San Fernando Valley State College

THE o-ANISYL GROUP IN PINACOL-LIKE REARRANGEMENTS

A thesis submitted in partial satisfaction of the requirements for the degree of Master of Science in Chemistry

by

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The thesis of Charles Edward Spivak is approved:

San Fernando Valley State College
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To my family
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2-Amino-1-(2-methoxyphenyl)-1-phenylethanol was synthesized and subjected to nitrous acid deamination in an effort to elucidate factors bearing on 1,2-shifts of the o-anisyl group. Besides the anticipated ketonic products, namely 2-methoxydeoxybenzoin and 2'-methoxydeoxybenzoin, a third product, 3-phenylbenzofuran, was obtained in substantial yield. This last compound resulted from intramolecular methoxyl interaction with the nitrous acid-generated cation and represents the first reported instance of o-MeO-5 participation in deamination. Attempts to synthesize the related aminoethanol 1,2-di(2-methoxyphenyl)-1,2-diphenyl-2-aminoethanol were unsuccessful. An outgrowth of this work was the synthesis of benzopinacol sulfite and 2,2'-dimethoxybenzopinacol sulfite. Studies of the former compound revealed that it is subject to pyrolytic decomposition leading mainly to benzpinacolone,
perhaps by a mechanism similar to that of the pinacol rearrangement.
CHAPTER I
INTRODUCTION

Generation of a carbonium ion on a carbon atom adjacent to a hydroxyl-bearing carbon atom usually induces a 1,2-shift which results in formation of a protonated carbonyl group on the formerly hydroxyl-bearing carbon atom. Some well known examples of this reaction are the following:

The purpose of the work described in this and in the following chapters was to attempt to study rearrangements of this type in which one of the potential migrating groups
is the o-methoxyphenyl (o-anisyl) group.

The pinacol rearrangement (d above) is a classical case of a 1,2-shift, and numerous reviews and discussions of it are available.\textsuperscript{1} Several studies of symmetrical pinacols (R\textsubscript{1}=R\textsubscript{4} and R\textsubscript{2}=R\textsubscript{3}) were undertaken in the 1930's,\textsuperscript{2} and it was found that migratory aptitudes (ratios of products resulting from migration of a substituted phenyl or other aryl group to those resulting from migration of the phenyl group) could be assigned with high internal consistency. Some of these migratory aptitudes are\textsuperscript{1a}

\begin{itemize}
  \item p-anisyl (500)*,
  \item p-tolyl (15.7),
  \item p-isopropylphenyl (9),
  \item p-ethylphenyl (5),
  \item m-anisyl (1.6),
  \item phenyl (1.0),
  \item p-chlorophenyl (0.7),
  \item o-anisyl (0.3),
  \item m-chlorophenyl (0.1).
\end{itemize}

This series shows, as might be expected, a trend which parallels ease of the migrating group to undergo electrophilic substitution (e.g., by the carbonium ion). The one outstanding irregularity of this series is the case of the o-anisyl group. Electronic considerations alone would indicate that the o- and p-anisyl groups should be of comparable migratory aptitude, and that only steric factors can be invoked to explain the huge disparity observed.

\*A migration ratio of 1000 (p-anisyl to phenyl) has recently been reported\textsuperscript{3} based on studies under slightly different conditions.
Indeed, Kharasch et al.\textsuperscript{4} have demonstrated that, in the absence of steric interactions at the migration terminus, \(\tau\)-anisyl migration predominates. They treated triarylcarbinols with tert-butyl hydroperoxide and a small amount of perchloric acid in acetic acid. The carbinol formed a hydroperoxide (which could be isolated under certain conditions) which then, they proposed, underwent protonation, dehydration, rearrangement, and hydrolysis to give a diaryl ketone and a phenol. When \(\tau\)-anisyl-diphenylcarbinol was so treated, benzophenone (a product resulting from \(\tau\)-anisyl migration) was recovered in 75\% yield and the starting material in 12\% yield.

The details of this steric inhibition to migration in the pinacol rearrangement have been the subject of some speculation. Ingold\textsuperscript{5} envisioned crowding of the ortho group (of the migrating aryl ring) with the groups present at the migration terminus: "At some stage in the migration involved in the reactions of Bachmann's pinacols, three bonds from one carbon atom to three aryl groups have to come into a plane, which would contain the migrating aryl ring, if its electrons are to be used effectively in the formation of the new bond. This is impossible in the presence of an ortho substituent."\textsuperscript{5} Brown\textsuperscript{6} postulated that the crowding occurred in the transition state when the migrating aryl group was between the migration origin and terminus, and resulted from unfavorable interaction of
the ortho group with groups attached to the glycol carbon atoms.

The effect of the ortho substituent in dehydration of meso and dl-disastereomers of symmetrical tetraaryl pinacols has recently been examined by Matsumoto and co-workers.\textsuperscript{7}

$$\begin{align*}
\text{meso} & \\
\text{dl} & \\
A &= \text{PhCOCPhAn}_2 \\
B &= \text{AnCOCPh}_2(\text{An})
\end{align*}$$
They found that, although the migratory aptitudes (i.e., A/B above) changed during the reaction, the ratio of A to B extrapolated to time zero was 0.85 for the meso and 0.3 for the dl isomer. They rationalized the difference in migratory aptitude for the meso vs. the dl isomers by proposing that eclipsing of bulky groups in the transition state suppresses that mode of rearrangement. The eclipsing of the bulky o-anisyl groups in the transition state b suppresses phenyl migration and thereby increases the migratory aptitude measured for the meso diastereomer in relation to that of the dl diastereomer, whose steric interactions in the two transition states (c and d above) are about the same. Although this work implicates another mode of steric interference, this additional mode alone does not account for the relative retardation of o-anisyl migration, since even the meso diastereomer showed a migratory aptitude (A/B) of less than one.

