaction of o-(1H-9-hydroxyphenalen-1-yl)benzaldehyde ethylene acetal, 47, with phenylmagnesium bromide.

To a Grignard reagent prepared from 0.48 g of magnesium, 1.9 g of 1,2-dibromoethane, 1.6 g (10 mmole) of bromobenzene, and 50 ml of ether was added a solution of 330 mg (1 mmole) of 47 in 30 ml of dry benzene. After being held at reflux for 30 min, the ether was distilled. The remaining benzene solution was held at reflux for 30 min, hydrolyzed with dilute hydrochloric acid, and worked up as usual. The crude product was dissolved in 5 ml benzene and added to a hot solution of 0.5 g of picric acid in 5 ml of ethanol. After standing at room temperature for 1 hr, 80 mg of picrate, mp 204-207° w. dec., was obtained by filtration. The picrate was chromatographed over basic alumina to yield 36 mg (11%) of yellow plates, mp 217-220°. The spectral data and elementary analysis were consistent with the structure of a phenylbenzo[a]-pyrene, 50; ir (KBr): 840, 830, 760, 700 cm⁻¹; nmr: δ 6.92-8.17 (m, 15, ArH), and 8.53-9.00 (m, 1, ArH); mass spectrum: calcd, 328.1259; found, 328.1257.

Anal. Calcd for C₂₀H₁₂O₂: C, 84.5; H, 4.3.
Found: C, 84.7; H, 4.5.

The remaining mother liquor was concentrated and chromatographed over basic alumina. The first fraction, obtained by using 250 ml benzene gave an oil which after crystallization from ligroin, yielded 28 mg of
yellow prisms, mp 185-203°. The material showed a mixture of at least two products by TLC. The UV spectrum showed that the products might be the benzo[a]pyrene derivatives. No attempt was made to identify the polar fractions.

Attempted preparation of benzo[a]pyrene by reaction of 48 with 2% sodium amalgam.

To a well stirred solution of 200 mg of 48 in 10 ml of ethanol and 10 ml of acetic acid was added 30 g of 2% sodium amalgam in portions. The solution was decanted onto 50 ml of water and worked up as usual. The crude product showed a mixture of compounds on a silica gel plate using benzene as eluant. None of the compounds corresponded to benzo[a]pyrene.

Attempted cyclization of 49 with trisdimethylaminophosphine (TDP) to 5a,6-epoxy-5a,6-dihydrobenzo[a]pyrene, 3.

A mixture of 50 mg (0.18 mmole) of 49, 200 mg (1.2 mmole) of TDP, and 5 ml of benzene was heated on a steam bath for 1 hr and worked up as usual. The crude product showed a fluorescent spot of Rf = 0.75 on a silica gel using benzene as eluant. After chromatography over alumina, the crude product yielded 3 mg (6%) of benzo[a]pyrene, mp 176.178°, not depressed by an authentic sample (mp 167-167°). No attempt was made to

identify the polar fraction. If a mixture of 29 and excess TDP was refluxed in dichlorobenzene for 24 hr, 32% of benzo[a]pyrene (isolated as picrate) was obtained.

In another run, 428 mg (1.5 mmole) of 29, 245 mg (1.5 mmole) of TDP, and 8 ml of benzene were mixed and stirred for 7 days. An aliquot showed only starting material and a polar substance by TLC. Benzene was replaced by o-dichlorobenzene and the mixture was held at reflux for 24 hr, and steam distilled. The crude product was chromatographed on alumina. The first fraction, obtained by using 1 A benzene, yields an oil which showed three major spots on silica gel plate using benzene as eluant. The first yellow spot, \( R_f = 0.76 \), was the major component, the second fluorescent spot corresponded to that of benzo[a]pyrene while the third spot, which is also fluorescent, had a \( R_f \) value of 0.17. The crude oil was treated with a solution of 0.3 g of picric acid in 3 ml each of benzene and ethanol to afford 110 mg (16%) of brown picrate, mp 170-172°. The picrate was chromatographed over basic alumina to give a yellow solid, mp 140-142°; \( \text{ir} (\text{KBr}): 1060, 840, 830, 755, 705, \text{and} 680 \text{ cm}^{-1} \); \( \text{nmr} (\text{CDCl}_3): \delta 3.30 (s, 6, (\text{CH}_3)_2\text{N}-) \), and 7.50-9.17 (m, 11, Ar-H). Based on this data, the yellow solid was tentatively assigned as 6-dimethylaminobenzo[a]pyrene, 51; mass spectrum: calcd, 295.1361; found, 295.1365.

**Anal. Calcd for C\(_{22}\)H\(_{17}\)N: C, 89.5; H, 5.8; N, 4.9.**

**Found: C, 89.3; H, 5.9; N, 4.7.**

The 6-dimethylaminobenzo[a]pyrene was unstable toward heating in the air. Attempted purification by recrystallization from hot ligroin caused colorization of compound.
o-Bromobenzyl bromide, 54.

