I. SELECTIVITY IN THE CYCLIZATION OF γ-ARYLBUTYRIC ACIDS

II. CHROMIC ACID OXIDATION AT THE BENZYLIC POSITION

By

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PART I

SELECTIVITY IN THE CYCLIZATION OF γ-ARYLBUTYRIC ACIDS

CHAPTER I

INTRODUCTION AND HISTORICAL

After a convenient procedure for hydrogenating phenanthrene to 9,10-dihydrophenanthrene (1) using copper chromite catalyst was reported by Burger and Mosettig[1] and Durland and Adkins[2], this hydrocarbon was widely used in the synthesis of polynuclear aromatic hydrocarbons. A range of partly and fully aromatic hydrocarbons can be prepared using 1 as starting material. This is possible because of the difference in the cyclizing properties of the resulting arylbutyric acids 3 and 4. In addition, the available cyclizing agents provide variation in selectivity. A choice of selectivity is not the only advantage in using 1. Friedel-Crafts reactions involve exclusive attack[3] at the 2-position of 1 whereas in phenanthrene the majority of attack is at the 3-position with some reaction at the 2-position.

Burger and Mosettig[3] initially reported that "carbon side chains attached to position 2, when forming six- and five-membered rings, will be directed entirely or chiefly to position 3, while in the phenanthrene series analogous side chains are directed from position 2 to position 1". Their predictions were based on earlier reports by

Bachmann[4] and Hillemann[5] that 2-phenanthrylpropionic acid cyclized to the 1-position compared to 9,10-dihydrophenanthrylpropionic acid which mainly cyclized to the 3-position. Burger and Mosettig[3] cyclized acid chlorides in the presence of aluminum chloride whereas Bachmann used stannic chloride[4].

Later Fieser and Johnson[6,7] showed cyclization selectivities not reported by the earlier workers. While acid 3 cyclized to the expected benzanthracene derivative, the chrysenone product from acid 4 resulted from selection of the cyclizing agent. Treatment of acid 4 with anhydrous hydrogen fluoride gave only the benzanthracenone, whereas use of cold stannic chloride yielded mostly the chrysenone[8]. The reaction temperature plays a significant role, at least in the case of stannic chloride, since increase of temperature results in a decrease in selectivity. Temperature effects on the polyphosphoric acid cyclizations are discussed in later pages. These observations led Johnson[9] to discuss "The influence of method on direction of cyclization" in his review, "The formation of cyclic ketones by intramolecular acylation". Johnson[9] also reviewed certain interesting topics as "The size of the ring", "Influence of the reactivity of the aromatic nucleus", "Steric factors other than ring size", "Direction of ring closure" and "Methods of cyclization". The ease of ring closure decreased from six to five to seven-membered rings. If cyclization can take place in two

different ways to yield two rings of different sizes, the more stable ring is formed. Effect of substituents has been widely studied. While ring-activating groups facilitate the reaction, ring closures meta to a deactivating group (carbonyl or nitro) have been reported. p-Methoxyphenylbutyric acid was found to cyclize less readily compared to phenylbutyric acid. Examples of cases wherein the cyclizations were either sterically too hindered or directed away by a substituent are known. Johnson's review[9] also refers to selectivities in ring closure when both positions ortho to the acid side chain are open. In the benzene series, a substituent at the meta position usually directs the ring closure to the para position (i.e. away from the meta substituent). Isolation of minor amounts of the other isomer have been reported in some cases. In the naphthalene series, the acid side chain at the 2-position usually cyclizes to the angular ketone unless the 1-position is sterically hindered. 2-Naphthylbutyric acid has been used in this study and a discussion is included in the following chapter.

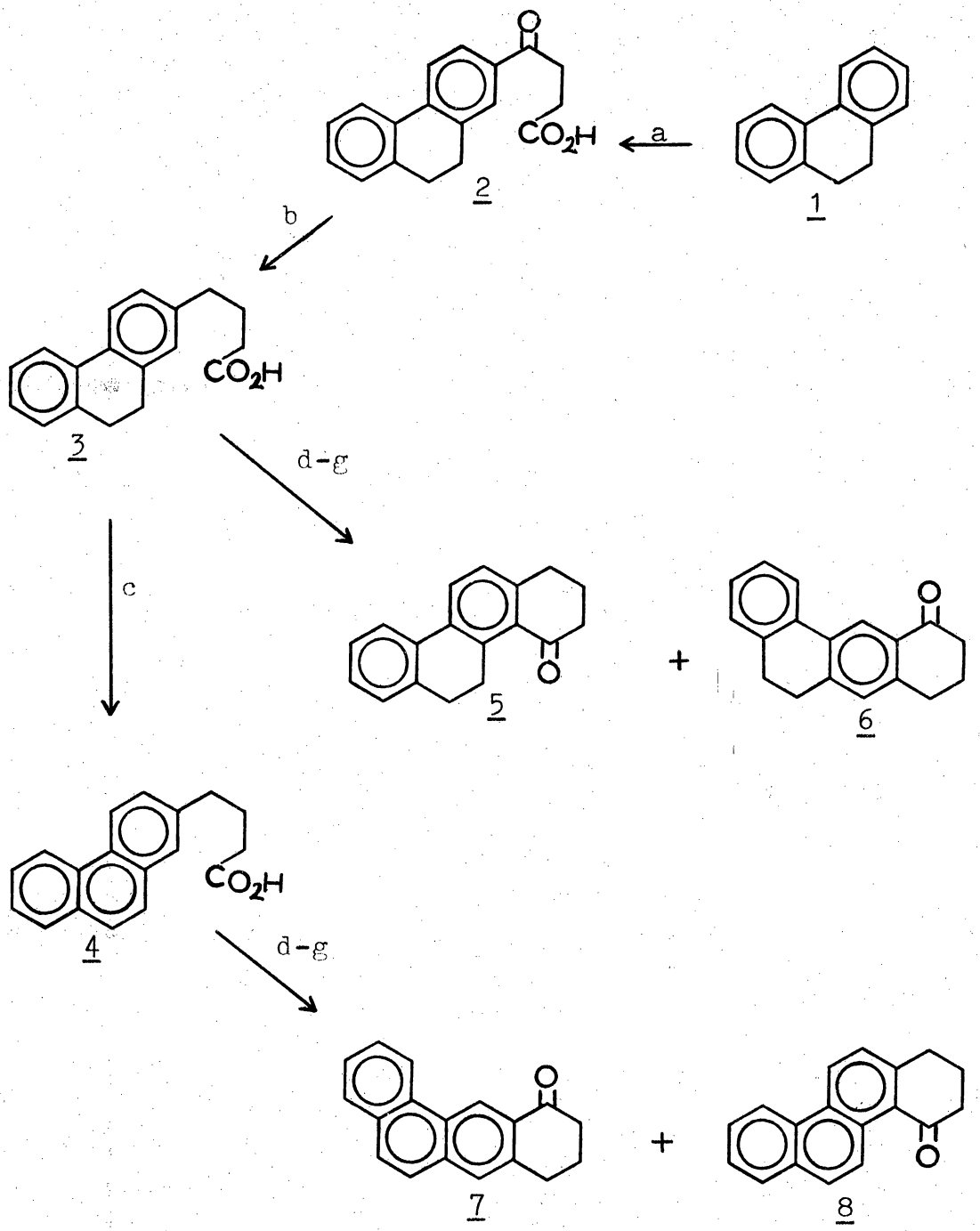
In the 1-naphthyl series, however, certain interesting results are available. The side chain can cyclize at the 2- and 8-positions giving a mixture or a single product. Three-carbon side chains and certain substituents promote the attack at the 8-position whereas four-carbon side chains are directed to the 2-position. For example, the ring closure of β-(1-naphthyl)propionic acid showed 6% at

the 2-position (five-membered ring) and 81% at the 8-position (six-membered ring). This compares with γ-(1-naphthyl)-butyric acid which exclusively cyclizes to the 2-position[9] (six-membered ring).

The conversion of γ-arylbutyric acids to cyclic ketones in general may be accomplished with several reagents and most of these give satisfactory yields. Of particular interest are those γ-arylbutyric acids which can cyclize in two different directions forming isomeric ketones. While the general cyclizing trend has been understood, adequate quantitative data to provide a clear picture of the ketone product ratios is not available.

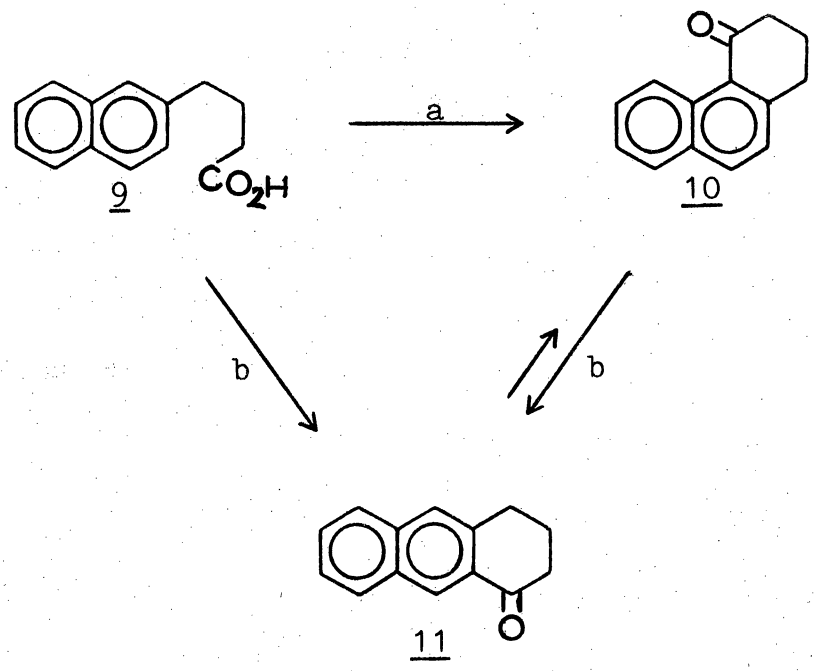
This study involves the reaction schemes represented in Figures 1 and 2, and the use of four common cyclizing agents- hydrogen fluoride, polyphosphoric acid (PPA), stannic chloride and zinc chloride. Sulfuric acid has been used on acids 3 and 4 to give the products shown in Figure 1 in 30-44% yields[3,6,7,10] but it was not included in this study.

The reactions of Figure 2 were investigated because they provide some insight into the temperature effects on polyphosphoric acid cyclization and the isomerization of the ketone 10 to 11. This reaction sequence has been studied by Agranat and Shih[11]. An investigation of selectivities in polyphosphoric acid cyclization which did not include isolation of individual products has been done by Patwardhan[12] using gas chromatography and NMR spectroscopy



[a]Succinic anhydride, $CH_3CH_2NO_2$, $AlCl_3$. [b]Zn(Hg), HCl. [c]Pd/C, xylene, Δ. [d]PPA, Δ. [e]$SOCl_2$; $SnCl_4$, benzene. [f]$ZnCl_2$, acetic acid. [g]HF.

Figure 1. Preparation of Acids 3 and 4 and Their Cyclization



[a]PPA, 110°C, 1 h. [b]PPA, 135°C, 4 h.

Figure 2. Preparation of Ketones 10 and 11

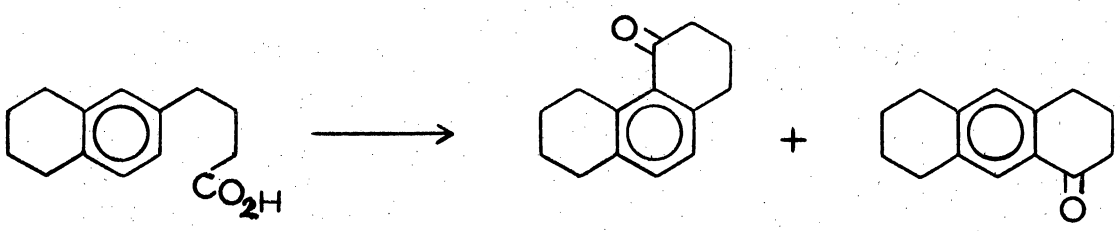


Figure 3. Cyclization of γ-(β-tetralyl)butyric Acid

for identification.

Several workers have studied the cyclization of γ-(β-tetralyl)butyric acid shown in Figure 3[12-16]. The major product has been reported to be the linear ketone though the ratio of the angular ketone was reported to increase to about 50% by using phosphorous pentachloride[15]. A 9:1 ratio in favor of the antular isomer was found when polyphosphoric acid was used[12]. Several other cyclizing agents (sulfuric acid and a mixture of phosphorus pentachloride and aluminum chloride as well as a mixture of phosphorus pentachloride and stannic chloride) have been used in this reaction[14]. A review of these reactions showing a range of product ratios are discussed in detail in the following chapter.