One might expect some involvement of the ortho methoxyl oxygen with the developing or full-fledged carbonium ion. Such interaction was shown by Winstein and co-workers to enhance rates of certain solvolyses and result in some formation of cyclic ethers. The intervention of the o-methoxyl group to form an n membered cyclic ether has been called by Winstein "o-MeO-n" participation, in which n is the number of members in the resulting cyclic ether. One such reaction was the following:
The rate of this solvolysis was found to be eight times as fast as the rate of the corresponding reaction using the \( p \)-methoxy isomer, for which no "\( o \)-MeO-5" participation was possible.

A similar participation was observed in the dehydration of 3,4-di(2-hydroxyphenyl)-hexane-3,4-diol, but not in the dehydration of the pinacols studied by Matsumoto. No cases of \( o \)-MeO-5 participation have been reported for deamination reactions, but such participation has been observed in the present work. This result will be discussed in Chapter III.

To elucidate further the behavior of the \( o \)-anisyl group in such rearrangements, the synthesis, separation into meso and dl diastereomers, and nitrous acid deamination of aminoalcohol I was proposed.

\[
\begin{align*}
\text{I} & & \text{II} \\
\text{OH} & & \text{OH} \\
\text{NH}_2 & & \text{NH}_2 \\
\text{An} \sim \text{C} \sim \text{An} & & \text{An} \sim \text{C} \sim \text{CH}_2 \\
\text{Ph} & & \text{Ph} \\
\end{align*}
\]

\( \text{An} = o\text{-Anisyl} \)
The steric and electronic factors which control the rearrangement of the corresponding glycol were expected to be viable in the proposed reaction, but modified by principles peculiar to deamination. In an effort to estimate the role of steric factors in this deamination and to search for possible "o-Me0-5" involvement, compound II, which was expected to display minimal steric hindrance at the migration terminus, was then to be deaminated and the resulting products compared to those arising from I.

Attempts to synthesize compound I, described in Chapter II, were unsuccessful, but did lead to cyclic sulfites. These sulfites did not react with ammonia to yield the corresponding aminoalcohols as expected. Instead they were subjected to pyrolysis in the hope that they would undergo pinacol-like rearrangements. A general discussion of such pyrolysis appears on page 11 and is taken up for the case at hand in Chapter IV.

Although having many superficial similarities, deamination of 2-aminoethanols (semipinacols) is known to differ in many details from dehydration of pinacols. Among these are differences in rates of rearrangement, solvent effects, role of the counter ion, reactive intermediates, and stereochemical outcome. Some of the factors important in deamination are treated briefly below and all are discussed in reviews.
Deamination of 1,2-aminoalcohols has long been known to be accompanied by a 1,2-shift. Although substituents on the basic 2-aminoethanol skeleton were selected so that rearrangements analogous to known symmetrical pinacol rearrangements could be investigated, some deamination experiments gave unexpected results. For example it was found\textsuperscript{12} that, in the deamination reaction below, phenyl migrated in preference to R, where R= alpha-naphthyl, p-tolyl, or p-anisyl. This preference was not in accord with the results of dehydration of appropriate pinacols. The problem was taken up by Curtin and co-workers\textsuperscript{13} who showed that migratory preference depended chiefly on the configuration of the semipinacol under consideration. The source of the high degree of stereospecificity in the semipinacolic deamination was believed by Curtin et al.\textsuperscript{13} to derive from eclipsing of bulky groups in the transition state of the rearrangement (which they envisioned as backside aryl migration concerted with loss of nitrogen from the diazonium ion). They lumped the various nonbonding interactions (steric strain, steric inhibition of resonance, dipole-dipole interactions, and entropy differences in the transition states resulting from unequal distribution of vibrational and rotational motions) under the
heading "cis effect."

Collins and co-workers pursued this work further. Their elegant study of the deamination of the stereochemically pure, isotopically labeled compound below revealed that nitrogen loss to form a secondary cation was not concerted with migration, and that the intermediacy of an open carbonium ion must be invoked. Though the migratory preferences above could be explained by the "cis effect," Collins demonstrated that in fact ground state conformation exclusively directed product distribution. Martin and Bentrupe, using the data of Collins et al. calculated the ratio of rate constants of phenyl migration to bond rotation to be \( k_2/k_1 = 6.3 \).

Evidence that diazonium salts do not spontaneously undergo C-N scission to leave a primary carbonium ion (in cases in which the hydroxyl group was absent from the
adjacent carbon) was provided by Guthrie\(^{18}\) and others.\(^{11a}\) Guthrie showed that deamination of \((+)-(R)-\text{neopentylamine-1-d}\) (below) gave products resulting from methyl migration

\[
\begin{align*}
\text{(CH}_3\text{)}_3\text{C} - \text{C} - & \xrightarrow{\text{NH}_2} \xrightarrow{\text{H}^+ \text{ONO}} \xrightarrow{\text{HOAc}} \text{(CH}_3\text{)}_2\text{C} - \text{C} - \\
\text{CH}_3 & \quad \text{CH}_3 \quad \text{CH}_3 \quad \text{D} \quad \text{H} \quad \text{CH}_3 \\
& \quad \text{D} \quad \text{H}
\end{align*}
\]

with at least 85% inversion of configuration at the migration terminus. He concluded that migration to a free carbonium ion could occur no more than 15% of the time.