A mixture of 188 g (1.10 mole) of o-bromotoluene, 178 g of N-bromosuccinimide, 1.50 g of benzoyl peroxide, and 350 ml of carbon tetrachloride was refluxed for 3½ hr. After cooling and filtration, carbon tetrachloride was removed on a rotary evaporator and the residue was fractionally distilled through column A to give 167 g (67%) of 54, bp 103-105° at 4 mm (lit bp 120-130° at 13 mm).

o-Bromobenzyl methyl sulfide, 55.

To a sodium ethoxide solution, prepared from 7.0 g of sodium and 150 ml of ethanol at 0°, was added 25 ml of cold methanethiol at once followed by 81 g (0.32 mole) of 29 during 30 min. The mixture was refluxed for 1 hr, after which 140 ml of ethanol was distilled. After adding 100 ml water the reaction mixture was worked up as usual to afford 66 g (93%) of 55, bp 97-101° at 3 mm (lit bp 104-107° at 5.2 mm).

1-[o-(Methylthiomethyl)phenyl]-1H-phenalen-9-ol, 56, and 9-[o-(methylthiomethyl)phenyl]phenalenone, 36.

To a solution of o-(methylthiomethyl)phenyllithium, 91 prepared from 117 ml of 2.2 M n-butyllithium and 57 g (0.027 mole) of 55 in 100 ml dry ether, at 0° was added 10 g (0.056 mole) of phenalenone in portions under nitrogen. After stirring at 0° for 2 hr, then at room temperature for 4 hr, the reaction mixture was held at room temperature for 4 hr.

the reaction mixture was held at reflux overnight, hydrolyzed with dilute hydrochloric acid and worked up as usual. The crude product was dissolved in 50 ml benzene then triturated with 300 ml of ether-ligroin (1:1) to give 4.5 g of tarry material. After treating this material with a solution of 10 g of benzoquinone in 100 ml of benzene, the benzene solution was washed successively with saturated sodium dithionate and 10% sodium hydroxide and worked up as usual. The residue was crystallized from benzene then recrystallized from dimethylformamide to yield 2.5 g (25%) of orange prisms, mp 250-251° w. dec. The spectral data and elementary analysis indicated that the compound was a phenalenone dimer, \( \text{mp} \); ir (KBr): 1630 (C=O) and 1618 cm\(^{-1}\) (C=C); mass spectrum: calcd, 358.0994; found, 358.0998.

**Anal.** Calcd for \( \text{C}_{26}\text{H}_{14}\text{O}_{2} \): C, 87.1; H, 3.9.

Found: C, 87.3; H, 3.8.

The remaining organic solution, obtained after removal of the tarry material, was concentrated on a rotary evaporator and the residue was chromatographed on 1 Kg of silica gel to give the following.
<table>
<thead>
<tr>
<th>Fraction</th>
<th>Eluant</th>
<th>Weight</th>
<th>Character</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$21 \ell$ of benzene-petroleum ether (1:9) and $21 \ell$ of benzene-petroleum ether (2:8)</td>
<td>24.4 g</td>
<td>oil</td>
</tr>
<tr>
<td>2</td>
<td>$18 \ell$ of benzene-petroleum ether (2:3)</td>
<td>6.4 g</td>
<td>a mixture of a solid and oil</td>
</tr>
<tr>
<td>3</td>
<td>$18 \ell$ of benzene-petroleum-ether (8:2)</td>
<td>4.0 g</td>
<td>oil</td>
</tr>
<tr>
<td>4</td>
<td>$10 \ell$ of benzene-petroleum-ether (8:2)</td>
<td>4.5 g</td>
<td>a mixture of a solid and oil</td>
</tr>
<tr>
<td>5</td>
<td>$4 \ell$ of benzene</td>
<td>1.0 g</td>
<td>morphorous solid</td>
</tr>
</tbody>
</table>

Fraction 1 contained benzylmethylsulfide and starting material indicated by GLC.

Fraction 2 was recrystallized twice from benzene-ligroin to give 3.0 g (17%) of yellow prisms of mp 147-148.5°, ir (KBr): 3200 cm$^{-1}$ (O-H); nmr (CDCl$_3$): $\delta$ 2.09 (s, 3, -SCH$_3$), 3.74 and 4.02 (AB q, 2, $J = 16.7$ Hz, -CH$_2$-), 5.51 (d of d, 1, $J = 4$ and 2 Hz, -CH=CH-CH-), 5.93 (d of d, 1, $J = 10$ and 4 Hz, -CH=CH-CH-), 6.55 (d of d, 1, $J = 10$ and 2 Hz, -CH=CH-CH-), 6.50 (s, 1, OH), and 6.90-8.20 (m, 9, Ar-H).

Anal. Calcd for C$_{12}$H$_{18}$OS: C, 97.2; H, 5.7; S, 10.1.

Found: C, 79.5; H, 5.6; S, 10.0.
Fraction 3 contained many compounds indicated by TLC. No attempt was made to separate them.

Fraction 4 was recrystallized twice from benzene-ligroin to yield 2.6 g (16%) of orange prisms of \( \text{36} \), mp 149-150°; ir (KBr): 1630 (C=O) and 1618 cm\(^{-1}\) (C=C); nmr (CDCl\(_3\)): \( \delta \) 1.90 (s, 3, -SCH\(_3\)), 3.41 and 3.52 (AB q, 2, \( J = 16 \text{ Hz} \), -CH\(_2\)-), 6.60 (d, 1, \( J = 10 \text{ Hz} \), H\(_2\)), and 7.02-8.25 (m, 10, H\(_3\) and Ar-H).