CHAPTER II

RESULTS AND DISCUSSION

β-[2-(9,10-Dihydrophenanthroyl)]propionic acid (2) was obtained in 77% yield by succinoylation of 9,10-dihydrophenanthrene (1), in nitroethane, in the presence of anhydrous aluminum chloride. As in earlier reports[3], acid 2 was free of product resulting from attack at the 3-position. Clemmensen reduction was found to be more satisfactory than the Wolff-Kishner procedure in removing the carbonyl oxygen to give acid 3. Dehydrogenation of 3 to 4 was readily accomplished in quantitative yields by heating in the presence of Pd/C in refluxing xylene. These reaction conditions are considerably milder and more convenient than those described by Fieser and Johnson[7] and Bachmann and Struve[8] who used sulfur and Pd/C respectively at temperatures around 240°C.

The cyclizations of 3 and 4 were carried out according to the procedures given in the next chapter. The crude mixtures of 5 and 6 were analysed on a 8-ft, 7% UC W-98 gas chromatographic column while the crude mixtures of 7 8 were analyzed on a liquid crystal column[16]. Ketones 6, 7 and 8 were separated and purified by Soxhlet extraction through neutral alumina followed by repeated recrystalli-

zations. Ketone 5 was preparatively separated from the enriched mother liquor of 6 using Waters Associates System 500 high pressure liquid chromatography (HPLC) equipment using two silica columns in series and dichloromethane solvent.

Ketone 7 was obtained as the only product with anhydrous hydrogen fluoride as the cyclizing agent whereas Ketone 8 was prepared as the major product (7:8;2:5) in the cyclization of the acid chloride of 4 in the presence of stannic chloride. Further purification of these compounds was accomplished by Soxhlet extraction and recrystallization as before. A mixture of 7 and 8 was difficultly separated during analysis using gas chromatography (UC W-98 column). However, a satisfactory separation was achieved with the liquid crystal column[16].

Numerous examples can be found in the literature describing the cyclization of aryl-substituted carboxylic acids. It is important to know the selectivity involved and whether the reaction will yield a mixture of isomeric ketones. Patwardhan[12] has studied polyphosphoric acid cyclizations of aryl-substituted propionic, butyric, and valeric acids wherein the aryl group was 6-tetralyl or 5-hydrindyl (Figure 4). While most of these reactions yielded mixtures rich in the linear isomer, β-(β-tetralyl)-propionic acid gave a 66% yield of the angular isomer. For the 6-tetralyl series, "as we go from the indanones to the tetralones and the benzosuberones, the amount of

angular ketone decreases consistently", while in the 5-hydrindyl series it is more gradual[12]. These results clearly illustrate the effect of the new ring size on the direction of cyclization in the presence of polyphosphoric acid. To an extent, the effect of the substituent attached to the aromatic ring (in this case rings of different sizes) is also illustrated. These cyclizations were carried out at 100°C compared to 110°C used in this study.

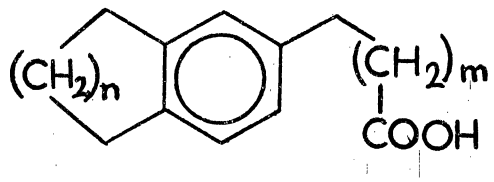


Figure 4. Aryl-Substituted Carboxylic Acids Studied with m=1,2,3; n=1,2.

Koo[17] has published certain guidelines for optimising reaction temperature in polyphosphoric acid cyclizations. Though these reactions are reasonably consistent over a temperature range, there is some selectivity associated with temperature as shown in Figure 2. It is interesting that polyphosphoric acid can cause the isomerization of 10 to 11 at 135°C while acid 9 gives mainly 10 during cyclization at 110°C[20]. The reaction at 135°C also

produced a number of side products, the major one being 1,2,3,4-tetrahydroanthracene. At this time we do not have a rationalization for its formation. In these studies, Agranat and Shih[11] claimed complete conversion of 10 to 11. There was no indication of side products. The present study, however, shows a ratio of 10:11 (1:4) when pure 10 is isomerized in the presence of polyphosphoric acid. Prolonged heating results in the increased formation of side products at the expense of the ketones. When pure 11 was subjected to the same conditions, a 12:1 ratio of 11 to 10 was observed in the product mixture.

While polyphosphoric acid showed less reaction selectivity in this investigation, the versatility and the ease of handling make it an ideal reagent for cyclization. If optimal reaction temperatures are used, high yields and clean products can be expected[17].

Stannic chloride is well established as a reagent for cyclization. Bachmann and Struve[8] reported their results on the cyclization of the acid chloride of 4 in the presence of stannic chloride. When the reaction was carried out in the cold, ketone 8 was formed as the major product. At room temperature, the reaction showed less selectivity. These findings vary from those reported by Fieser and Johnson[7] that ketone 7 was two-thirds of the product obtained in the intramolecular acylation of the acid chloride of 4 using stannic chloride and aluminum chloride. Our GC analysis of the product mixture showed a 2:5 ratio in

favor of 8 (the reaction was carried out at 0°C). However, these workers[7] made no mention of the reaction temperature which determines the product ratio. When acid chlorides of β-(2-phenanthryl)butyric acid[18] and β-(2-phenanthryl)propionic acid[19] were cyclized with aluminum chloride and stannic chloride respectively, exclusive (five-membered) ring closures at the 1-position was reported. These results compare with those of Patwardhan[12] who reported the formation of a greater proportion of the angular ketone when a five-membered ring is formed than a six-membered one.

Use of stannic chloride in cyclization usually required prior conversion of the acid to its acid chloride. Two reagents, phosphorus pentachloride and thionyl chloride, have commonly been used for this conversion. High cyclization yields[9] of the product ketones were reported. In some cases the free acids were used, but the yields were lower.

Zinc chloride was more selective than stannic chloride despite carrying out the reaction in boiling acetic acid. A similar result was reported by Fieser and Johnson[7]. Acid 4 was not converted to its acid chloride prior to cyclization with zinc chloride.

Hydrogen fluoride has become a popular cyclizing agent[9] since 1939. The method is simple and gives high yields. This reagent was found to be the most selective. The product from acid 3 or 4 showed only one isomer. There is practically no work-up involved in these reactions,

since the excess hydrogen fluoride can be easily evaporated using a gas stream or a steam bath leaving the crude product.

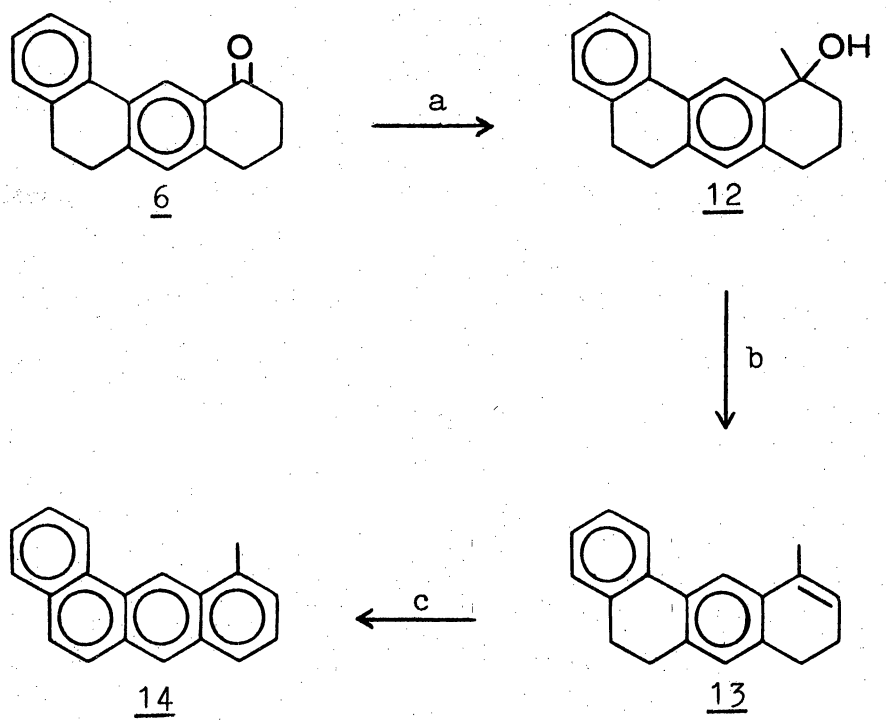
Rahman and coworkers[14] studied the cyclization of γ-(β-tetralyl)butyric acid (Figure 3) in the presence of three different reagents. With phosphorus pentachloride and stannic chloride mixture (0°C), the linear isomer predominated. When phosphorus pentachloride and aluminum chloride were used at 100°C, the angular ketone resulted as the major product. When the above reaction was carried out in the presence of sulfuric acid, some interesting selectivities were observed. At room temperature the linear ketone predominated while the angular isomer resulted after four hours of heating. The authors[14] pointed out: "Possibly, under the vigorous conditions of cyclization ketone VI isomerizes to VII". Considering the results of Agranat and Shih[11] and those obtained in this study on the isomerization of 10 to 11, this is reasonable. Several authors[12,13,15,21] have reported mixtures of varying proportions in the cyclization of γ-(β-tetralyl)butyric acid. The difference in the cyclizing properties of the above acid (Figure 3) and γ-(2-naphthyl)butyric acid (Figure 2) is remarkable. Figure 2 represents the naphthylbutyric acid undergoing ring closure to the linear isomer at high temperatures[11] (140°C) and the angular isomer at temperatures around 100°C[20]. The relation between the direction of cyclization and the temperature seems much less obvious

in meta-substituted phenylbutyric acids which cyclize mainly to the para-position[9].

The isomerization in ring systems caused by Lewis catalysts (aluminum chloride and boron trifluoride) has been studied by several authors[22-29]. However, very little information is available on the isomerization of cyclic ketones. This study[11] shows that polyphosphoric acid can cause ketone 10 to isomerize to 11 under vigorous conditions. Rahman and coworkers[14] believe that hot sulfuric acid can isomerize 3,4,5,6,7,8-hexahydro-1(2H)-anthracenone to its angular isomer.

Figure 5 shows the reaction scheme used by Fieser and Johnson[6] to obtain 11-methylbenz[a]anthracene from ketone 6. This scheme has been used as part of this investigation. Interestingly, our GC and LC analysis of the crude and pure samples of alkene 13 showed four different peaks, two of them major, in spite of the sharp melting point and a characteristic ^{1}H NMR spectrum. The ratio of the peaks was easily influenced by temperature, chromatography, etc., and our efforts to separate the peaks by liquid chromatography were unsuccessful.

Table I includes the data obtained on the cyclization of 3 and 4 in the presence of polyphosphoric acid, stannic chloride, zinc chloride and hydrogen fluoride.



[a]CH_3MgBr, ether; NH_4Cl. [b]Oxalic acid, toluene, Δ.

[c]Pd/C, methylnaphthalene, Δ.

Figure 5. Preparation of 11-Methylbenz[a]anthracene (14) from Ketone 6

TABLE I

CYCLIZATION OF γ-ARYLBUTYRIC ACIDS

γ-Arylbutyric Acid	Cyclizing Agent	Crude Product % Yield	Ratio 5:6
3	PPA	92	10:1
3	$SnCl_4$[a]	80	20:1
3	$ZnCl_2$[b]	96	9:1
3	HF	96	6 only
			Ratio 7:8
4	PPA	61	10:9
4	$SnCl_4$[a]	79	2:5
4	$ZnCl_2$[b]	68	1:10
4	HF	96	7 only

[a]With prior conversion to acid chloride.

[b]In acetic acid and acetic anhydride (3:2) at reflux.

CHAPTER III

EXPERIMENTAL

β-[2-(9,10-Dihydrophenanthroyl)]-propionic Acid (2)

Succinic anhydride (490 g, 4.6 mol) was added to a 12-L flask equipped with mechanical stirrer, inlet and outlet for nitrogen, thermocouple, and Gooch tubing for the addition of aluminum chloride. 9,10-Dihydrophenanthrene (1) (940g, 5.1 mol) was added to the flask along with 2120 mL of nitroethane. The mixture was stirred and the temperature was maintained at 5°C. Aluminum chloride was transferred in small amounts from a bottle attached to the Gooch tubing. The color of the mixture during $AlCl_3$ addition turned from yellow to greenish yellow to dark green. Hydrogen chloride was evolved continuously. The reaction was stopped after the addition of 1350 g of aluminum chloride. The mixture was then poured over ice and the flask was washed with conc. hydrochloric acid. A white solid separated which was filtered, washed with water, dissolved in ether, and the ether layer extracted with 10% sodium hydroxide solution. The aqueous layer was acidified to give a white crystalline solid which was

recrystallized twice from an acetone-water mixture to yield 988 g (77%) of 2, mp 159-160°C (lit.[3] mp 157.5-158.5°C); IR (KBr) 1690 (CO) (s), 1720 (COOH) (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.02-8.76 (m,4,Ar-H), 8.42-8.24 (m,3,Ar-H), 3.36 (t,2,Ar-CO-CH_2-), 2.94 (t,4,Ar-CH_2-CH_2-Ar), 2.86 (t,2,CH_2-COOH); MS m/z (rel intensity) M^+ 280(1), 262(100), 207(92), 179(34), 178(42), 55(27).