Rearrangements of 1,1-diaryl-2-aminoethanols by nitrous acid lead to products resulting from aryl migration, and migratory preferences follow the order discovered in the pinacol rearrangement, although to much less pronounced degree, as shown by the migration ratios\(^{19}\) \((\text{Ar/Ph})\), \(\text{p-}\text{anisyl, 1.56; p-tolyl, 1.28; phenyl, 1; and p-chlorophenyl, 0.88.}\) It seems, then, that the intermediate cation in these reactions (diazonium ion or perhaps free carbonium ion) is highly reactive and rearrangement takes place without the high selectivity which accompanies the pinacol rearrangement.
The cyclic sulfites, III and IV below, which arose in the course of attempted preparation of aminoethanol I, seemed to be good candidates for further study. Pyrolysis of such sulfites, it was hoped, would lead to rearranged products, in a manner similar to the pinacol rearrangement. Most of the work done on pyrolysis of sulfites has been designed to elucidate the mechanism and scope of the beta elimination which these groups induce. Some of the consequences of sulfite pyrolysis when beta elimination is not possible (as in III and IV) are reviewed below.

III: \[ R = \text{OCH}_3 \]  
IV: \[ R = \text{H} \]

The pyrolysis of five-membered cyclic sulfites of compounds which do not have beta hydrogens usually yields rearranged carbonyl compounds. One case is known in which an epoxide was also formed.\(^{20}\) The rearrangement is probably synchronous with C-O scission. For example Price and Berti\(^{22}\) have pyrolyzed the sulfites below and found that either hydride shift or ring contraction resulted depending on whether the starting sulfite was the cis or trans isomer.
Price and Berti\textsuperscript{21} have also pyrolyzed the sulfites of hydrobenzoin which gave either deoxybenzoin or diphenylacetaldehyde depending on whether they pyrolyzed the \textit{cis} or \textit{trans} isomer. The mechanism they proposed for this reaction requires a phenonium ion intermediate. They cite

\[ \text{cis} \]

\[ +\text{SO}_2 \]

\[ \text{trans} \]

\[ +\text{SO}_2 \]

\[ \text{cis} \]

\[ \text{trans} \]

\[ \text{A} = \text{PhCOCH}_2\text{Ph} \quad \text{B} = \text{Ph}_2\text{CHCHO} \]
as evidence of a carbonium ion intermediate in such reactions the observation that, when the anticipated carbonium ion is a particularly stable one, the temperature at which pyrolysis begins (evidenced by loss of sulfur dioxide) is low compared with that of a compound which would be expected to yield a less stable carbonium ion. 22

Results similar to the above were obtained by Coxon et al. 23, who pyrolyzed the cyclic sulfites of cis and trans 2,3-butanediol. They obtained 2-methylpropionaldehyde (the product resulting from 1,2-shift of a methyl group) in less than one percent yield from the cis isomer and in ten percent yield from the trans isomer. Since a bridged intermediate is not expected to be as viable here as it is in the hydrobenzoin sulfites studied by Price and Berti (vide supra), the low yield of the aldehyde product is not surprising.
CHAPTER II
SYNTHETIC TRIALS AND APPROACHES

Synthetic route to 2-amino-1-(2-methoxyphenyl)-1-phenylethanol (II). The problem of synthesizing II was really one of synthesizing the precursor, 2-amino-2'-methoxyacetophenone hydrochloride (V), which yields the desired product upon reaction with phenylmagnesium bromide. An acidic reaction medium must be maintained or else the aminoketone will dimerize to form dihydropyrazines and, by air oxidation, pyrazines:

```
2 ArCH2NH2 → ArHN1 → ArNNAr
N
```

Tiffeneau et al. 25 first synthesized II by the reaction of 2-methoxyacetophenone with amyl nitrite and sodium ethoxide followed by reduction with stannous chloride in hydrochloric acid. The similar nitrosation method of Claisen and Manesse 26 was followed, but the yield was not acceptable.

Of the many alternative routes 27 to V, the following were attempted:
\begin{align*}
\text{VI} & \xrightarrow{\text{Br}_2} \text{VII} & \text{HCl, Et}_2\text{O} & \text{VIII} \xrightarrow{\text{HCl}} \text{IX} \\
\text{VI} & \xrightarrow{\text{NaN}_3} \text{VIII} & \text{HCl, Et}_2\text{O} & \text{X} \xrightarrow{\text{HCl}} \text{XI} \\
\text{V} & \xrightarrow{\text{PhMgBr}, \text{Et}_2\text{O}, \text{H}_2\text{O}} \text{XII}
\end{align*}

\text{Ref. 28} \  \text{Ref. 29} \  \text{Ref. 30} \  \text{Ref. 31}
The product mixture from reaction 1 showed no oxime bands in the infrared spectrum, and for this reason work along this line was discontinued.

Bromination of 2-methoxyacetophenone in chloroform\textsuperscript{32} gave an 80\% yield of VI. Brominations in ether, with\textsuperscript{33} and without\textsuperscript{34} use of aluminum chloride catalyst, gave only fair yields (42\%) of VI and some 2,5'-dibromo-2'-methoxyacetophenone by-product, which was identified by spectroscopic means.

When VI was allowed to react with hexamethylenetetramine in chloroform (the Delepine reaction, \#3) the only precipitate recovered was a substance which appeared to be hexamethylenetetramine hydrochloride (the infrared spectrum of this product was very similar to an authentic sample of hexaminetetramine hydrochloride and completely lacked typical aromatic bands) and not the anticipated salt. In contrast, when the 2-bromo-4'-methoxyacetophenone was prepared and allowed to react in the same way, a white precipitate formed immediately (mp 168-170\° decomp), whose complicated infrared spectrum resembled that of the parent compound but was significantly different. This result was taken as evidence that the presence of the \(\alpha\)-methoxy group in VI was inhibiting its successful reaction.

The Gabriel synthesis (reaction 4) was successful to the extent that the phthalyl derivative was prepared in 40\% yield (the nuclear magnetic resonance spectrum of this
compound was compatible with this conclusion). Preliminary attempts to hydrolyze this material failed, and only starting material was recovered.