Anal. Calcd for C\(_{22}\)H\(_{16}\)O\(_5\): C, 79.7; H, 5.1; S, 10.1.

Found: C, 79.5; H, 5.0; S, 10.0.

Fraction 5 contained a mixture of \( \text{36} \) and phenalenone indicated by TLC. An attempt to crystallize more \( \text{36} \) was not successful.

No attempt was made to identify the polar fractions.

In another run, a solution of phenalenone in benzene was added initially at 0° to the \( o \)-(methylthiomethyl)phenyllithium solution during 24 hr while the solution was allowed to warm up to room temperature. After chromatography of the crude product only 7% of \( \text{36} \) was obtained after oxidation of the crude 1-[\( o \)-(methylthiomethyl)phenyl]-1H-phenalen-9-ol, \( \text{56} \), isolated. Substantial amount (50%) of phenalenone was recovered. Also when tetrahydrofuran was used as solvent in the reaction, TLC analysis of an aliquot showed little reaction.

It was found that if one oxidized the crude reaction mixture with benzoquinone before separation on a silica gel column, the yield of desired product decreased due to the difficulty of separating the desired product \( \text{36} \) from the unreactive phenalenone by chromatography.
Alumina is not recommended for chromatography because little separation occurred when alumina plates were used for TLC.

After discovering that low reaction temperatures increased the yields from reactions of phenalenone or benzathrone with Grignard reagents or aryllithium reagents, a reaction of phenalenone with o-(methylthiomethyl)phenyllithium was run at -30 to -10°. Analysis of aliquots by TLC showed that most of phenalenone had reacted as indicated by the absence of a yellow spot at \( R_f = 0.24 \) corresponding to phenalenone and the product was mainly \( \text{56} \). When the reaction mixture was worked up, TLC analysis showed a substantial amount of 9-[o-(methylthiomethyl)phenyl]phenalenone, \( \text{36} \), was present probably because of oxidation. The reaction mixture was oxidized with benzoquinone hoping to get the crystalline \( \text{36} \) directly failed. It is recommended to future workers to prepare \( \text{56} \) and \( \text{36} \) by reaction of phenalenone and o-(methylthiomethyl)phenyllithium at -30 to -10° and isolation of products by chromatography over silica gel.

**Oxidation of \( \text{56} \) with benzoquinone.**

A mixture of 1.97 g of \( \text{56} \), 40 ml of benzene, and 4.0 g of benzoquinone was heated on a steam bath for 20 min. After working up as described before, 1.71 g (86%) of \( \text{36} \) was obtained.

**Dimethyl-[o-(9-phenalenonyl)benzyl]sulfonium tetrafluoroborate, \( \text{30} \).**

To a solution of 1.00 g (3.05 mmole) of \( \text{36} \) in 20 ml of acetonitrile was added 6.6 g of methyl iodide. The mixture was stirred for 30 min,
0.560 g (3.17 mmole) of silver tetrafluoroborate added, and the stirring was continued for 3 hr. The solution was filtered and the filtered silver iodide was washed several times with acetonitrile. The combined acetonitrile solution was concentrated on a rotary evaporator to yield a residue which, after crystallization from ethanol-acetonitrile, yielded 1.06 g (83%) of yellow plates of 30, mp 197-199°C w. dec.; ir (KBr): 1630 (C=O) and 1618 cm⁻¹ (C=C); nmr (DMSO-d₆): δ 2.71 and 2.80 (two s, 6, (CH₃)₂-S⁺), 4.46 and 4.62 (AB q, 2, J = 14 Hz, -CH₂-), 6.60 (d, 1, J = 10 Hz, H₂), 7.05-8.60 (m, 10, H₃ and ArH); nmr (CF₃CO₂H): δ 2.80 (s, 6, (CH₃)₂S⁺), 4.50 and 4.73 (AB q, 2, J = 14 Hz, -CH₂-), and 7.35-9.20 (m, 11, Ar-H).

Anal. Calcd for C₂₂H₁₉BF₄OS: C, 63.2; H, 4.7; S, 7.7.

Found: C, 63.2; H, 4.5; S, 7.7.

The sulfonium salt 30 was not stable to heating. Attempted recrystallization from hot ethanol-acetonitrile reduced the yield of 30 to 73%. In the best run, before acetonitrile was removed completely, the solution was diluted with ethanol to afford 90% of 30.

6-Acetoxybenzo[a]pyrene, 19a.

A solution of 0.99 g of lead tetraacetate in 30 ml of glacial acetic acid was added to a solution of 0.50 g benzo[a]pyrene in 20 ml of benzene. After standing for 30 min, the benzene was distilled and water was added to saturation. On cooling 0.50 g of greenish yellow precipitate was isolated which after recrystallization from glacial
acetic acid yielded 0.30 g (50%) of 19a, mp 208-209° (lit mp 208.5-
209.5°).