γ-[2-(9,10-Dihydrophenanthryl)]-butyric Acid (3)

Mossy zinc (660 g) was amalgamated using a solution of 34 g of mercuric chloride in 780 mL of water and 33 mL of conc. hydrochloric acid. The amalgam was added to a 12-L, two-necked flask containing 420 g (1.5 mol) of 2, 700 mL of water and 1150 mL of conc. hydrochloric acid. The mixture was heated to reflux while the excess hydrogen was led outside to bubble through water in a beaker. The reaction was carried out for a total of 46 h with five 165-mL additions of conc. hydrochloric acid at regular intervals. When the reaction was stopped, the methyl ester of the product showed only one GC peak. The mixture was allowed to cool, transferred to a 12-L separatory funnel and then extracted with ether. The ether extract was washed with water, dried ($MgSO_4$) and evaporated to obtain 400 g of crude 3 (quantitative yield based on the crude). The product was recrystallized from a toluene-isohexane mixture to give a pale yellow solid, mp 90-91°C (lit.[3] mp 92°C).

Impure samples of 3 recovered from the mother liquors were purified by esterification with methanol and vaccum-distilling in a Kugelrohr apparatus. Ir (KBr) 1695 (COOH) (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.78-7.60 (m,3,Ar-H), 7.37-7.00 (m,4,Ar-H), 2.83 (t,4,Ar-CH_2-CH_2-Ar), 2.67 (t,2,Ar-CH_2), 2.38 (t,2,CH_2-COOH), 1.97 (quintet,2,Ar-CH_2-CH_2-CH_2); MS m/z (rel intensity) M^+ 266(81), 206(50), 193(100), 178(30).

γ-(2-Phenanthryl)butyric Acid (4)

Acid 3 (10 g) and 1 g of 10% Pd/C were magnetically stirred in 100 mL of xylene in a 300-mL flask equipped with a condenser. The condenser was connected to a rubber tube which dipped in water in a beaker. This served as a bubble trap. The mixture was heated at reflux and hydrogen was observed to bubble out through the water. After hydrogen evolution ceased, the hot solution was filtered through Dicalite to remove catalyst. Concentration of the filtrate by means of a rotary evaporator gave a solid which was then recrystallized from a toluene-isohexane mixture to give 9.6 g (97%) of shiny white flakes: mp 135-136°C (lit.[7] mp 134-135.5°C); IR (KBr) 1705 (COOH) (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.70-8.52 (m,2,Ar-H), 7.92-7.20 (m,7,Ar-H), 2.87 (t,2,Ar-CH_2-), 2.40 (t,2,CH_2-COOH), 2.10 (quintet,2,Ar-CH_2-CH_2-CH_2); MS m/z (rel intensity) M^++1 265(72), M^+ 264(100), 204(56), 191(98), 189(88), 178(20), 165(22).

5,6,8,9-Tetrahydro-11(10H)-benz[a]-anthracenone (6)

Cyclization of Acid 3 with Polyphosphoric Acid

Polyphosphoric acid (350 mL) was heated in a 3-necked flask fitted with a mechanical stirrer and a thermometer, the third neck being open. When the temperature of the acid reached 95°C, 50 g of 3 was added in small amounts over a period of 20 min. The color changed from yellow to dark green to fluorescent dark green. The mixture was stirred for 2 h at 110°C. The cooled mixture was poured over 2500 g of ice to hydrolyze the polyphosphoric acid. The yellow solid which separated the filtered and dissolved in ether. The ether layer was washed with sodium bicarbonate solution (no unreacted acid was recovered from this) and then with water. The ether layer was filtered through Dicalite and anhydrous $MgSO_4$, the solvent was removed and the yellow solid was distilled in a Kugelrohr apparatus to give 43 g (92%) of a pale yellow oil which solidified on standing. The ratio of the isomers (by GC) in the crude material was 10:1 (6:5). The distilled material was recrystallized from benzene-isohexane to give large pale green crystals of 6, mp 95-97°C (lit.[6] mp 97-98°C).

Cyclization of Acid 3 with
Stannic Chloride

Acid 3 (1.0 g) was stirred in 15 mL of anhydrous ether contaning a drop of pyridine. To this was added 2 mL of thionyl chloride and the mixture was stirred for 30 min to give a clear solution. The ether and the thionyl chloride were evaporated under reduced pressure to yield a reddish solid. This solid was dissolved in about 20 mL of dry benzene, cooled in ice and 1.5 mL of stannic chloride was added under a nitrogen atmosphere over a period of 10 min. The reddish complex was decomposed with ice and dil. hydrochloric acid and then extracted with ether. The ether layer was washed with sodium bicarbonate solution, then water, dried ($MgSO_4$), filtered and concentrated to 0.75 g (80%) of brown crystals. The GC ratio was 10:1 (6:5).

Cyclization of Acid 3 with
Zinc Chloride

Acid 3 (1.0 g), 0.5 g of freshly fused zinc chloride, 10 mL of acetic acid and 2 mL of acetic anhydride were heated at reflux for 1 h. After cooling the dark brown mixture, water was slowly added until a semi-solid separated. The aqueous solution was decanted and the product was dissolved in ether. The ether solution was then washed with sodium bicarabonate solution and with water, dried ($MgSO_4$), filtered, and concentrated to 0.9 g (96%) of a brown solid. The GC ratio of 6:5 was 9:1.

Cyclization of Acid 3 with Anhydrous Hydrogen Fluoride

Hydrogen fluoride (150 mL) was condensed into a plastic bottle and then the acid 3 (10 g) was added in small quantities with constant shaking. The bottle was kept in an ice bath during the addition. When the addition was complete, the mixture was allowed to react for a few minutes and the excess hydrogen fluoride was evaporated (overnight) in a stream of nitrogen into a trap containing alkali. The crude product in benzene solution was washed with saturated potassium carbonate solution and water, and then dried ($MgSO_4$), filtered, and concentrated to 9.0 g (93%) of a pale green powder. GC analysis showed no detectable amount of ketone 5. This material was recrystallized from benzene-isohexane to give 6, mp 95.5-97.0°C; IR (KBr) 1680 (CO) (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.41 (s,1,Ar-H), 7.90-7.77 (m,1,Ar-H), 7.34-7.13 (m,3, Ar-H), 7.06 (s,1,Ar-H), 2.91 (t,2,Ar-CH_2), 2.84 (t,4, Ar-CH_2-CH_2-Ar), 2.64 (t,2,CO-CH_2), 2.10 (quintet,2,CO-CH_2-CH_2); MS m/z (rel intensity) M^++1 249(22), M^+ 248(100), 220(22), 192(42), 191(28).

1,2,5,6-Tetrahydro-4(3H)-chrysenone (5)

The mother liquor from the above recrystallizations was concentrated to a solid material richer in ketone 5. The mixture was separated using preparative liquid chroma-

tography with two silica columns in series and dichloromethane solvent. The fraction containing 5 was evaporated and the compound was further purified by recrystallization from 95% ethanol; mp 88-89°C; IR (KBr) 1675 (CO) (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.82 (d,2,Ar-H), 7.24 (s,4,Ar-H), 3.36 (t,2,Ar-CO-CH_2), 3.06-2.62 (m,6,all benzylic), 2.11 (quintet,2,Ar-CO-CH_2-CH_2); MS m/z (rel intensity) M^+ 248 (62), 247(30), 246(23), 237(19), 236(100), 230(17), 204 (21), 190(35), 189(23), 188(30). Anal. calcd for $C_{18}H_{16}O$: C, 87.10; H, 6.45. Found: C, 87.25; H, 6.30.

8,9-Dihydro-11(10H)-benz[a]anthracenone (7) and 1,2-Dihydro-4(3H)-chrysenone (8)

Cyclization of Acid 4 with Anhydrous Hydrogen Fluoride

The procedure for cyclization of 4 was similar to that used for the cyclization of acid 3. A GC analysis of the product (96% yield) showed no trace of the chrysenone 8. It was purified by recrystallization from benzene-isohexane, mp 118-119.5°C (lit.[7] mp 117-118°C); IR (KBr) 1680 (CO) (s), 1620 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.40 (s,1, Ar-H), 8.79 (d,1,Ar-H), 7.94-7.48 (m,6,Ar-H), 3.15 (t,2, Ar-CO-CH_2), 2.78 (t,2,Ar-CH_2), 2.21 (quintet,2,Ar-CO-CH_2-CH_2); MS m/z (rel intensity) M^+ 246(100), 218(34), 190(50), 189(47).

Cyclization of Acid 4 with Polyphosphoric Acid

Using the same procedure as before, a 61% yield of a mixture of ketones 7 and 8 (10:9) was obtained as shown by GC analysis.

Cyclization of the Acid Chloride of 4 with Stannic Chloride

Acid 4 (15.0 g) was first converted to the acid chloride using thionyl chloride and then cyclized in the presence of anhydrous stannic chloride using the procedure for cyclization of acid 3. After the work-up, 11.0 g of the crude product mixture (79% yield) was obtained. The ratio was 2:5 (7:8). The melting point increased from 115-123°C after five recrystallizations.

Cyclization of Acid 4 with Fused Zinc Chloride

Using the procedure adopted for acid 3, acid 4 was converted to a mixture of ketones 7 and 8 (1:10) in 81% yield. Purification of this material using Soxhlet extraction and recrystallization from methanol yielded pale green crystals, mp 124-126°C (lit.[7] mp 125-125.5°C); IR (KBr) 1660 (CO) (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.30 (d,1,Ar-H), 8.77 (d,1,Ar-H), 8.63 (quintet,1,Ar-H), 8.00-7.78(m, 2,Ar-H), 7.78-7.38 (m,3,Ar-H), 3.13 (t,2,Ar-CO-CH_2), 2.81

(t,2,Ar-CH_2), 2.18 (quintet,2,Ar-CO-CH_2-$\underline{CH_2}$); MS m/z (rel intensity) M^+ 246(100), 218(66), 190(69), 189(55).

11-Hydroxy-11-methyl-5,6,8,9,10,11-hexahydrobenz[a]anthracenone (12)

Methyl magnesium bromide (100 mL of 3M solution in ether) was stirred mechanically in a 3-necked, 250 mL flask fitted with a dropping funnel, condenser, nitrogen inlet and an outlet. The exit gases were bubbled through toluene in a beaker. A saturated solution of the ketone 6 (6.0 g) was slowly added from the dropping funnel over a period of 30 min. After addition, refluxing was continued for 5 h. The mixture became turbid during the second hour. The reaction complex was then decomposed by addition of a saturated solution of ammonium chloride and the product was extracted into ether. The ether layer was washed with water, dried ($MgSO_4$), filtered and concentrated to 5.2 g (81%) of a viscous oil. This product was subsequently extracted through alumina in a chromatographic column and used in the next reaction. IR (NaCl) 3340 (OH) (s) cm^{-1}.

11-Metyl-5,6,8,9-tetrahydrobenz[a]anthracene (13)

Alcohol 12 (5.2 g) was heated in refluxing toluene in the presence of a few crystals of oxalic acid using a Dean-Stark trap to collect water. Droplets of water con-

densed into the trap during the two hours of reaction. The cooled solution was extracted with sodium bicarbonate solution and then water. The toluene layer was dried ($MgSO_4$), filtered and concentrated to yield a yellowish oil which was extracted with isohexane through alumina in a Soxhlet column. A colorless oil (3.7g, 76% yield) was obtained which solidified as a pale green solid on standing. Repeated recrystallizations improved the mp from 59-63°C to 69.5-71.0°C. GC analysis of the crude and purified samples showed four peaks inspite of the sharp melting point. The ratios varied with each run, two of the peaks being major. Picrate formation followed by decomposition of the recrystallized picrate yielded a white crystalline material which still showed the four peaks. Preparative liquid chromatography was also unsuccessful in separating the peaks. This material was dehydrogenated in the following step. MS m/z (rel intensity) M^+ 246(100), 244(91).