The reaction of VI with sodium azide (see the experimental section) was rapid and gave a high yield (89%). All attempts to reduce this azide to II at more than one atmosphere pressure of hydrogen (5% palladium on charcoal was used as the catalyst throughout) caused some reduction of the keto group, but reduction at atmospheric pressure was successful.

Reaction of V with phenylmagnesium bromide yielded the desired product II.

Synthetic routes to 1,1,2,2-tetrayl-2-aminoethanols. Neither the parent compound (VIII) nor the di-o-methoxy derivative (I) has ever been isolated, though two groups have postulated the transitory existence of VIII during acid treatment of 2,2,3,3-tetraphenylazirane35 or of the oxazoline36 below:

\[
\begin{align*}
\text{Ph}_2\text{C} & \quad \text{CPh}_2 \\
\text{Ph}_2\text{C} & \quad \text{CPh}_2 \\
\text{Ph}_2\text{C} & \quad \text{CPh}_2
\end{align*}
\]

1) MeOH \[ \text{OH} \quad \text{NH}_2 \]

2) 50% H\text{SO}_4 \[ \text{OH} \quad \text{NH}_2 \]

\[
\begin{align*}
\text{Ph}_2\text{C} & \quad \text{CPh}_2 \\
\text{Ph}_2\text{C} & \quad \text{CPh}_2 \\
\text{Ph}_2\text{C} & \quad \text{CPh}_2
\end{align*}
\]

VIII IX 72%
Since both I and VIII are unknown, many attempts were made to synthesize VIII from its more readily available precursors with the intention of using the successful route for the synthesis of I. The most reasonable approach to this synthesis was through the tetraarylethylene oxides which, it was hoped, would react readily with ammonia to yield the desired compounds. A scheme and description of the attempts made to synthesize I is presented below.

The reaction of o-anisoyl chloride with benzene in the presence of aluminum chloride\textsuperscript{37} yielded unidentified products, none of which was 2-methoxybenzophenone or xanthone, a conceivable by-product.\textsuperscript{38}

The Grignard reaction leading to 2-methoxybenzhydrol and subsequently to 2-methoxybenzophenone was successfully executed according to the method of Stoerm\textsuperscript{er} and Friderici\textsuperscript{39} and is described in the experimental section.

The reaction of 2-methoxybenzophenone with phosphorus pentachloride\textsuperscript{40} yielded the dichloro compound in 82% yield, and reaction of this product with iron pentacarbonyl\textsuperscript{41} resulted in a red solid which contained several unidentifiable products. The dichloride was then allowed to react with copper powder in pyridine.\textsuperscript{42} This reaction is known to be sensitive to the copper source.\textsuperscript{43} After work up only 2-methoxybenzophenone and 2-methoxybenzhydrol were identified by infrared analysis and, for the 2-methoxybenzhydrol, melting point.
The photoreaction of 2-methoxybenzophenone to yield the corresponding pinacol is described in the experimental section. This product was then allowed to react with thiocarbonyldiimidazole. The reaction, carried out under dry nitrogen, was monitored by thin layer chromatography until a growing product spot seemed to reach its maximum size. After passing the product through a short chromatography column, a still somewhat impure product was obtained whose infrared spectrum was almost identical with that of 2-methoxybenzophenone. An hydroxyl and another characteristic band gave evidence that significant amount of the benzopinacol was also present (the infrared spectra of the benzopinacol and the ketone are very similar).

Benzopinacol reacted with thionyl chloride (as described in the experimental section) to yield the cyclic sulfite, IV. Attempts to convert this sulfite to the aminoalcohol VIII frequently resulted in formation of tetraphenylethyleneoxide (IX). These attempts as well as those on the epoxide (IX) are described below.

\[
\begin{align*}
\text{Ph}_2C\overset{\text{O}}{\text{CPh}_2} & \xrightarrow{\text{NH}_4\text{OH} / /} \quad \text{VIII} \\
& \xrightarrow{1) \text{NaNH}_2 / /} \quad \text{IX} \\
& \xrightarrow{2) \text{H}_2\text{O} / /}
\end{align*}
\]
A solution of the epoxide (IX), ammonium hydroxide, and butanol were sealed in a glass tube and heated to 205° overnight. The epoxide was recovered unchanged. Sodamide was fused with the epoxide, but most of the epoxide was recovered. Amine bands were absent in the infrared spectra of the product mixture.

Attempts to convert sulfite IV to the aminoalcohol by reaction with ammonia resulted only information of the epoxide (IX) and benzpinacolone (X). Similar reaction of the sulfite with sodium azide were also fruitless.

The benzopinacol sulfite (IV) was oxidized with potassium permanganate in acetic acid, acetone, or acetonitrile. Infrared bands at 1390 and 1225 cm⁻¹ (very strong) indicated the presence of the sulfate, but that
compound, being extremely labile, was not obtained in pure form. By-products of this reaction were the epoxide (IX) and the ketone (X). When one crude sulfate preparation was recrystallized once from acetonitrile it was converted entirely to benzpinacolone (X), mp 180.8-181.2° (lit. 181°).

Reactions of the sulfate with sodium azide in acetone yielded, besides the usual epoxide (IX) and ketone (X), an azide whose presence was manifested by bands at 2140 and 2110 cm⁻¹ (very strong) in its infrared spectrum. Thin layer chromatography of the crude mixture showed three spots at Rf = 0.51 (strong, yellowish), 0.35 (strong, epoxide IX by comparison with an authentic sample) and 0.10 (very weak). Since sulfate and hydroxyl infrared bands were absent, this approach to the aminoalcohol was abandoned.