6-Methoxybenzo[a]pyrene, 19b.

A mixture of 50 mg of 19a, 16 ml of methyl iodide, 10 ml of di-
methylformamide, and 6 ml of 2 N methanolic sodium hydroxide was
stirred at room temperature for 6 hr. After adding 50 ml of water,
the reaction mixture was worked up as usual and the crude product was
chromatographed over alumina to give 46 mg (92%) of 19b, mp 168-170°.
One recrystallization from benzene-ligroin afforded pure 19b, mp 173-
174° (lit mp 174-175°).

Reaction of 30 with sodium methoxide in methanol-acetonitrile.

To a sodium methoxide solution prepared from 1.0 g of sodium and
20 ml of methanol was added a solution of 0.60 g (1.44 mmole) of 30 in
10 ml of acetonitrile and 10 ml of benzene. The mixture was stirred
under nitrogen for 3 hr. A TLC analysis of an aliquot on a silica gel
plate, pretreated with triethylamine, using benzene-ethyl acetate (1:9)
as eluant showed a major spot of Rf = 0.33 corresponding to that of 6-
hydroxybenzo[a]pyrene, 19. Since 6-hydroxybenzo[a]pyrene was known

92. L. F. Fieser and E. B. Hershberg, J. Amer. Chem. Soc., 60, 2542
(1938).


94. Benzene was used hoping to extract the desired benzo[a]pyrene epox-
ide, 3, into it and prevent 3 from reaction with sodium methoxide.

95. Crude 19 was prepared from treatment of 19a with butyllithium.
to be unstable, it is best to be isolated as the acetate. After adding 10 ml of acetic anhydride, the reaction mixture was stirred for 30 min, diluted with 30 ml of water, and extracted with benzene. The benzene solution was washed with saturated sodium bicarbonate solution and worked up as usual. The crude product was chromatographed over 70 g of silica gel to give the following data.

<table>
<thead>
<tr>
<th>Fraction</th>
<th>Eluant</th>
<th>Weight</th>
<th>Character</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 &amp; ether: petroleum ether (1:99)</td>
<td>nil</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>225 ml of ether: petroleum ether (1:99)</td>
<td>56 mg</td>
<td>solid</td>
</tr>
<tr>
<td>3</td>
<td>675 ml of ether: petroleum ether (1:99)</td>
<td>58 mg</td>
<td>solid</td>
</tr>
<tr>
<td>4</td>
<td>675 ml of ether: petroleum ether (1:99)</td>
<td>nil</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>675 ml of ether: petroleum ether (2:8), and 1500 ml of ether: petroleum ether (3:7)</td>
<td>294 mg</td>
<td>solid</td>
</tr>
</tbody>
</table>

Fraction 2 was a light yellow solid, mp 130-135°C, which after recrystallization from ligroin afforded 40 mg of light yellow prisms of 6-methylthiobenzo[a]pyrene, 19c, mp 168.5-169°C (lit mp 169-170.5°C);
ir (KBr): 840, 770, 762, 752, and 692 cm\(^{-1}\); nmr (CDCl\(_3\)): \(\delta 2.34\) (s, 3, -SCH\(_3\)), and 7.68-9.30 (m, 11, Ar-H); mass spectrum, m/e = 298 (p); uv (CHCl\(_3\)): 235 (4.14), 258 (4.36), 270 (4.14), 282 (4.16), 294 (4.38), 305 (4.53), 350 (3.54), 364 (3.84), 383 (4.12), 403 (4.15).

**Anal.** Calcd for C\(_{21}\)H\(_{14}\)S: C, 84.5; H, 4.7; S, 10.8.

Found: C, 84.3; H, 4.6; S, 11.0.

Fraction 3 was shown to be a mixture of two components by TLC and was rechromatographed over silica gel using ether:petroleum ether (1:99) as eluant. The first cut, obtained by using 300 ml of eluant, gave 14 mg of light yellow prisms, which after recrystallization yielded additional 8 mg of 19c. The total yield of 19c was 48 mg (10%). The second cut, obtained by using 500 ml eluant yielded 45 mg (10%) of 6-methoxybenzo[a]pyrene, 19b, mp 166-168\(^\circ\), which after recrystallization from benzene-ligroin afforded light yellow prisms of pure 19b, mp 173-174\(^\circ\), not depressed by authentic sample prepared before; ir (KBr): 1090, 762, 752, and 705 cm\(^{-1}\); nmr (CDCl\(_3\)): \(\delta 4.32\) (s, 3, -OCH\(_3\)), and 7.63-9.12 (m, 11, Ar-H); uv (CHCl\(_3\)): 235 (4.38), 257 (4.53), 269 (4.54), 277 (4.33), 290 (4.55), 303 (4.68), 359 (4.21), 378 (4.30), 398 (4.34), 411 (3.81); mass spectrum, m/e = 282 (p).