11-Methylbenz[a]anthracene (14)

Alkene 13 (2.0 g) and 0.2 g of 10% Pd/C were heated in refluxing xylene for 18 h. The mixture was cooled, filtered through Dicalite to remove the catalyst and then concentrated with rotary evaporation. The crude product was extracted through alumina (Soxhlet extractor) using isohexane. This solution deposited 1.1 g of pale yellow

needles on cooling. The mother liquor was evaporated and the resulting oil was again refluxed with 0.1 g of 10% Pd/C in boiling methylnaphthalene for 20 h. Evaporation of the solvent yielded an additional 0.9 g of a brown material (quantitative yield based on the crude). This product was also recrystallized from isohexane to give 14, mp 116.5-117.0°C (lit.[6] mp 118.0-118.5°C); ^{1}H NMR ($CDCl_3$) δ 9.04 (s,1,Ar-H), 8.65 (q,1,Ar-H), 8.07 (s,1,Ar-H), 7.74-7.27 (m,8,Ar-H), 2.71 (s,3,Ar-CH_3); MS m/z (rel intensity) M^++1 243(20), M^+ 242(100).

1,2-Dihydro-4(3H)-phenanthrenone (10)

Acid 9 (5.0 g), prepared by succinoylation of tetralin followed by reduction of the carbonyl and dehydrogenation in the presence of Pd/C, was added slowly to 50 mL of polyphosphoric acid heated to 110°C. The mixture was stirred by means of a mechanical stirrer at constant temperature for 1 h. The hot, light brown reaction mixture was poured into 600 mL of water. The turbid mixture was then extracted with toluene, and the organic layer was washed with water, saturated sodium bicarbonate solution, then water. The toluene layer was dried ($MgSO_4$) and rotary evaporated to give an amber oil (4.8 g, quantitative yield based on the crude). GC analysis showed one impurity (<2%) in the crude mixture. The material was purified by recrystallization from isohexane to obtain white flakes, mp 66-67°C (lit.[11] mp 69°C); IR (KBr) 1670 (CO) (s) cm^{-1};

^{1}H NMR ($CDCl_3$) δ 9.37 (d,1,Ar-H on C-5), 7.90-7.21 (m,5, Ar-H), 3.08 (t,2,Ar-CO-$\underline{CH_2}$); 2.76 (t,2,Ar-$\underline{CH_2}$), 2.15 (quintet,2,Ar-CO-CH_2-$\underline{CH_2}$); MS m/z (rel intensity) M^++1 197 (18), M^+ 196(100), 168(23), 140(51).

3,4-Dihydro-1(2H)-anthracenone (11)

Isomerization of 10

Polyphosphoric acid (200 mL) was stirred mechanically in a 500-mL flask at 135°C. Ketone 10 (4.0 g) waa added slowly and the mixture was stirred for 4.5 h. The reaction mixture turned black during this period. The contents of the flask were poured into ice-water to obtain tar-like material which was filtered off. The crude product was then extracted through alumina (Soxhlet column) using isohexane. The extract was then concentrated and distilled in a Kugelrohr apparatus to yield 2.7 g (68%) of a crystalline solid. A red residue remained in the pot. GC analysis of the crude material prior to distillation showed ketones 10 and 11 (3:10) in addition to a minor impurity. Ketone 11 was successfully separated from the mixture by semicarbazone formation and subsequent hydrolysis of the first crop of the derivative. It was further purified by recrystallization from isohexane to obtain white flakes of 11; mp 92.0-92.5°C (lit.[11] mp 95°C); IR (KBr) 1690 (CO) (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.40 (d,1,Ar-H), 7.89-7.28 (m,5,Ar-H), 3.05 (t,2,Ar-CO-$\underline{CH_2}$); MS m/z (rel intensity) M^+ 196

(100), 168(44), 140(56), 139(30). Anal. calcd for $C_{14}H_{12}O$: C, 85.71; H, 6.12. Found: C, 85.57; H, 6.13.

Cyclization of 9 to 11

Acid 9 (3.0 g) was slowly added to 100 mL of polyphosphoric acid, stirred at 135-140°C by means of a mechanical stirrer, in a 250 mL round-bottomed, two-necked flask equipped with a thermometer. The mixture turned black while the stirring was continued for 4 h. The mixture was poured into 700 mL of water, stirred, cooled and then transferred to a 3-L separatory funnel. The product was extracted with ether and the ether layer was washed successively with water, sodium carbonate solution, and water. The ether layer was dried ($MgSO_4$) and concentrated to 2.2 g (81% yield) of tar-like material. GC analysis of this crude product showed a mixture of 10 and 11 (1:4).

Isomerization of 11 to 10

Ketone 11 (200 mg, 98% pure) was isomerized in 100 mL of polyphosphoric acid at 135°C using the procedure described for isomerization of 10. The crude mixture (147 mg, 76% yield) showed a ratio of 12:1 (11:10) by LC analysis (silica gel using dichloromethane).

PART II

CHROMIC ACID OXIDATION AT THE BENZYLIC POSITION

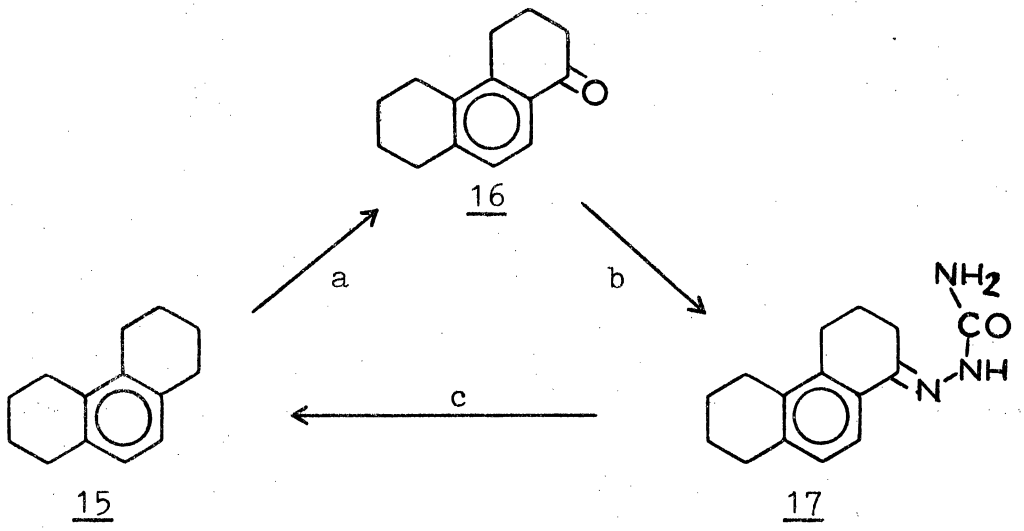
CHAPTER IV

INTRODUCTION AND HISTORICAL

Our interest in high purity 1,2,3,4,5,6,7,8-octahydrophenanthrene (15) and 1,2,3,4,5,6,7,8,9,10,11,12-dodecahydrotriphenylene (25) led us to investigate chromic acid oxidations as part of our purification effort. While 15 is commercially available, purification of this hydrocarbon posed serious problems. The main impurities were found to be 1,2,3,4,4a,9,10,10a-octahydrophenanthrene, 1,2,3,4-tetrahydrophenanthrene and a third unidentified compound, besides other partially saturated phenanthrenes. Though it was easy to eliminate the more aromatic impurities, two impurities could not be separated using spinning band distillation, column chromatography or preparative open-column liquid chromatography. Oxidation of the hydrocarbon to a ketone and processing the crystalline ketone was considered as an alternative. We were successful in obtaining pure samples of the ketone 16 which yielded the pure hydrocarbon by catalytic hydrogenation. However, the hydrocarbon needed careful handling and storage under argon in the cold since impurities were found to increase if the sample was exposed to air. We noted that Bushick[22] and Schneider[23] isomerized 15 to its anthracene analog while

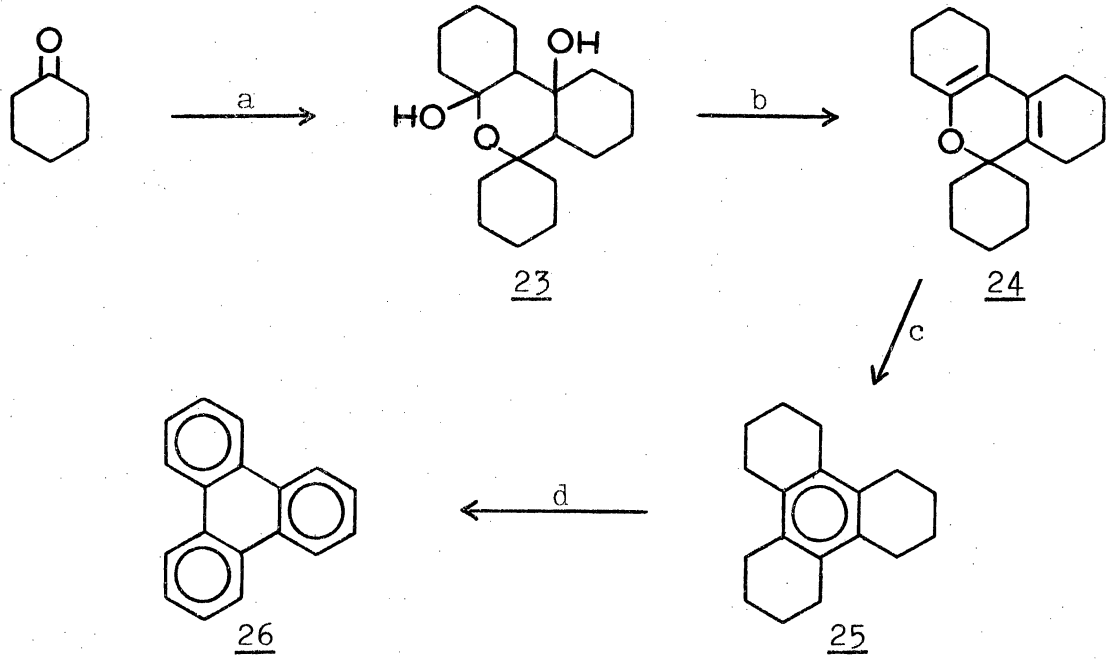
Shadmanov[30] isolated 1,2,3,4,4a,9,10,10a-octahydrophenanthrene as one of the products of condensation of 1,4-dichlorobutane with tetralin in the presence of aluminum chloride. The isomerization reaction has been described in the patent literature[23-29]. Known methods of preparation of 15 include catalytic hydrogenation of phenanthrene, isomerization of octahydroanthracene in the presence of HX and AlX_3 (or BF_3) followed by separation of the mixture[22-29], reaction of tetralin with 1,4 dichlorobutane in the presence of aluminum chloride[30,50], conversion of tetralin to a mixture of octahydrophenanthrene and octahydroanthracene in the presence of HX-AlX_3[23] or HF-BF_3[24,25,26], and Diels-Alder addition of maleic anhydride to 1,1'-dichlohexenyl followed by decarboxylation with P_2O_5 at 350°C[31].

Ketone 16, obtained by chromic acid oxidation of 15 as the major product, was purified by formation of the semicarbazone 17. This derivative exhibited greater stability than the hydrocarbon or the ketone. Ketone 18, which was obtained as a minor product in the above oxidation, was easily removed by the slow rate of semicarbazone formation. The high solubility of 18 in common organic solvents and its low melting point (40.0-40.5°C) were other factors helpful in the purification of 16. Figure 6 represents the scheme used for obtaining pure samples of 15. The other minor products of the oxidation, 19 and 20, were also removed easily.



[a]Chromic acid, acetic acid, 2 h. [b]$H_2NCONHNH_2.HCl$, CH_3COONa. [c]H_2, Pd/C, acetic acid.

Figure 6. Purification of 15



[a]NaOH, 72 h. [b]C_6H_5COCl, pyridine. [c]350°C. [d]Pd/C, 300°C.

Figure 7. Preparation of 25

The second compound used in this study was 1,2,3,4,-5,6,7,8,9,10,11,12-dodecahydrotriphenylene (25). It was prepared using the synthesis route shown in Figure 7. This route has been explored earlier by several workers[37-44] and the best yielding reagents[37] were used in this study with a few modifications. Direct conversion of cyclohexanone to 25 has also been reported[47] in low yields. Other methods of synthesis include reaction of 1,4-dichlorobutane with benzene or tetralin[48-53], action of heat on phenol[54], and reactioon of hexasubstituted benzenes with sulfuric acid[55]. This hydrocarbon was found to be very stable compared to 15. A series of common purification techniques including sublimation[56] were used to obtain very pure samples of 25. This compound was also dehydrogenated in the presence of Pd/C to pure triphenylene 26.