Reaction of the sulfate with ammonium hydroxide in acetone or acetonitrile produced only mixtures of the epoxide (IX) and benzpinacolone (X), as determined by infrared spectroscopy and thin layer chromatography.

When benzopinacol sulfate (XI) was allowed to react in a sealed tube with liquid ammonia in dimethylformamide, a greenish solid was obtained, mp 235.0-235.8°. Since the infrared spectrum of this compound had all of the bands of tetraphenylethylene (common peak positions were
identical), but had a few others as well, it seemed likely that the unknown reaction product would be closely related to tetraphenylethylene. One such related compound is 9,10-diphenylphenanthrene, mp 235°. The mechanism proposed for this reaction is given below:

This product has been shown to result from the action of chromyl chloride on tetraphenylethylene, and a mechanism involving a similar cyclic ester was proposed. Two reactions involving addition to benzil monohydrazone were then attempted. Benzil, which was recrystallized from ethanol, reacted smoothly with hydrazine hydrate in ethanol to produce the hydrazone in a 91% yield, mp 144-149° (lit. 151°).

The unpurified benzil monohydrazone was allowed to react with phenylmagnesium bromide. Thin layer chromatography of the product mixture indicated the presence of six components. Mild acid extraction yielded a drop of foul smelling purple-brown fluid. Two major components were evident by thin layer chromatographic analysis.
Although an amine and possibly a hydroxyl band was present in the infrared spectrum of this fluid, the low yield discouraged pursuit of the Grignard reaction and suggested the trial of phenyllithium. Reaction of benzil monohydrazone with phenyllithium in refluxing tetrahydrofuran produced several products. The infrared spectrum of the crude mixture was very similar to deoxybenzoin, the product expected from Wolff-Kishner reduction. Dilute acid extraction provided a film of greenish residue. Although the infrared spectrum of this product showed a band at 3340 cm\(^{-1}\) (possibly an amine band), strong bands at 1650 and 1610 cm\(^{-1}\) intimated the presence of undesirable C=O or C=N bonds.

Two other approaches to 1,1,2,2-tetraphenyl-2-amino-ethanol (VIII) were embarked upon but terminated in inchoate stages. The proposed routes and their weaknesses are given below. Since Bittner et al.\(^{36}\) postulated the transient existence of the desired product upon acidic hydrolysis of a \(\Delta^2\)-oxazoline, the possibility of an oxazo-
line precursor was investigated. The questions which arose were 1) which tetraphenyloxazolines have been synthesized and 2) could they yield the desired aminoethanol. Bittner et al. synthesized one such oxazoline, and a synthesis of a similar compound was also reported by Gerhart and Schollkopf. A literature investigation suggested that once a suitable oxazoline was formed, it could yield the aminoethanol by hydrolysis or by hydrogenation followed by hydrolysis. For example, the reactions below are known.

\[
\begin{align*}
R & \xrightarrow{H_2O} XNH_3CH_2O\text{CR} \\
H_3C-\text{Ph} & \xrightarrow{H_2O} H_3CO\text{NHCHPhC(Ph)}_2\text{OH} \\
\text{Ph} & \xrightarrow{\text{Na/C}_5\text{H}_2\text{OH}} \text{PhCH}_2\text{NHCH}_2\text{CH}_2\text{OH}
\end{align*}
\]

As a first step leading to the oxazoline synthesized by Bittner et al., 2-methoxybenzhydrylamine hydrochloride was prepared by the Leuckart reductive amination of 2-methoxybenzophenone according to the procedure described by Kalamár and Ryban. Further work on this route was deferred for lack of time.
The highly successful Knoevenagel-like reaction of benzophenone with diphenylmethane in sodamide leading to 1,1,2,2-tetraphenylethanol in 91-96% yield\textsuperscript{54} suggested the Henry reaction below.

\[
\begin{align*}
\text{Ph-} & \text{-C-Ph} + \text{Ph-} & \text{-C-Ph} \\
\text{H} & \text{ base} & \text{OH NO}_2 \\
\text{Ph}_2 & \text{-C-C-Ph} & \text{VIII}
\end{align*}
\]

Bordwell and Garbish,\textsuperscript{55} however, have synthesized 1,1-diphenyl-2,2-dimethyl-2-nitroethanol by a different method and found that their compound is unstable in 20% alkali and reverts to benzophenone and 2-nitropropane. Therefore the above sequence was not attempted.
CHAPTER III
THE DEAMINATION OF
2-AMINO-1-(2-METHOXYPHENYL)-1-PHENYLETHANOL

The deamination of 2-amino-1-(2-methoxyphenyl)-1-phenylethanol (II) was carried out in acetic acid-water at 0° and at 30°. The crude product mixture was analyzed by thin layer chromatography (silica gel G developed in chloroform-petroleum ether, 1:2). Upon visualization with iodine, four spots were seen at \( R_F = 0.75, 0.20, 0.10 \) and 0.00 (referred to as the A, B, C, and Z products respectively in the discussion below). Percolation through a short alumina column eliminated the yellow, polymeric material responsible for the origin spot (the Z product), and column chromatography on a silica gel column separated the remaining products. The product C was a mixture of isomeric ketones XII and XIII (vide infra) resulting from phenyl and o-anisyl migration respectively. Product B was eluted from the column in such small quantity that there was enough only for a very weak infrared spectrum, which was not very informative. Product A was 3-phenylbenzofuran, a result of o-MeO-5 participation!
Although the ketones XII and XIII were not separated from each other, infrared and nuclear magnetic resonance spectra and gas liquid partition chromatography (GLPC) retention times of the mixture were the same as those of artificial mixtures of the authentic compounds. The identity of 3-phenylbenzofuran (XIV) was also proved by comparison of its infrared spectrum and GLPC retention times with those of an authentic sample. The synthesis of the authentic products is described in the experimental section.