Fraction 5 yielded 66\% of 6-acetoxybenzo[a]pyrene, mp 201-205\(^\circ\), which after recrystallization from benzene-ligroin gave 268 mg of pure 6-acetoxybenzo[a]pyrene, 19a, mp 208-209\(^\circ\), not depressed by authentic sample prepared before; ir (KBr): 1740 (C=O), 840, 830, 762, 753, and 700 cm\(^{-1}\); nmr (CDCl\(_3\)): \(\delta 2.69\) (s, 3, -OCOCH\(_3\)), and 7.63-9.08 (m, 11, Ar-H); uv (CHCl\(_3\)): 256 (4.59), 267 (4.63), 277 (4.47), 288 (4.66),
301 (4.73), 337 (3.94), 354 (4.20), 373 (4.43), 393 (4.49), 407 (4.05); mass spectrum, m/e = 310 (p).

Reaction of 30 with sodium methoxide in dimethylsulfoxide (DMSO).

To a solution of 0.70 g of sodium ethoxide in 6 ml DMSO was added 150 mg (0.36 mmole) of 5 under nitrogen. After stirring for 2 hr, the reaction mixture was worked up as described above to give 13 mg (13%) of 19b and 48 mg (43%) of 19a.

Reaction of 30 with sodium hydroxide in water and acetonitrile.

To a solution of 0.80 g of 30 in 40 ml of acetonitrile and 10 ml of benzene was added 10 ml of 50% sodium hydroxide solution. After stirring at room temperature for 1 hr, the reaction mixture was worked up as described above to afford 12 mg (2.3%) of 19c, 10 mg (2%) of 19b, and 140 mg (22%) of 19a.

Reaction of lithium methoxide with 30 in methanol-acetonitrile.

To a solution of 620 mg of 30 in 25 ml of acetonitrile and 40 ml benzene was added a lithium methoxide solution prepared from 0.5 g of lithium and 40 ml of methanol. The mixture was stirred for 2 hr at room temperature and worked up as described to give 60 mg (14%) of 19c and 310 mg (68%) of 19a.
o-Bromoethylbenzene, 62.

To 1215 g (6.00 mole) of 40% hydrobromic acid was added slowly with stirring 153.0 g (1.25 mole) of o-ethylaniline at 20-30° during 1 hr. The slurry was cooled to 5° and 121 g (1.70 mole) of sodium nitrite (97%) added with stirring in 5-10 g portions during 1 hr at 5-10°. Copper powder (5.0 g) was added and the mixture was heated to start the decomposition of diazonium salt then cooled immediately with an ice bath. The temperature was maintained at 15° for 1 hr and then raised to 90-95° for 30 min. After adding 1 l of water, the reaction mixture was steam distilled. The distillate was made basic with 10 g sodium hydroxide and taken into 500 ml of benzene. The benzene solution was washed with 10% sodium hydroxide solution and worked up as usual to afford 96 g (42%) of 62, bp 68-70° at 8 mm (lit bp 64° at 8 mm); nmr (CCl₄): 6 1.12 (t, 3, J = 8 Hz, -CH₃), 2.75 (q, 2, J = 8 Hz, ArCH₂-), and 6.75-7.50 (m, 4, Ar-H).

o-Bromo-(1-methylthioethyl)benzene, 63.

A mixture of 96.5 g (0.52 mole) of 62, 93 g (0.52 mole) of N-bromo-succinimide, 1 g of benzoyl peroxide, and 250 ml of carbon tetrachloride was held at reflux for 2 hr. After cooling, solid was removed by

96. Obtained from Aldrich Chemical Company.

97. Reaction would get out of control if not cooled immediately after nitrogen evolution started.

filtration and the solvent removed by evaporation. The residue was added to a sodium methylmercaptide solution prepared from 29 g of methanethiol and a sodium methoxide solution (12 g of sodium in 250 ml of methanol). The mixture was refluxed for 30 min and worked up as usual. The residue was fractionally distilled through column B to afford 103 g (86%) of 63, bp 84-85° at 0.6 mm; nmr (CCl$_4$): $\delta$ 1.48 (d, 3, $J = 7$ Hz, -CH$_3$), 1.90 (s, 3, -SCH$_3$), 4.51 (q, 1, $J = 7$ Hz, Ar-CH-CH$_3$), and 6.90-7.70 (m, 4, Ar-H).

Anal. Calcd for C$_4$H$_{11}$BrS: C, 46.8; H, 4.8; Br, 34.6; S, 13.9.

Found: C, 46.9; H, 4.9; Br, 34.5; S, 13.7.

Reaction of phenalenone with o-(1-methylthioethyl)phenyllithium, 64, at room temperature.

To a solution of 26 mg of 2.2 M n-butyllithium in hexane was added 13 g (0.057 mole) of 63 in 10 ml ether at 0° during 30 min. After stirring at 0° for 1 hr, a solution of 4.0 g (0.022 mole) of phenalenone in 40 ml of benzene was added dropwise during 10 min, the reaction mixture was stirred at room temperature overnight, treated with dilute hydrochloric acid, and worked up as usual. The crude product was chromatographed over 400 g of silica gel to give the following data.