Two other compounds were subjected to benzylic oxidation: 6-nitro-1,2,3,4-tetrahydronaphthalene (31) and 5-nitro-1,2,3,4-tetrahydronaphthalene (36). These were obtained commercially.

In earlier studies on the benzylic oxidation of substituted tetralins in our laboratory, Burnham, Duncan and Eisenbraun[57,58] used chromic acid and evolved an optimized procedure. This was satisfactory for low molecular weight and unhindered hydrocarbons but needed some modification of reaction time and temperature for hindered and electronically less favored ones. A majority of the oxidations

done in this latter study required more vigorous conditions. The conversion of the monoketones to the diketones was more difficult than preparing monoketones from the hydrocarbon except in the case of 25 which was also slow to react. The nitrotetralins were as difficult to oxidize as the monoketones from the other hydrocarbons.

The results published by the above authors[57,58] offer ample evidence for electronic and steric factors operating in oxidation at the benzylic positions. When there are at least two different benzylic positions available, the ketone isomer ratio is determined by the steric factor and also by the nature of the substituent attached to the aromatic ring. In the case of alkyl-substituted tetralins, a definite activating influence was observed when the alkyl group was suitably placed on the aromatic ring (6-methyltetralin, for example). However, if the alkyl group hinders one of the benzylic positions (as in 5-methyltetralin), the amount of the electronically favored product decreases.

The selective influence of steric and electronic factors on the ratio of products resulting from chromic acid oxidation at the benzylic position can be used in the synthesis of certain interesting ketones. Chromic acid oxidation has been used occasionally by chemists as a means of preparing benzylic ketones. The disadvantages are low to fair yields and lack of clean products. When there are two or more different benzylic positions

available in the hydrocarbon, the reaction usually produces a mixture of isomeric ketones. It is possible to predict the major product, but it is not easy to predict the ratio. However, if separation techniques can be worked out, chromic acid oxidation can be an asset to the formation of otherwise less accessible benzylic ketones[12-15,21,32-36,57,58].

The current availability of HPLC and the conventional semicarbazone reaction made it possible to separate and isolate several of the ketone products from chromic acid oxidations. As early as 1924, Schroeter[59] reported the isolation of ketones 16 and 18 from the oxidation of 15 using chromic acid. This author was unable to provide an exact ketone ratio, since the isomers were separated by their different rates of semicarbazone formation and subsequent hydrolysis of the individual semicarbazones. The current study resulted in the isolation of the diketones 19 and 20 using preparative liquid chromatography. With the advent of newer and more efficient separation techniques, the use of chromic acid in oxidation should increase.

CHAPTER V

RESULTS AND DISCUSSION

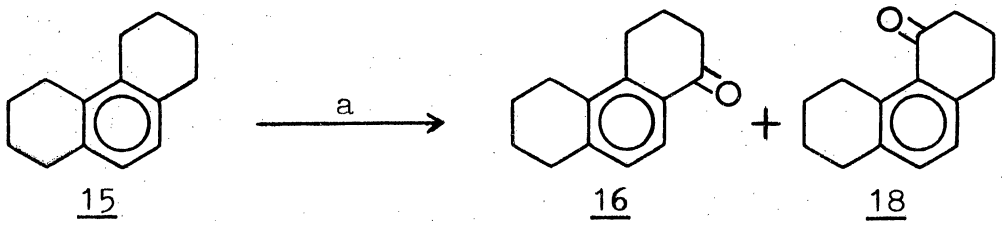
Two partially saturated aromatic hydrocarbons and two nitro-substituted tetralins were used in this study of oxidation at the benzylic position. The hydrocarbons, 1,2,3,4,5,6,7,8-octahydrophenanthrene (15) and 1,2,3,4,5,-6,7,8,9,10,11,12-dodecahydrotriphenylene (25), differed in their steric hindrance to oxidation. The nitro-tetralins (31 and 36) were included because the nitro groups were expected to exert an electronic influence. While 31 was expected to show only an electronically deactivating effect of the nitro group, 36 seemed to experience the steric as well as the electronic effects of the nitro substituent favoring the formation of the expected isomer. The nitrotetralins also provided a comparison to results published from our laboratory[57,58] on the oxidation of several alkyl-substituted tetralins. The monoketones obtained from 15 and 25 were further oxidized to the corresponding diketones and some of these diketones were isolated and identified. Oxidation of 16, 18 and 27 to the diketone stage offered an interesting study of the extent of steric and electronic factors governing the product ratio. For example, the formation of the major

product from oxidation of monoketone 27 was controlled by the electronic influence of the carbonyl group, since all but one of the available benzylic positions are sterically equivalent. It should also be recognized that two of these benzylic positions are identical in that their oxidation leads to the same product. In 16, the electronically favored benzylic position was sterically most hindered while in 18 the position was sterically least hindered. In other words, a comparison of the diketone ratios from 16 and 18 would reflect only the steric influence on oxidation, since the electronic factor is the same.

For this study, it is necessary to obtain pure starting materials. Though all the compounds used as starting materials in this investigation were commercially available, they contained several impurities. In particular, 15 was found to have impurities which could not be removed using the usual techniques. Figure 6 shows the scheme used to purify 15. Large amounts of commercial 15 were oxidized at room temperature to ketone 16 as the major product. This crystalline compound was purified and then converted to its semicarbazone (17). Either 16 or 17 in pure state yielded pure hydrocarbon upon catalytic hydrogenation. Storage of 15 also needed special conditions as described in the earlier chapter.

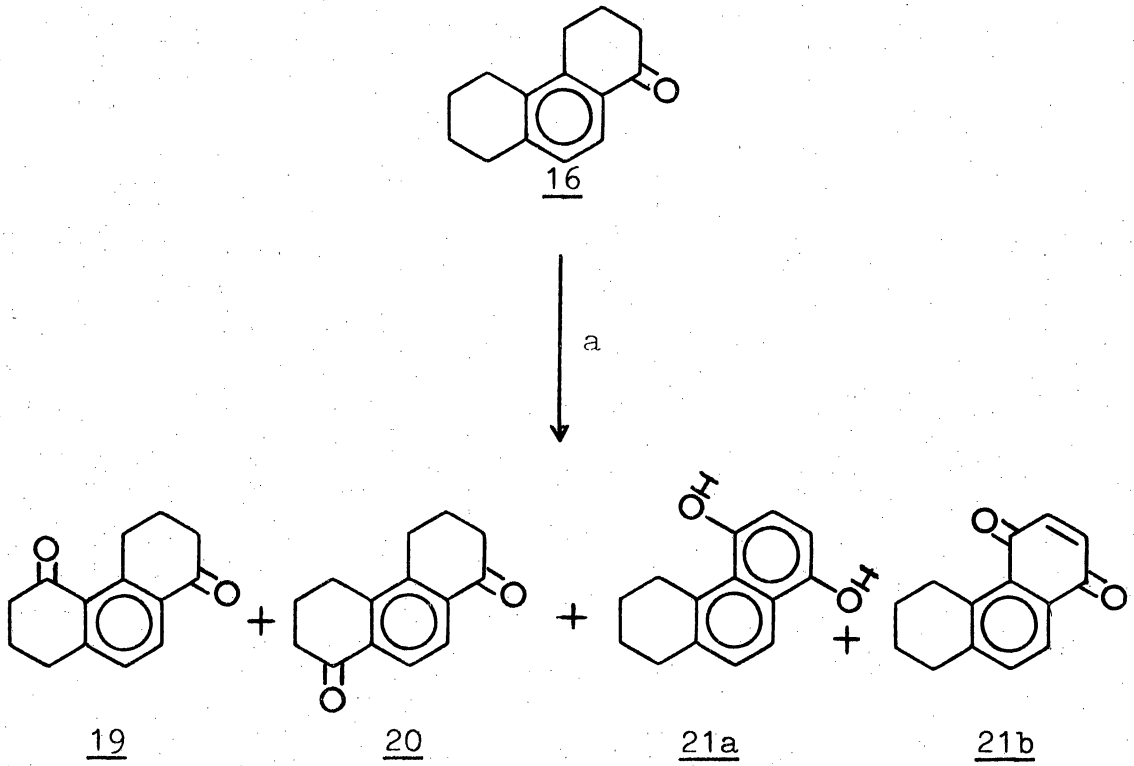
Oxidation of 15 offered the most interesting range of compounds. This liquid hydrocarbon was highly soluble

in organic solvents, especially acetic acid. The compound is sterically less hindered compared to 25. These factors make it possible to easily oxidize the compound at room temperature to monoketones 16 and 18 (5:1) (Figure 8). Ketones 16 and 18 were obtained pure from this mixture. Each of these, when oxidized further, were expected to yield two different diketones, a diphenol and possibly a quinone (Figures 9 and 10). One of the diketones and the diphenol were common products from 16 and 18. Oxidation of 16 yielded two diketones but no quinone or phenolic materials were found. When a 50% excess of chromic acid was used, the reaction gave two diketones and some starting material after one hour, and two diketones and a third minor neutral product after two hours. The two diketones, 19 and 20, were formed in the ratio 4:1. The identities of these compounds were verified using ^{13}C NMR spectroscopy after a successful separation was achieved using preparative liquid chromatography. Ketone 18 also yielded two diketones when oxidized. One of these, the major product, was 19 obtained from 16 (according to GC analysis) while the minor product was assigned to 22. The ratio of these isomers in the crude oxidation product was 9:1 (19:22). Ketones 16, 18 and 27 (Figure 11) have been cited in the literature often but most workers[12-15,21,32-36] have used long synthesis routes instead of chromic acid oxidation[59,60] to obtain these ketones.



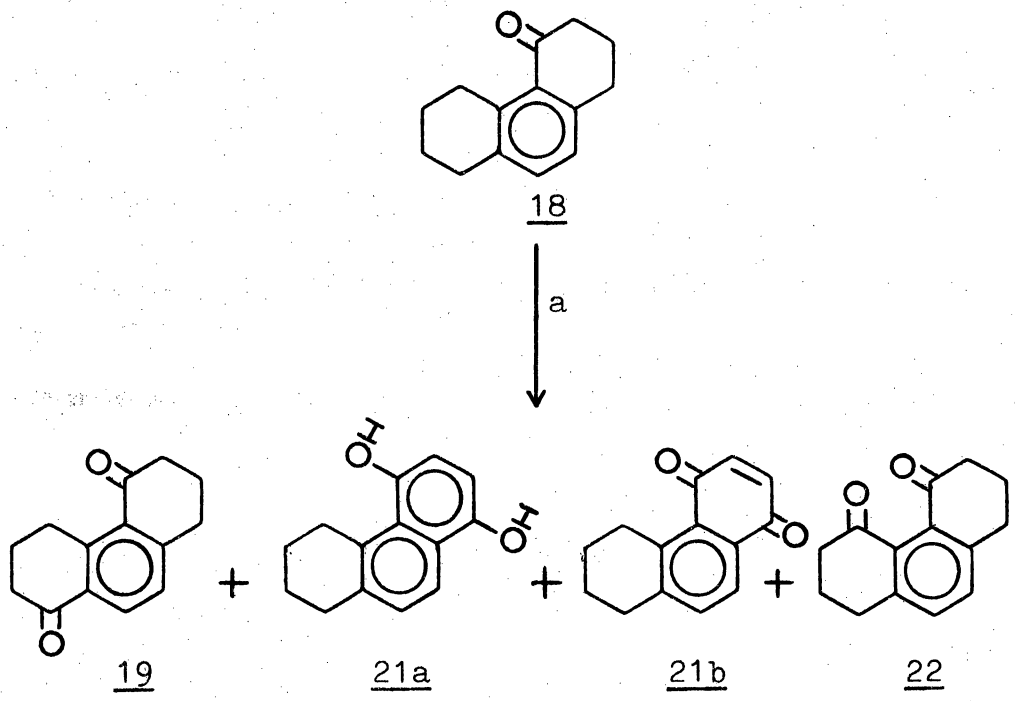
[a]Chromic acid, acetic acid, 2 h.

Figure 8. Oxidation of 15 to the Monoketones 16 and 18



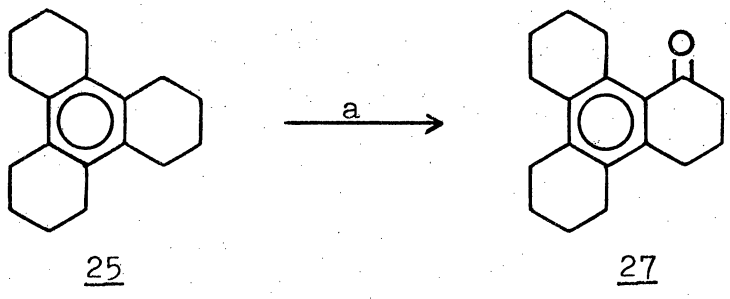
[a]chromic acid, acetic acid, 2 h, Δ.