Several deaminations were run at 0°C, and the proportions of the ketonic fraction were determined by nuclear magnetic resonance spectroscopy. The average composition thus calculated differed from that found in the last run (reported in Table 1) by less than 1%. The ratio of XIV to the mixture of deoxybenzoins (XII and XIII) in the
neutral reaction product, which had been freed from the polymeric material, was accomplished by glpc analysis. The assay details of this work are described in the experimental section, and the results are reported in Table 1.

Table 1
Product Composition from Deamination of II

<table>
<thead>
<tr>
<th>Product</th>
<th>Yield, Mole Percent of Theoretical</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0°</td>
</tr>
<tr>
<td>XII</td>
<td>47.1</td>
</tr>
<tr>
<td>XIII</td>
<td>11.6</td>
</tr>
<tr>
<td>XIV</td>
<td>26.7</td>
</tr>
<tr>
<td></td>
<td>30°</td>
</tr>
<tr>
<td>XII</td>
<td>42.5</td>
</tr>
<tr>
<td>XIII</td>
<td>12.6</td>
</tr>
<tr>
<td>XIV</td>
<td>18.8</td>
</tr>
</tbody>
</table>

Deviations of the total mole percents of identifiable products in Table 1 from 100% reflect loss of polymeric material upon alumina filtration and normal handling and transfer losses.

Because further reaction of ketone XIII leading to 2-phenylbenzofuran seemed possible in the acidic reaction medium, a control reaction was carried out. After subjecting XIII to exactly the same reaction and work up conditions suffered by the aminoalcohol II, XIII was recovered as a white, crystalline solid which was shown by glpc analysis to be free of other products. The 3-phenylbenzofuran (XIV) was expected to be stable under the deamination conditions, since vigorous conditions are required
to convert it cleanly to 2-phenylbenzofuran.\textsuperscript{56} Stability of the products is further enhanced by their low degree of solubility in the reaction medium.

In view of the work by Curtin and Crew\textsuperscript{19} and Kharasch\textsuperscript{4}, deamination of II would be expected to result in migration of the aryl group more susceptible to electrophilic attack without regard to steric restrictions, since the migration terminus is relatively uncluttered. Despite the low selectivity of the reactive cation (presumably the diazonium ion\textsuperscript{11a, 18}) migration of the o-anisyl group would be expected to at least equal (as incorrectly reported previously\textsuperscript{25}) or exceed migration of phenyl. The much-reduced product ratios (XIII/XII) actually found, which were 0.25 and 0.30 (see Table 1), can be explained with the aid of Chart 1.

The rate of rotational interconversion of the diazonium ions is speculative, but the low specificity of the rearrangement observed in other cases\textsuperscript{19} suggests that ground state conformation may be important, and that the rate of bond rotation may be comparable to the rate of migration. A higher ground state population of the amino-ethanol leading to XII may be expected on the basis of hydrogen bonding between the hydroxyl and amino groups and also between the amino group and the methoxyl oxygen (to form quasi 5- and 7-membered rings, respectively). Molecular models indicate that such an arrangement would be
possible, and Matsumoto gives evidence for similar hydrogen bonding in the meso and dl isomers of 2,2'-dimethoxybenzopinacol.\textsuperscript{7c} The fact that the amount of phenyl migration (favored by the hydrogen bonded ground state) decreases with increased temperature as the three possible ground state populations tend toward equality, gives support to this hypothesis.

If the aryl migrations leading to the phenonium-bridged intermediates and finally to the deoxybenzoins
(XII and XIII) were the only two courses for the reaction to take, the prediction that the migration ration of XIII/XII would possibly be observed. It seems, however, that the ground state conformation which would lead ultimately to XIII is diverted by the intervention of the well-positioned methoxyl oxygen to the oxonium intermediate (o-MeO-5 route). Such unique intervention could not accompany deamination in other cases studied since a nearby oxygen function was absent. It may be that oxygen intervention accompanies diazotization and also allows the equilibrium between the diazonium ion and the neutral diazo compound to favor the ionized form. This equilibrium has been shown to exist in several cases studied.57

\[ R-\text{CH}_2-N_2OAc \rightleftharpoons R-\text{CHN}_2^+ + HOAc \]

o-MeO-5 participation in solvolysis reactions, discussed in the introduction, has been studied by Winstein and co-workers, and carbonyl oxygen participation in the deamination of glutamine to yield 4-carboxy-gamma-butyrolactone has been described by Austin and Howard. Huffman and Elliott have shown that a favorably positioned hydroxyl group was capable of reacting intramolecularly with a nearby cation. They found that erythro-1,2-diphenyl-2-aminoethanol gave 15 mole percent of trans-stilbene oxide on deamination whereas the threo isomer gave only a trace of this product. A similar intramolecular reaction involving an alkene with a cation
resulting from deamination has been reported. The present case represents, however, the first example of \_\textsubscript{\textalpha}-\textMeO-5 participation in deamination.

The oxonium intermediate (see Chart 1) probably reacts with the solvent to form methyl acetate (or perhaps methanol) and thereby lead to 3-phenylbenzofuran (XIV). This same intermediate, however, may also give rise to the yellow polymeric material which was removed from the reaction products by filtration through alumina. Evidence that the polymer does so arise comes from the fact that Curtin and Crew\textsuperscript{19} reported 97-100\% of theoretical recovery of ketonic products resulting from deamination of \textit{para} substituted \textit{1,1-diaryl-2-aminoethanols}, from which such an intermediate could not be expected.

That the weight of polymer lost was more than three times greater when the reaction was carried out at 30\textdegree than it was at 0\textdegree is in keeping with the general observation that polymer formation increases with temperature.