99. Column B is a 30 in Widmer column topped with a total reflux partial take-off condenser.
Fraction 1 contained three fluorescent components, incompletely separated from each other, and a nonfluorescent component as indicated by TLC. This fraction was then treated as described below. Fraction 2 was crystallized from ligroin followed by recrystallization from benzene-ligroin to yield 40 mg of light yellow prisms, mp 209-211°. The uv spectrum agreed with that reported 100 for 6-methylbenzo[a]pyrene, 67; ir (KBr): 835, 825, 750, and 685 cm⁻¹; nmr (CDCl₃): δ 3.17 (s, 3, -CH₃), and 7.23-9.22 (m, 11, Ar-H); mass spectrum, m/e = calcd for C₂₁H₁₄: 266.1095; found m/e = 266.1101.

The mother liquor of the Fraction 2 was combined with Fraction 1 and rechromatographed over silica gel. The first cut obtained by using 1 L of petroleum ether as eluant, yielded 40 mg (0.5%) of light yellow needles, mp 147-148°, after several recrystallizations from benzene-ligroin. The spectral data indicated that the compound might be a di-butyl-6-methylbenzo[a]pyrene, \( \text{C}_{28} \text{H}_{30} \); nmr (CDCl\(_3\)): \( \delta 0.75-2.25 \) (m, 14, \(-\text{CH}_{2}\text{CH}_{2}\text{CH}_{3}\)), \( 2.75-3.42 \) (m, 7, Ar-CH\(_3\) and ArCH\(_2\)-), and \( 7.50-8.33 \) (m, 9, Ar-H); mass spectrum calcd for \( \text{C}_{28}\text{H}_{30} \), m/e = 378,2427, found m/e = 378.2433; uv (CHCl\(_3\)): 263 (4.38), 272 (4.43), 282 (4.30), 294 (4.41), 307 (4.47), 345 (3.80), 365 (4.06), 383 (4.27), 405 (4.31), 416 (3.98). The second cut, obtained by using 1 L of benzene-petroleum ether (1:20) as eluant, gave 1.0 g of yellow prisms, mp 85-120°, which showed a mixture of three fluorescent components incompletely separated from each other by TLC. No attempt was made to separate the mixture in this cut. The third cut, obtained with 1 L of benzene-petroleum ether (1:20), yielded an additional 70 mg of 67. The total yield of 6-methylbenzo[a]pyrene, 67, was 1.8%.

Fraction 3 contained mainly 1-methylthioethylbenzene and starting material 63 as determined by GLC.

Fraction 4 showed many components by TLC, therefore no further work was done in this fraction.

In another run, phenalenone was reacted with 64 prepared from butyllithium and excess bromide 63 to yield 4.5% of 6-methylbenzo[a]-pyrene. No improvement in yield was obtained when \( \text{N,N,N',N'-tetramethylethylenediamine} \) was added.

To 23 ml of 2.2 M n-butyllithium in hexane at 0° was added a solution of 13 g (0.056 mole) of 63 in 30 ml of dry ether during 10 min under nitrogen. After stirring at 0° for 30 min, the solution was cooled to -60°. To this solution was added 8.0 g (0.044 mole) of phenalenone in portions. The mixture was stirred at -60 to -50° for 40 min and poured onto dilute hydrochloric acid. After standing at room temperature overnight, 3.3 g of yellow solid, mp 170-178°, was collected by filtration. The yellow solid was recrystallized from benzene-ligroin to yield 2.5 g (17%) of light yellow prisms of 65, mp 177-179°; ir (KBr): 3300 (O-H), 1600 cm⁻¹ (C=C); nmr (DMSO-d₆): 6
1.64 (d, 3, J = 7 Hz, -CH₂CH₃), 1.93 (s, 3, -SCH₃), 4.81 (q, 1, J = 7 Hz, Ar-CH₂CH₃), 5.59 (br, 1, -CH=CH-CH₂-), 6.06 (d of d, 1, J = 10 and 5 Hz, -CH=CH-CH₂-), 6.66 (d of d, 1, J = 10 and 2 Hz, -CH=CH-CH₂-), and 6.85-6.70 (m, 9, Ar-H).

Anal. Calcd for C₃₂H₂₀O₆S: C, 79.5; H, 6.1; S, 9.7.

Found: C, 79.6; H, 5.9; S, 9.6.

The combined mother liquor was extracted with benzene-ether. The organic solution was treated with 10 g benzoquinone, heated on a steam bath for 30 min and worked up as described before. The crude product was chromatographed over 400 g alumina. The first fraction, obtained by using 2 l of benzene as eluant, gave 3.0 g of an oily mixture which contained 63 and 1-methylthioethylbenzene as indicated by GLC. The
second fraction, obtained by using 5 L of benzene-ether (4:1), gave 7.6 g of orange prisms, mp 121-128°, which was recrystallized from benzene-ligroin to yield 6.3 g (43%) of 66, mp 129-133°. An analytical sample (mp 146-147.5°) was obtained after four recrystallizations from benzene-ethanol; ir (KBr): 1630 (C=O), 1610 cm⁻¹ (C=C); nmr (CDCl₃): 8 1.37 (d, 3, J = 6 Hz, -CH₂-CH₃), 1.83 (s, 3, -SCH₃), 3.32 (q, 1, J = 6 Hz, -CH₂-CH₃), 6.60 (d, 1, J = 10 Hz, H₂), and 7.10-8.25 (m, 10, H₃ and Ar-H).