Figure 9. Expected Products from Oxidation of 16



[a]Chromic acid, acetic acid, 2 h, Δ.

Figure 10. Expected Products from Oxidation of 18



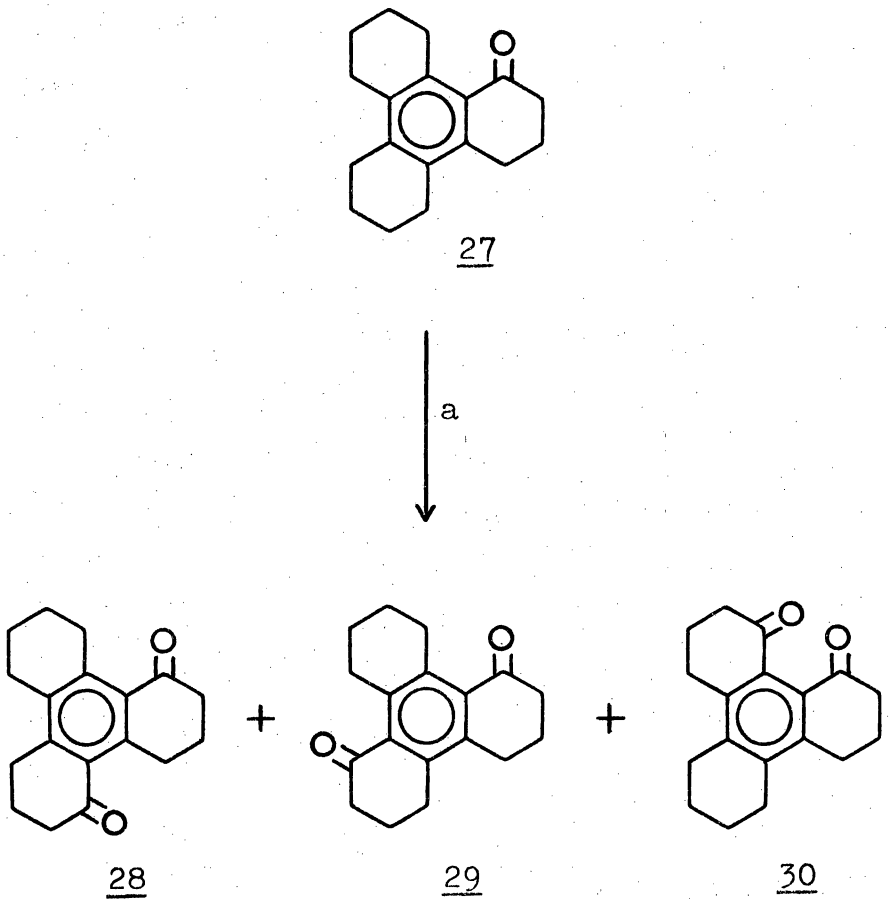
[a]Chromic acid, acetic acid, 6 h, Δ.

Figure 11. Oxidation of 25 to the Monoketone 27

It is of interest that oxidation of 16 produces 19 and 20 (4:1) whereas oxidation of 18 produces 19 and 22 (9:1). These results clearly show that absence of steric hindrance causes an increase in the formation of the electronically favored product. The increase, however, is less significant when the electronic effect is considered in the absence of steric effect as in the oxidation of 27 (Figure 12). This monoketone has sterically equivalent benzylic positions available for further oxidation. The crude product showed one major diketone (identified as 28 using ^{13}C NMR spectroscopy) and traces of two other products. This shows that the electronic influence is strong enough to provide considerable selectivity, at least in the oxidation of 27 to 28.

Schroeter[59] was the earliest to report a synthesis of 16 by the oxidation of 15 using chromic acid. This author also synthesised 16 by the cyclization of γ-(α-tetralyl)butyric acid and confirmed the structure of the major product in the above oxidation. Ketones 16 and 18 were separated using the difference in the rates of semicarbazone formation. Schroeter reported about 90-95% of 16 and the remainder as 18 in the crude mixture. The present study showed a ratio of 5:1 (16:18).

The synthesis of 25 from cyclohexanone has been described[37-46] and we were able to use this synthesis to prepare very pure hydrocarbon as shown in Figure 7. The preparation of ketone 27 required the strongest conditions



27

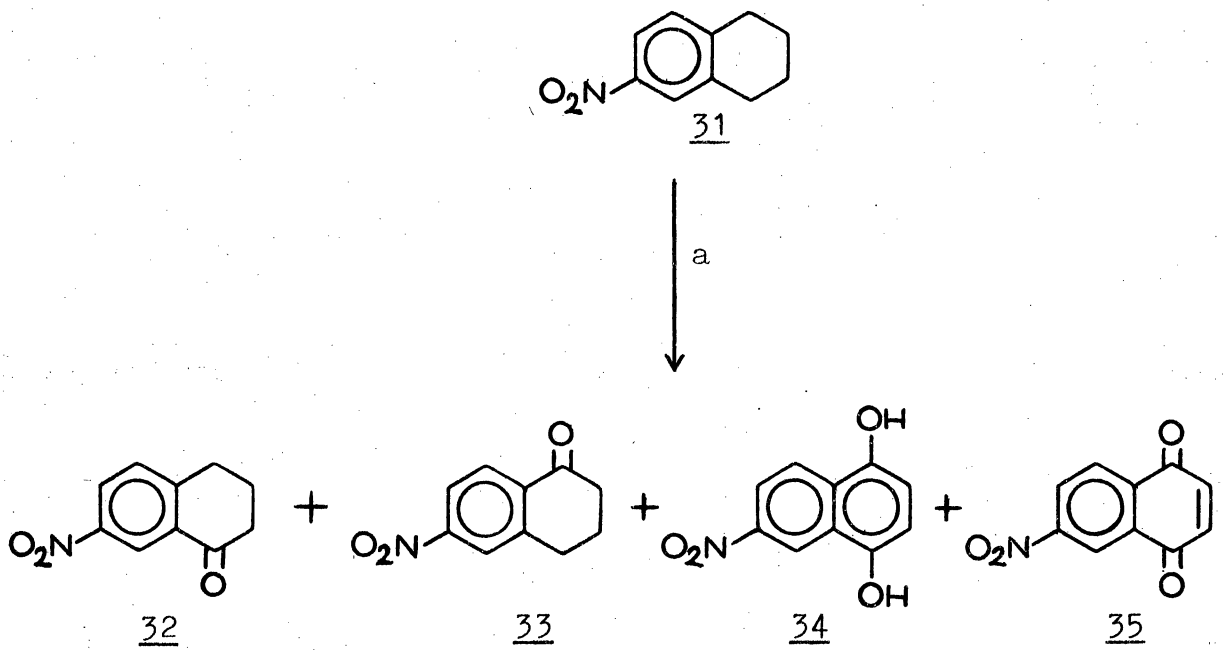
28 29 30

[a]Chromic acid, acetic acid, 6 h, Δ.

Figure 12. Expected Diketones from Oxidation of 27

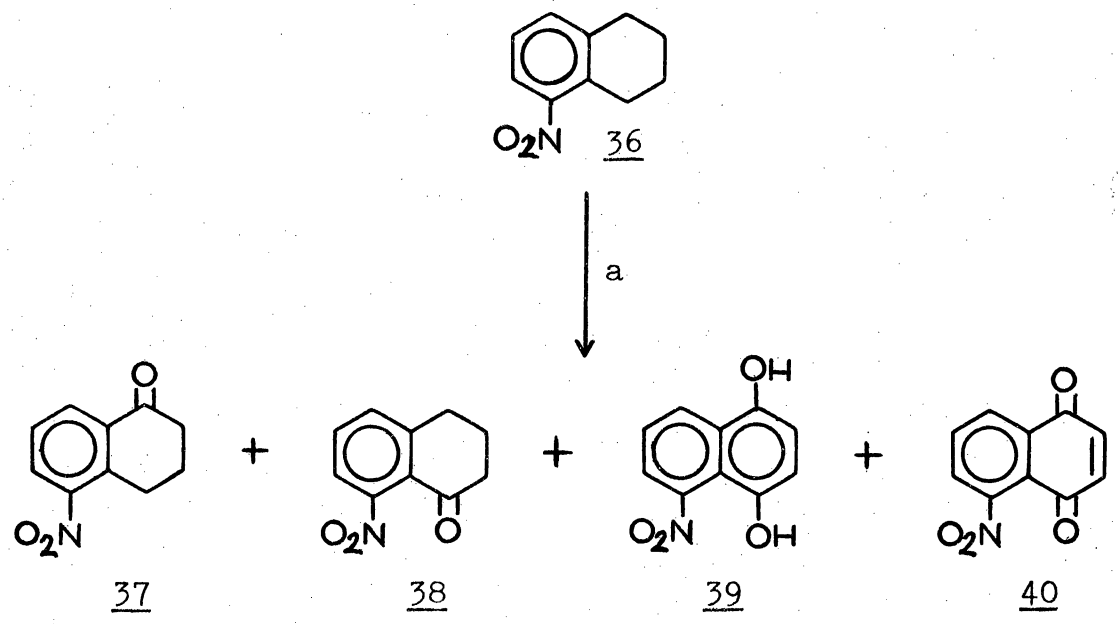
for oxidation[60]. Part of the starting material remained and the reaction usually produced a mixture of the monoketone 27 and the diketone 28. The relative amounts of 27 and 28 were controlled by the amount of chromic acid used and the reaction time. Unlike octahydrophenanthrene (15), hydrocarbon 25, as shown by GC, yielded one diketone (28) as the major product. Traces of two other compounds detected in the product mixture were assigned to the symmetrical diketones 29 and 30 which were not isolated. The structure of diketone 28 was confirmed by observing 18 peaks in the ^{13}C NMR spectrum. Diketones 29 and 30 are symmetrical and would show 9 peaks in the ^{13}C NMR spectrum. The crude mixture containing 25, 27 and 28 was conveniently separated using two silica columns and dichloromethane in preparative liquid chromatography to isolate 27 and 28.

The nitrotetralins (Figures 13 and 14) provided an extension of oxidation studies carried out in this laboratory. The procedure[58], involving two hours of stirring the oxidation mixture at 20°C, which was adequate for the more reactive alkyl-substituted tetralins, was found to be too mild for 31 and 36. However, these compounds were conveniently oxidized under the conditions used for 16, 18 and 25. While 31 and 36 differed sterically, the product ratios showed interesting results. Oxidation of 31 produced two ketones in the ratio 1.1:1, but the major product was not the one predicted on the basis of electro-



[a]Chromic acid, acetic acid, 2 h, Δ.

Figure 13. Expected Products from Oxidation of 31



[a]Chromic acid, acetic acid, 2 h, Δ.

Figure 14. Expected Products from Oxidation of 36

nic factors. This was realized when the product mixture was matched against a standard of commercially available 7-nitro-3,4-dihydro-1(2H)-naphthalenone (32). Possibly there is preferential destruction of ketone 32 to account for the preponderence of ketone 31.

When 36 was oxidized, two ketones in the ratio 4.3:1 were obtained. In the absence of standards, the major product was assigned to 37 and the minor one to 38.

Table II lists the results obtained from the oxidation studies discussed in this chapter.