Apparent migratory aptitude in cases such as this in which \_\textsubscript{\textalpha}-\textMeO-5 participation is a reality, is not a true reflection of the inherent vulnerability of aryl groups to electrophilic attack. The \_\textsubscript{\textalpha}-\textMeO-5 route diverts the intermediate which would otherwise lead to an aryl-migrated product and thereby diminish its proportion in the final product mixture.
CHAPTER IV
PYROLYSIS OF BENZOPINACOL SULFITE

Hauptmann and Dietrich\(^6\) attempted the synthesis of benzopinacol sulfite (IV) by refluxing a solution of benzopinacol with thionyl chloride in pyridine for ten hours. In view of the results of the present work it is not surprising that the vigorous conditions employed by these workers yielded only benzpinacolone. In the course of the present work, this sulfite and the 2,2'-di-\(\text{-}\text{\textbeta-}\text{-anisyl}\) analog (III) were successfully prepared by the action of thionyl chloride on the parent pinacols in dry pyridine at room temperature. Tetraaryl, five-membered cyclic sulfites of this type were unknown heretofore. Details of these syntheses are given in the experimental section.

The ultimate objective of the following investigation was to separate III into its meso and dl forms, pyrolyze...
each disastereomer, assay the products, calculate migration ratios (if rearrangement did occur), and rationalize the results. Before attempting this pyrolysis, however, it seemed prudent to make a preliminary investigation of the pyrolysis of the simpler, unsubstituted sulfite, IV, and it is to the findings of this investigation that the remainder of this chapter is devoted.

When IV was pyrolyzed neat at 137° for one hour, four products could be detected upon thin layer chromatographic analysis (silica gel GF-254 developed in chloroform-hexane, 1:2) at $R_F = 0.52, 0.33, 0.18,$ and $0.00$ (designated A, B, C, and D, respectively). Product B, which was the major product, was readily identified as benzpinacolone (X) by comparison of the infrared spectrum of the pyrolysate with that of an authentic sample of X and by its ultraviolet spectrum and $R_F$ value, both of which were identical to those of an authentic specimen. Product A was identified as tetraphenylethylene (XV) by its $R_F$ value and ultraviolet spectrum, and product C was identified as tetraphenylethylene oxide (IX) by the same evidence. Substance D was apparently polymeric. Although

\[
\begin{align*}
\text{SO} & \quad \text{Ph}_2\text{C} - \text{CPh}_2 \xrightarrow{\Delta} \text{PhCOCPh}_3 + \text{Ph}_2\text{C} = \text{CPh}_2 + \text{Ph}_2\text{C} - \text{CPh}_2 \\
\text{IV} & \quad \text{X} & \quad \text{XV} & \quad \text{IX}
\end{align*}
\]

identification of A as tetraphenylethylene is not positive,
it can be stated that this product was positively not 9,10-diphenylphenanthrene (see Chapter II), for the published ultraviolet spectrum of the latter\textsuperscript{61} is readily distinguished from that of the former.

Ultraviolet analysis of the products formed upon pyrolysis of IV gave the results reported in Table 2.

<table>
<thead>
<tr>
<th>Product</th>
<th>Mole Percent Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>99.7±7</td>
</tr>
<tr>
<td>XV</td>
<td>3.5±0.3</td>
</tr>
<tr>
<td>IX</td>
<td>trace*</td>
</tr>
</tbody>
</table>

*An estimate of 0.2 mole percent was based on visual comparison with standards on another plate.

In view of the ready appearance of tetraphenylethylene oxide (IX) resulting from various reactions of the sulfite IV (see Chapter II) and the observation that this epoxide was the major product formed when pyrolysis was carried out in various organic solvents (diglyme, dimethylformamide, and nitrobenzene), the low yield of IX upon neat pyrolysis was surprising. As a control reaction, therefore, IX was pyrolyzed under the same conditions as IV and was found to be converted to benzpinacolone (X) to the extent of only 2.5%, the rest remaining unchanged (the pure epoxide was found to rearrange to a slight extent under the influence
of the silica gel on a thin layer chromatographic plate).

The epoxide was found to be more reactive when pyrolyzed in the presence of the sulfite, however. A series of intimate mixtures of IV and IX was prepared by adding a measured volume of a standard solution of one compound (in tetrahydrofuran) to the other compound contained in a culture tube. After enough tetrahydrofuran was added to dissolve all solid matter at room temperature, the solvent was rapidly removed in vacuo to leave a thin crust of the mixed solids. This solid was then pyrolyzed and analyzed in the usual manner. When various mixtures of epoxide and sulfite, in gram ratios between 0 and 2.0 epoxide to sulfite, respectively, were pyrolyzed and the pyrolysis products analyzed by thin layer chromatography, epoxide spots were either completely absent or barely perceptible (artificial mixtures of the epoxide and ketone spotted and developed on a thin layer chromatographic plate showed that as little as 1.5 microgram of epoxide could be readily detected). Pyrolysis of mixtures of epoxide and sulfite in proportions of 10:1 or greater left large amounts of the epoxide unchanged, however. The fate of the epoxide, as may be deduced from Table 3, was to be largely if not completely converted to benzpinacolone (X).