The material, mp 129-133°, showed two doublets at 8 1.37 and 1.47 for C-methyl group.

When the material, mp 146-147.5°, was melted and mp was taken again, the mp dropped to 131-135°. The nmr spectrum of the once melted material again showed two doublets at 8 1.37 and 1.47 for C-methyl group. This phenomenon can be explained by the formation of 4 diastereomers (see Results and Discussion, page 75).

Dimethyl-[α-methyl-α-(9-phenalenonyl)benzyl]sulphonium tetrafluoroborate, 69.

To 820 mg (2.48 mmole) of 66, mp 146-147.5°, was added 10 g of methyl iodide followed by a solution of 500 mg (2.52 mmole) of silver tetrafluoroborate in 20 ml acetonitrile. After stirring at room temperature for 2 hr, the reaction mixture was filtered, and the silver iodide was washed with acetonitrile. The acetonitrile solution was concentrated on a rotary evaporator to give a crude product which after crystallization from ethanol yielded 850 mg (80%) of 69, mp 218-220°.
w. dec.; ir (KBr): 1630 (C=O), 1610 cm\(^{-1}\) (C=C); nmr (DMSO-\(d_6\)): \(\delta\) 1.82 (d, 3, J = 8 Hz, -CH-CH\(_3\)), 2.60 and 2.85 (two s, 6, -S\(^+\)(CH\(_3\))\(_2\)), 4.60 (q, 1, J = 8 Hz, -CH-CH\(_3\)), 6.60 (d, 1, J = 10 Hz, H\(_2\)), and 7.08-8.60 (m, 10, H\(_3\) and Ar-H).

Analytical. Calcd for C\(_{23}\)H\(_{21}\)OSBF\(_4\): C, 63.9; H, 4.9; S, 7.4. Found: C, 63.8; H, 5.0; S, 7.4.

When nmr spectrum was taken in trifluoroacetic acid, the two S-methyl groups appeared at \(\delta\) 2.65 and 2.78.

**Attempted Synthesis of 5a,6-epoxy-6-methylbenzo[a]pyrene.**

To a sodium ethoxide solution, prepared from 0.30 g of sodium and 20 ml of methanol, was added 300 mg of 69 and 10 ml of benzene. After stirring at room temperature for 1 hr, the reaction mixture was diluted with 50 ml of water and extracted with benzene. The benzene solution was dried over anhydrous sodium carbonate and concentrated on a rotary evaporator. The crude product was analyzed on a silica gel plate, pretreated with triethylamine, using benzene as eluant. A blue spot of \(R_f = 0.54\) and a small yellow spot which did not move with solvent were found under UV light. However when a regular silica gel plate was used, a yellow spot, covered by a blue spot with \(R_f = 0.54\), and a big yellow spot which did not move with solvent were found under UV light. An attempt to obtain crystalline material by trituration with 5 ml of benzene and 40 ml of ligroin isolated only an amorphous

---

101. Using anhydrous magnesium sulfate as drying reagent caused decomposition of the benzene solution as indicated by the red color on the surface of magnesium sulfate.
substance which showed besides the expected molecular ion m/e = 282, also m/e = 312, 296, and 281 with highest intensity at m/e = 296. The nmr spectrum showed many peaks. No conclusion can be drawn from these spectral data.

**Attempted synthesis of 6-[o-methylthiomethyl]phenyl]-7H-benz[d,e]-anthracene-7-one, 39.**

To a o-(methylthiomethyl)phenyllithium solution prepared from 12.9 g (0.052 mole) of o-bromobenzyl methyl sulfide, 26 ml of 2.2 M butyl-lithium and 40 ml of ether at 0° was added a solution of 6.0 g (0.026 mole) of 7H-benz[d,e]anthracen-7-one in 50 ml of tetrahydrofuran. After stirring at 0° for 30 min then room temperature for 30 min, the reaction mixture was refluxed for 2 hr, hydrolyzed with dilute hydrochloric acid and worked up as usual to give 15.2 g of crude product which was chromatographed over 400 g of silica gel. The first fraction, obtained by using 2 l of benzene-petroleum ether (1:1), gave an oily mixture which after crystallization from ligroin yielded 50 mg of colorless needles, mp 233-235°. One recrystallization from benzene-ligroin raised the mp to 238-239°. The uv spectrum and mp agreed to that reported for naphtho[1,2,3,4-def]chrysene, 67-69. The mass spectrum showed a molecular ion, m/e = 302.

---

102. Obtained from Aldrich Chemical Company and recrystallized from chlorobenzene before use.
7-[o-(Methylthiomethyl)phenyl]-7H-benz[d,e]anthracen-7-ol, $\mathcal{T}_3$.