TABLE II

PRODUCT RATIOS IN BENZYLIC OXIDATIONS

Compound Oxidized	Products
15	16:18 (5:1)
16	19:20 (4:1)
18	19:22 (9:1)
25	27
27	28:29:30 (25:1:2)
31	32:33 (1:1.1)
36	37:38 (4.3:1)

CHAPTER VI

EXPERIMENTAL

Purification of Commercial 1,2,3,4,5,6,-7,8-Octahydrophenanthrene (15)

A solution of chromium trioxide (160 g, 1.6 mol) in 160 mL of water was added to a well-stirred solution of 15 (160 g, 0.86 mol) in 8 L of acetic acid. The temperature of the mixture was maintained at 20°C using a water bath during the addition. When the temperature stabilized, the water bath was removed and the mixture was stirred for another 2 h. At the end of the reaction, the acetic acid was removed using a rotary evaporator. The residue was diluted with about 6 L of water and extracted with ether. The extract was washed with water, dried ($MgSO_4$) and evaporated to 145 g (84%) of a partly crystalline dark brown material (about a fourth of this was found to be unreacted 15 by GC) which was boiled with 1 L of isohexane and cooled. The unreacted hydrocarbon and part of the ketone products stayed in the mother liquor while ketone 16 was deposited as yellow crystals. This material was distilled in a Kugelrohr apparatus to obtain a pale yellow crystalline solid which was extracted through

neutral alumina in a Soxhlet column using isohexane. This gave shiny colorless crystals of 16 which showed one impurity on the GC. Liquid chromatographic analysis using UV detector showed traces of two other impurities. At this stage, ketone 16 was converted to its semicarbazone (17). This derivative was found to be extremely insoluble in common organic solvents and partly soluble in pyridine. The material was leached successively with hot 2-propanol twice and hot toluene twice and extracted with isohexane in a Soxhlet column. A part of the semicarbazone sample was then hydrolyzed to the ketone by partitioning it between 20% hydrochloric acid and ether. The ether layer was washed with water, dried ($MgSO_4$) and concentrated to obtain colorless crystals of 16 which showed some impurities by LC analysis. Recrystallization from 2-propanol followed by catalytic hydrogenation yielded 15 which showed one impurity on the GC. Direct hydrogenation of 17 yielded 15 which, after elution through silica gel in a chromatography column using isohexane, was found to have one impurity. Hydrogenation of the 2,4-dinitrophenylhydrazone of 16 gave a pure sample of 15: ^{1}H NMR ($CDCl_3$) δ 6.81 (s,2,Ar-H), 2.72 (t,4,CH_2 at C-4 and C-5), 2.55 (t,4, CH_2 at C-1 and C-8), 1.78 (m,8,CH_2 at C-2, C-3, C-6 and C-7); MS m/z (rel intensity) M^+ 186(100), 158(64), 145(33), 143(24), 129(24).

Aldol-Condensation of Cyclohexanone: Preparation of 6-Spirocyclohexane-4a,10a-dihydroxy-perhydrodibenzo-[b,d]pyran (23)

Distilled cyclohexanone (850 g) was placed in a 2-L, round-bottomed flask fitted with a mechanical stirrer. Sodium hydroxide flakes (85 g) were added and the mixture was stirred for 72 h. During this time the mixture turned from colorless to yellow to white with the formation of a solid white product. When the reaction was stopped, the mixture was poured over 2 Kg of ice and then stirred. The product (300 g, 35% yield) was filtered off. The filtrate containing unreacted cyclohexanone was extracted with isohexane and the organic layer was washed with water and dried ($MgSO_4$) and filtered. Evaporation of the solvent yielded about 400 g of unreacted cyclohexanone. Repetition of the experiment in a nitrogen atmosphere caused no significant increase in the yield. A cleaner product was obtained when the reaction mixture was diluted with ethanol and water and then filtered. The recovery of the unreacted cyclohexanone, however, was more difficult in this case. The crude product (mp 175-188°C) was recrystallized from 2-propanol to give colorless crystals of 23; mp 181-185°C (lit.[37] mp 175°C; lit.[39] mp 210°C); IR (KBr) 3220 (OH) (s) cm^{-1}; MS m/z (rel intensity) M^+ 294(3),

258(64), 215(100), 131(68), 77(88), 55(78).

Dehydration of 23 to 6-Spirocyclohexane-1,2,3,4,7,8,9,10-octahydrodibenzo[b,d]pyran (24)

Using Benzoyl Chloride

The cyclohexanone trimer 23 (50 g) was dissolved in 500 mL of pyridine in a 1-L, round-bottomed flask. Benzoyl chloride (50 mL) was added and the mixture was stirred at 80°C for 1 h using a magnetic stirrer. The clear brown solution was cooled and then poured into 1 L of water and the solution acidified with conc. hydrochloric acid. The product was then extracted three times with benzene and the combined benzene extracts were washed with sodium bicarbonate solution and then with water. After drying ($MgSO_4$) and filtering the solvent was evaporated to a brown oil (44 g, theoretical yield).

Using p-Toluenesulfonyl Chloride

Trimer 23 (50 g), p-toluenesulfonyl chloride (35 g) and pyridine (300 mL) were added to a 500-mL, round-bottomed flask fitted with a Vigreux column. The mixture was heated to 80°C and stirred at that temperature for 30 min. The solution was then cooled and poured into 500 mL of water and acidified with hydrochloric acid. The product was extracted three times with benzene and the

combined extract was washed successively with water, sodium bicarbonate solution and water. The organic layer was dried ($MgSO_4$) and filtered through Dicalite. It was concentrated to a dark brown oil. The yield was not calculated, but the material was subsequently converted to dodecahydrotriphenylene (25) in 90% overall yield based on 23.

Using Amberlyst-15

Trimer 23 (5.0 g), Amberlyst-15 (2.0 g) and toluene (100 mL) were mixed in a 200-mL round-bottomed flask equipped with a Dean-Stark trap. The solution was refluxed for 1 h until no more water condensed in the trap. At the end of the reaction, the solution was filtered and the solvent evaporated to obtain 4.4 g (theoretical yield) of 24. GC analysis showed a trace (1%) of dodecahydrotriphenylene (25) in the product.

Preparation of 1,2,3,4,5,6,7,8,9,10,11,-12-Dodecahydrotriphenylene (25)

A 44-g sample of 24 (prepared using benzoyl chloride as above) was heated in a fused salt bath of KNO_2:$NaNO_2$ (10:7) at 350°C under nitrogen for 90 min. A Vigreux column was attached to the flask containing the reaction mixture. Droplets of water condensed on the sides as the reaction proceeded. At the end, the flask was cooled to room temperature and the brown mass obtained was washed with methanol to remove any unreacted starting material

and the residue was filtered off. The residue was again passed through neutral alumina in a Soxhlet column using isohexane solvent to obtain 36.5 g (89% yield) of white crystalline 25; mp 228-230°C (lit.[37] mp 232°C; lit.[39] mp 236°C); ^{1}H NMR ($CDCl_3$) δ 2.57 (m,all benzylic protons) and 1.77 (m,allnon-benzylic protons); MS m/z (rel intensity) M^+ 240(100), 212(33), 211(24), 199(30), 198(35), 183(26).

Purification of 25

The crude 25 was passed through alumina as mentioned earlier. Following this, the material was recrystallized three times from benzene-isohexane. This procedure removed traces of oily impurities resulting from the pyrolysis. Some amount of solvent was retained in the crystals even after extensive pumping. The compound was found to be devoid of detectable impurities, by GC, at this stage. A final sublimation procedure[56] was adopted in order to remove the solvent and to improve the purity of the compound. When the major portion of the compound had sublimed, the material was scraped out and sealed in oven-baked, pre-weighed vials. Combustion calorimetry by the Energy Relations Research Group at the Bartlesville ERDA station showed 25 to be 99.987% pure.

Conversion of 25 to Triphenylene (26)

A mixture of 25 (15 g) and 10% Pd/C (1.5 g) were heated using a fused salt bath in a round-bottomed flask

attached to a bubble tube dipped in a beaker of water. Hydrogen gas started bubbling out when the temperature reached 300°C. The flask was heated at this temperature for 2 h until nomore hydrogen evolved. The flask was cooled and the hard residue was dissolved in benzene. The catalyst was removed by filtering the solution through Dicalite. Evaporation of the solvent gave a quantitative yield of 26. Two intermediate compounds were observed by GC, but the reaction always yielded a mixture of products which were finally converted to 26. The crude material was purified by Soxhlet extraction through alumina, recrystallization from benzene-isohexane, picrate formation followed by decomposition of the recrystallized picrate, and finally, sublimation to give mp 195-197°C (lit.[47] mp 199°C); ^{1}H NMR ($CDCl_3$) δ 8.54-8.74 (m,6,protons on C-2, C-3, C-6, C-7, C-10, C-11), 7.54-7.74 (m,6,protons on C-1, C-4, C-5, C-8, C-9, C-12); MS m/z (rel intensity) M^++1 229(21), M^+ 228(100), 227(11), 114(11), 113(13), 112(11).

Oxidation of 1,2,3,4,5,6,7,8-Octahydrophenanthrene (15)

Purified 15 (1.3 g) was dissolved in 160 mL of glacial acetic acid in a 500-mL Erlenmeyer flask, stirred with a magnetic stirrer at 17-21°C by using an ice-water bath. A 10% solution of chromium trioxide in acetic acid (30 mL) was added from a dropping funnel over a period of

30 min. The mixture was stirred for 2 h and poured into 950 mL of water. The product was extracted with ether and the ether layer was successively washed with water, ammonium hydroxide, and water. Evaporation of the solvent yielded 1.3 g (93% yield) of a solid material which showed four products, the major one being 16. The first peak in the GC was identified as 18 while the last two peaks were later identified as 19 and 20 respectively. The ratio was 3:15:5:1 (18:16:19:20). Recrystallization of this material from isohexane yielded 3,4,5,6,7,8-hexahydro-1(2H)-phenanthrenone (16) while 18 was isolated from the mother liquor by column chromatography on alumina to give 16, mp 81-82°C (lit.[33] mp 82°C; lit.[59] mp 81-82°C); IR (KBr) 1670 (CO) (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.82 (d,1, Ar-H at C-10), 7.01 (d,1,Ar-H at C-9), 2.78 (t,4,CH_2 at C-2 and C-4), 2.58 (t,4,CH_2 at C-5 and C-8), 2.10 (quintet,2,CH_2 at C-3), 1.96-1.68 (m,4,CH_2 at C-6 and C-7); MS m/z (rel intensity) M^+ 200(100), 172(82), 144(60), 129(44).

1,2,5,6,7,8-Hexahydro-4(3H)-phenanthrenone (18)

This compound was obtained from the mother liquor of 16 and further purified by column chromatography using neutral alumina and ether; mp 40.5-41.0°C (lit.[13,15] mp 40°C); IR (KBr) 1675 (CO) (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.02 (q,2,Ar-H), 3.15 (s,2,CH_2 at C-5), 2.80 (quintet,4,CH_2 at

C-1 and C-3), 2.58 (t,2,CH_2 at C-8), 2.00 (quintet,2,CH_2 at C-2), 1.71 (m,4,CH_2 at C-6 and C-7); MS m/z (rel intensity) M^+ 200(100), 185(62), 172(33), 129(34), 115(32). Anal. calcd for $C_{14}H_{16}O$: C, 84.00; H, 8.00. Found: C, 84.16; H, 8.20.

Oxidation of 16 to diketones 19 and 20

Ketone 16 (5.5 g, 0.028 mol), 60 mL of 10% chromic acid solution in acetic acid and 200 mL of glacial acetic acid were heated at reflux for 2 h followed by 2 h stirring at room temperature. The greenish solution was poured into 3 L of water and extracted with ether twice in a 5-L separatory funnel. The combined ether extracts were washed with sodium bicarbonate solution, 10% sodium hydroxide solution, and finally with water. The ether layer was dried ($MgSO_4$) and concentrated to 4.3 g (73% yield) of a dark brown material. A sample of this crude material showed two peaks in addition to the starting material in the ratio 4:1 (19:20). Preparative liquid chromatographic separation of the product mixture afforded the two diketones which were further purified by recrystallization from isohexane; 3,4,7,8-tetrahydro-1(2H),5(6H)-phenanthrenedione (19), mp 96-97°C; IR (KBr) 1680 (CO) (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.19 (d,1,Ar-H), 7.27 (s,1,Ar-H), 3.40 (t,2,CH_2 at C-4), 3.01 (t,2,CH_2 at C-8), 2.67 (quintet,4, CH_2 at C-2 and C-6), 2.10 (m,4,CH_2 at C-3 and C-7); MS m/z (rel intensity) M^++1 215(39), M^+ 214(100), 186(58),

185(26), 171(28), 158(51), 130(20). Anal. calcd for $C_{14}H_{14}O_2$: C, 78.50; H, 6.54. Found: C, 78.71; H, 6.64.

3,4,5,6-Tetrahydro-1(2H),8(7H)-phenanthrenedione (20)

mp 166-168°C; IR (KBr) 1695 (CO) (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.93 (s,2,Ar-H), 2.90 (t,4,CH_2 at C-4 and C-5), 2.66 (t,4,CH_2 at C-2 and C-7), 2.17 (m,4,CH_2 at C-3 and C-6); MS m/z (rel intensity) M^++1 215(33), M^+ 214(83), 187(29), 186(100), 158(46), 130(29), 129(25), 115(25), 28(71). Anal. calcd for $C_{14}H_{14}O_2$: C, 78.50; H, 6.54. Found: C, 78.30; H, 6.71.

Oxidation of 18 to diketones 19 and 22

Ketone 18 (200 mg), 3 mL of 10% chromic acid solution and 15 mL of glacial acetic acid were refluxed for 2 h, cooled and poured into 150 mL of water. The product was extracted with ether and the ether layer washed with sodium bicarbonate solution, 10% sodium hydroxide solution and then water. The ether layer was dried ($MgSO_4$) and concentrated to obtain 170 mg (79% yield) of a partly crystalline brown material. GC analysis showed two products, the major one being 19. The minor product, probably 22, was not isolated. The ratio of the isomers in the crude mixture was 9:1 (19:22).

Oxidation of 25

The procedure used by Farina and Audisio[60] was slightly modified by dropping a suspension of the hydrocarbon 25 (5.0 g) in 100 mL of acetic acid into a magnetically stirred solution of CrO_3 (5.0 g) in 125 mL of acetic acid. When the addition was complete, the mixture was heated on a stream bath for 6 h. The solution was then poured into 1 L of water and the product was allowed to separate. The solid was filtered off, dissolved in ether and extracted with sodium bicarbonate solution and water. The ether layer was dried ($MgSO_4$) and evaporated to 3.0 g (57% yield) of a brown solid. Extraction of this material through neutral alumina in a Soxhlet column with isohexane yielded two fractions, the first rich in hydrocarbon and the second in the product ketones. The mixture of 27 and 28 was separated by preparative liquid chromotography. Further purification was achieved by repeated recrystallizations from isohexane to give 3,4,5,6,7,8,9,10,11,12-decahydro-1(2H)-triphenylenone (27), mp 220.5-222°C (lit.[60] mp 224°C); IR (KBr) 1690 (CO) (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.12 (m,2,Ar-CO-CH_2), 2.77 (t,2,CH_2 at C-12), 2.59 (m,8,CH_2 at C-4, C-5, C-8 and C-9), 2.05 (quintet,2, CH_2 at C-3), 1.78 (m,8,CH_2 at C-6, C-7, C-10 and C-11); MS m/z (rel intensity) M^+ 254(100), 239(96), 198(25), 28(67). Anal. calcd for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 85.15; H, 8.53. In addition, 3,4,7,8,9,10,11,-

12-octahydro-1(2H),5(6H)-triphenylenedione (28) was obtained and purified similarly: mp 225.5-228°C; IR (KBr) 1675 (CO) (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.24 (m,4,CH_2 at C-2 and C-6), 2.83 (t,4,CH_2 at C-4 and C-12), 2.65 (m,4,CH_2 at C-8 and C-9), 2.04 (m,4,CH_2 at C-3 and C-7), 1.79 (m,4, CH_2 at C-10 and C-11); MS m/z (rel intensity) M^++1 269(21), M^+ 268(100), 253(18), 212(30). Anal. calcd for $C_{18}H_{20}O_2$: C, 80.60; H, 7.46. Found: C, 80.46; H, 7.52.

Oxidation of 6-Nitro-1,2,3,4-tetrahydronaphthalene (31)

A mixture of 31 (1.8 g, 0.01 mol), 40 mL of 10% chromic acid solution in acetic acid and 125 mL of glacial acetic was heated at reflux for 2 h. The cooled mixture was poured into 1200 mL of ice-water, and then transferred to a 5-L separatory funnel. The product was extracted twice with ether and the combined ether extracts were washed successively with saturated sodium bicarabonate solution, 10% sodium hydroxide solution and then water. The ether layer was dried ($MgSO_4$) and evaporated to 0.9 g (50% yield) of a pink material which showed two LC peaks in addition to the starting material in the ratio 1:1.1. A standard of 7-nitro-3,4-dihydro-1(2H)naphthalenone (32) obtained commercially showed 32 to be the minor product. The sodium bicarbonate extract was neutralized with hydrochloric acid and extracted with ether. The ether layer was washed with water, dried ($MgSO_4$) and evaporated to

obtain 0.4 g (20%) of a brown oil which solidified on standing. Similar work-up of the sodium hydroxide extract yielded 0.1 g (5%) of a reddish brown material.

Oxidation of 5-Nitro-1,2,3,4-tetrahydronaphthalene (36)

The procedure used for the oxidation of 31 was adopted for this reaction. Following a similar work-up, 0.8 g (40% yield) of neutral product, 0.4 g (20%) of an acidic product and 0.1 g (5%) of a phenolic product were obtained. The neutral material showed the presence of more starting material than the previous reaction. LC analysis showed two peaks in the ratio 4.3:1.

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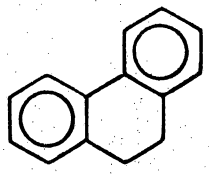
APPENDIX

GLOSSARY OF STRUCTURES



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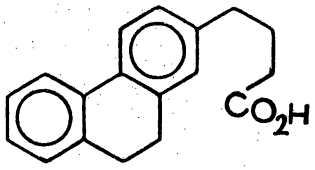

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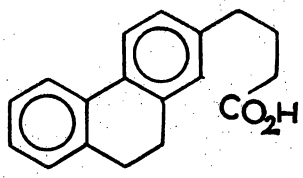

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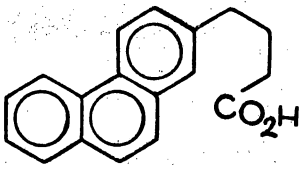

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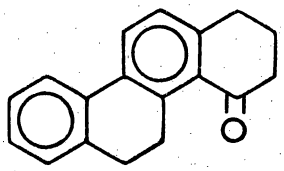

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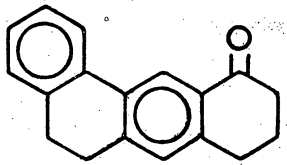

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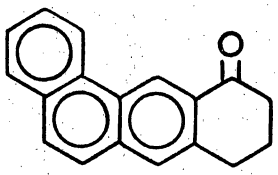

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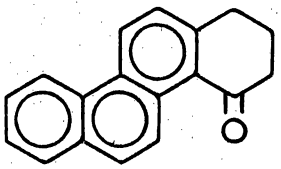

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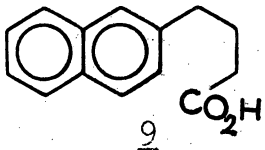

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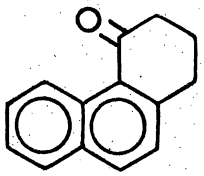

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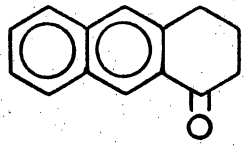

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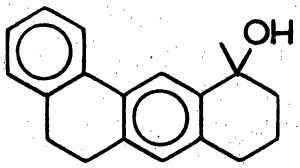

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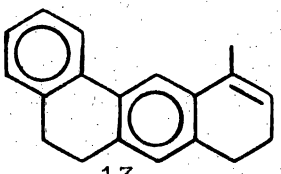

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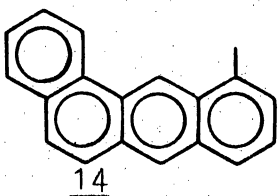

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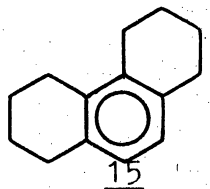

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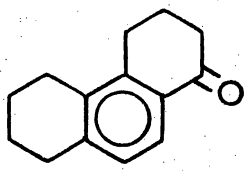

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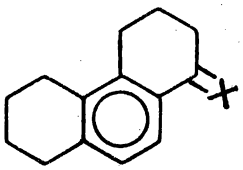

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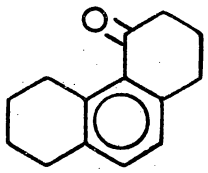

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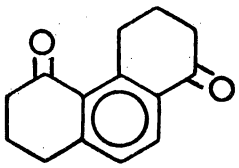

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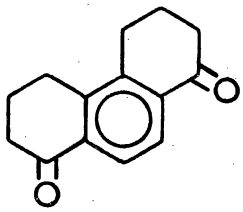

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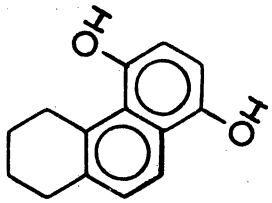

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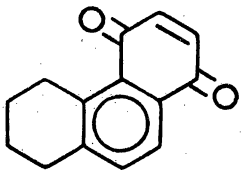

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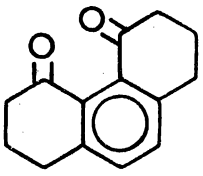

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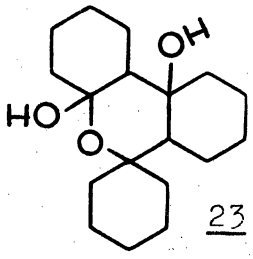

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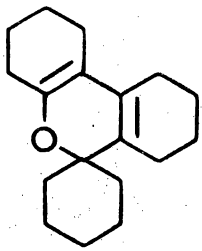

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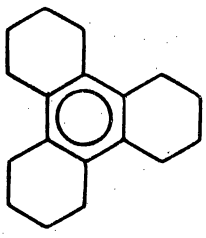

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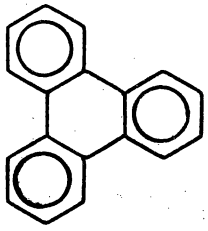

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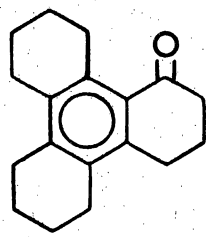

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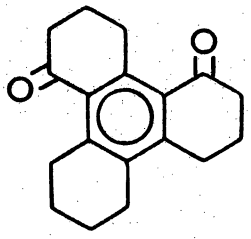

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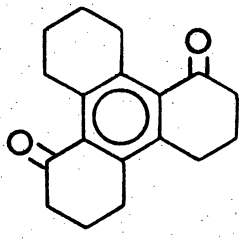

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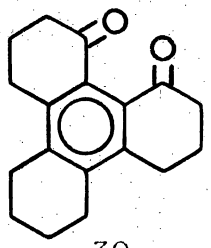

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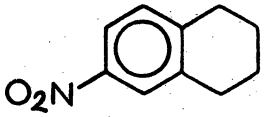

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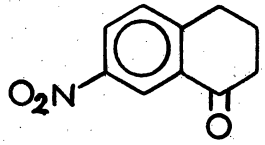

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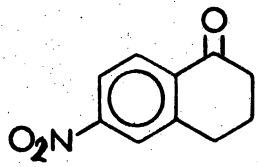

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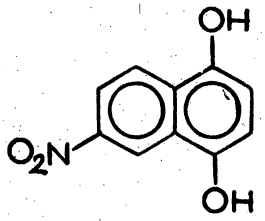

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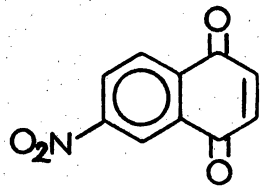

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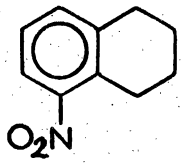

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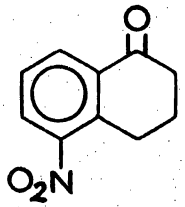

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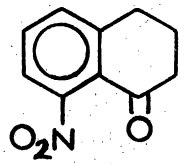

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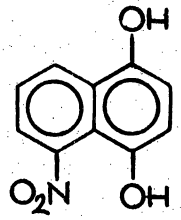

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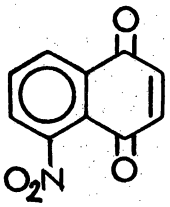

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VITA

Premasagar Vuppalapaty

Candidate for the Degree of

Doctor of Philosophy

Thesis: I. SELECTIVITY IN THE CYCLIZATION OF γ-ARYLBUTYRIC ACIDS
II. CHROMIC ACID OXIDATION AT THE BENZYLIC POSITION

Major Field: Chemistry

Biographical:

Personal Data: Born in Penugudurupadu, India, June 2, 1952, the son of Dr. Baliah and Mrs. Anasuya Vuppalapaty.

Education: Graduated from Rani Seethaiachi High School, Annamalainagar, India; received the Bachelor of Science degree from Annamalai University, India, in May, 1972, with a major in Chemistry and minors in Physics and Mathematics; completed requirements for the Doctor of Philosophy degree at Oklahoma State University in July, 1979.

Professional Experience: Graduate Teaching Assistant, Oklahoma State University, September 1973-May 1974, September 1974-May 1975, September 1975-May 1976, September 1976-July 1977, June 1978-July 1978; Graduate Research Assistant, American Petroleum Institute, June 1974-December 1974; Graduate Research Assistant, Environmental Protection Agency, January 1975-January 1976, September 1976-May 1977, September 1978-November 1978; Graduate Research Assistant, Energy Research and Development Administration, January 1976-May 1976; Gulf Summer Fellow, 1976.