To 70 ml of 2.2 M n-butyllithium was added at 0°, a solution of 33.5 g (0.124 mole) of o-bromobenzyl methyl sulfide in 50 ml of dry ether during 40 min. After stirring at 0° for 1 hr, the reaction mixture was cooled to -60°. To this cold solution was added 16.5 g (0.072 mole) of benz[d,e]anthracen-7-one in portions. After stirring at -60 to -50° for 1.5 hr, the reaction mixture was poured onto dilute hydrochloric acid and worked up as usual. The crude product was crystallized from ether-ligroin to yield 15.4 g (59%) of yellow prisms of $\mathcal{T}_3$, mp 109-116°. An analytical sample (mp 114-116°) was obtained after recrystallization from benzene-ligroin; ir (KBr): 3350 cm$^{-1}$ (O-H); nmr (CDCl$_3$): 6 1.10 (s, 3, -SCH$_3$), 2.60 (s, 1, -O-H), 2.90 (s, 2, -CH$_2$-), and 7.11-8.60 (m, 14, Ar-H); mass spectrum, m/e = 368 (p).

Anal. Calcd for C$_{25}$H$_{20}$OS: C, 81.5; H, 5.5; S, 8.7.

Found: C, 81.6; H, 5.4; S, 8.7.

2-[o-(Methylthiomethyl)phenyl]tropone, $\mathcal{O}_b$.  

To a o-(methylthiomethyl)phenyllithium solution prepared from 60 ml of 2.2 M n-butyllithium, 28.5 g of o-bromobenzyl methyl sulfide and 50 ml of ether was added a solution of 4.0 g tropolone in 50 ml of ether during 10 min. The reaction mixture was stirred at room temperature for 4 hr, and hydrolyzed with dilute hydrochloric acid. After standing at room temperature overnight, 6.4 g of yellow solid, mp 96-110° w.dec.,

103. Heating of $\mathcal{T}_3$ in hot recrystallization solvent tended to decompose $\mathcal{T}_3$ indicated by appearance of green color.
was obtained after filtration. Since this yellow solid was not stable
toward heating, no attempt was made to purify it through recrystallization. The nmr and ir spectra indicated that the material might be
1-[c-(methylthiomethyl)phenyl]cycloheptatriene-1,7-diol, $\text{I}_4$; ir (KBr): 3500-3000 cm$^{-1}$ (O-H); nmr (CDCl$_3$): $\delta$ 1.92 (s, 3, -SCH$_3$), 2.55 (s, 2, 
-CH$_2$-), 6.63 (s, br, 2, -OH), and 7.00-8.80 (m, 9, -CH=CH- and Ar-H).

The yellow solid was dissolved in 100 ml of methylene chloride.
The methylene chloride solution was shaken with 30% sulfuric acid and
worked up as usual. The crude product was recrystallized from ethanol
to yield 2.7 g (35% from tropolone) of $\text{I}_b$, mp 84.5-85.5°; ir (KBr): 1626 (C=O), 1560 cm$^{-1}$ (C=C); nmr (CDCl$_3$): $\delta$ 1.92 (s, 3, -SCH$_3$), 3.57 (s, 2, 
-CH$_2$-), and 6.90-7.50 (m, 9, -CH=CH- and Ar-H).

**Anal. Calcd for C$_{15}$H$_{14}$OS:** C, 74.3; H, 5.8; S, 13.2.

**Found:** C, 74.2; H, 6.0; S, 13.2.

If the reaction mixture was hydrolyzed with dilute sulfuric acid,
it was difficult to isolate $\text{I}_b$ by crystallization.

**Dimethyl-[c-(2-troponyl)benzyl]sulfonium tetrafluoroborate, $\text{I}_c$.**

A mixture of 1.03 g of $\text{I}_b$, 10 g of methyl iodide, 827 mg of sil-
ver tetrafluoroborate, 10 ml of acetonitrile was stirred for 1 hr.
Silver iodide precipitate was filtered and washed with acetonitrile.
The acetonitrile solution was concentrated on rotary evaporator to give
a non-crystalline substance. All attempts to crystallize this material
failed; therefore, no elementary analysis was made. The nmr spectrum
of this material showed the absorptions of a sulfonium salt, $\delta$ 2.25
(s, 6, -S$^+$ (CH$_3$)$_2$) and 4.49 (s, 2, -CH$_2$-S$^+$).
Reaction of sodium methoxide with 40c.

To a solution of crude sulfonium salt, 40c, obtained above in 20 ml of methanol and 10 ml of acetonitrile was added a solution of 2.0 g sodium methoxide in 20 ml methanol. The mixture was stirred for 2 hr and worked up as usual to give 700 mg of crude product which showed many products by TLC. Attempted separation over silica gel to obtain pure substance failed.
BIBLIOGRAPHY


Cooke, R. G., Johnson, B. L., and Segal, W., ibid., 11, 231 (1958).


Dewar, M. J. S., ibid., 74, 3357 (1952).


Fieser, L. F. and Hershberg, E. B., ibid., 60, 2542 (1938).


Jones, R. N., ibid., 67, 2127 (1945).

Kasperek, G. J. and Bruice, T. C., ibid., 94, 198 (1972).

Kaubisch, N., Daly, J. W., and Jerina, D. M., Biochemistry, 11, 3080 (1972).


Koelsch, C. F. and Rosenwald, R. H., ibid., 2, 462 (1938).


Newman, M. S. and Blum, S., ibid., 86, 5508 (1964).