The catalyzed rearrangement of this epoxide to the ketone could be mediated by 1) sulfur dioxide released upon pyrolysis, 2) sulfur trioxide released as the sulfite
Table 3
Pyrolysis of a Mixture of IV and IX

<table>
<thead>
<tr>
<th>Pyrolysis Mixture</th>
<th>Micromoles</th>
<th>Mole Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfite (IV)</td>
<td>2.66</td>
<td>46.6</td>
</tr>
<tr>
<td>Epoxide (IX)</td>
<td>3.06</td>
<td>53.5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>5.73</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>

**Products**

<table>
<thead>
<tr>
<th>Product</th>
<th>Value</th>
<th>Mole Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketone (X)</td>
<td>5.26±0.35</td>
<td>92.0±6.3</td>
</tr>
<tr>
<td>Tetraphenyldienelethylene (XV)</td>
<td>0.13±0.01</td>
<td>2.3±0.1 (4.9±0.3)*</td>
</tr>
<tr>
<td>Epoxide (IX)</td>
<td>trace</td>
<td>trace</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>5.39</strong></td>
<td><strong>94.3</strong></td>
</tr>
</tbody>
</table>

*Based on micromoles sulfite pyrolyzed only.

It was observed that the epoxide was soluble in liquid sulfur dioxide contained in a sealed glass tube at the pyrolysis temperature, and when such a tube was heated for 1.5 hours and the products analyzed, only a small amount of the ketone was found and the bulk of the epoxide was recovered unchanged. An attempt at similarly pyrolyzing the epoxide in liquid sulfur dioxide into which a small amount of sulfur trioxide had been dissolved resulted in dark colored pyrolysis products which did not migrate from the origin of a thin layer chromatogram. The
results of this experiment are, however, inconclusive, since the preparation and entry of the sulfur trioxide into the reaction tube was not done under a strictly anhydrous atmosphere, and since the amount of sulfur trioxide thus admitted was not carefully controlled. It does seem unlikely, however, that the small amount of sulfur trioxide released (if it is released at all as such) should catalyze the conversion of so much of the epoxide to the ketone, especially since the pyrolyses were conducted under a gentle stream of dry nitrogen, and the catalytic role of the sulfite itself remains as a strong possibility.

As pointed out in the introduction, only one previous case of epoxide formation resulting from pyrolysis of a five-membered cyclic sulfite has been reported. The present research, however, has demonstrated that the epoxide is the major product upon pyrolysis in solution. The question of whether the epoxide is an intermediate whose catalyzed rearrangement yields the ketone in the absence of a solvent is an important one. It is to be expected that the rearrangement of the epoxide would yield products in different proportion from the rearrangement of the corresponding sulfite, and the extent of partition between routes requiring and not requiring the intermediacy of the epoxide should be determined in order correctly to account for product distributions. At present no evidence
is extant to confirm the intermediacy of this epoxide in neat pyrolysis (no more than a trace of epoxide has ever been observed in thin layer chromatographic analysis of pyrolysis products), but neither has there been found anything which would preclude this possibility.

Pyrolyses executed in organic solvents yielded mostly the epoxide with a small amount of tetr phenylethylene and traces of other products. Rates of these pyrolyses were faster in polar solvents than in non-polar ones. This observation, which is in keeping with results previously reported for pyrolysis of non-cyclic sulfites having no beta hydrogens, suggests the existence of ionic intermediates.

The epoxide (and ethers in the case of non-cyclic sulfites) may result either from successive or synchronous C-0 and S-0 scission. In cyclic sulfites the possibility exists for attack of the carbonium ion generated by C-0 cleavage on the sulfite S-0-C oxygen. In the case of the non-cyclic sulfites that yield ethers on pyrolysis, the ion pair R-0-...+CR3 is believed to exist after loss of sulfur dioxide. Were this mechanism followed in the case of a five-membered cyclic sulfite, a 1,3-dipole would result. These possibilities are illustrated below:

\[
\begin{align*}
\text{ROSO}_2 & \quad \text{R}^+ \quad \text{SO}_2^-
\end{align*}
\]
The ketonic products could arise \textit{via} the same intermediates if rearrangement is faster than epoxide formation.

That the amount of tetraphenylethylene formed in solvent pyrolyses increased with the polarity of the solvent was an unexpected observation. Large amounts of tetraphenylethylene resulted from pyrolysis in nitrobenzene and dimethylformamide, and considerably smaller amounts resulted from pyrolysis in diglyme and tetralin. It would be premature to speculate on details of this reaction, however, since pyrolysis in solvents of low polarity also favored formation of colored matter ($R_F=0.00$, after usual analysis) and small amounts of other unidentified by-products. Further work is required better to understand details of this pathway. It would be interesting to see, for example, to what extent the sulfite of a disubstituted, tetraaryl \textit{meso} glycol gave \textit{cis} and \textit{trans} olefins on pyrolysis.

In summary, it was shown that pyrolysis of neat benzopinacol sulfite yields predominately the rearranged ketone (benzpinacolone). Since a carbonium ion or partial
carbonium ion was suggested by this and previous work, it seems that this rearrangement provides another member in the series of carbonium-ion induced rearrangements of the type below.

Further work remains to be done to determine details of this reaction, such as 1) to what extent the epoxide is formed in neat pyrolysis, 2) the kinetic order of the rearrangement (unimolecular, bimolecular, etc.), and 3) the mechanism of tetraphenylethylene formation.
CHAPTER V

EXPERIMENTAL

All melting points were determined in open capillary tubes in a Thomas Hoover melting-point apparatus and are uncorrected. Infrared (ir) spectra were recorded on Beckman IR 8 and Perkin-Elmer 700 spectrophotometers. Nuclear magnetic resonance (nmr) spectra were taken on a Hitachi Perkin-Elmer R-20 60MHZ spectrometer. Ultraviolet (uv) spectra were recorded on Perkin-Elmer 202 and Cary 14 spectrophotometers in solvent ethanol. Gas-liquid partition chromatography (glpc) was performed on a 6' x 1/4" SE-30 column at 209° in a Loenco 2400 Gas Chromatograph with a helium carrier-gas flow-rate of about 60 cm3/min. Combustion analyses were carried out by Schwarzkopf Microanalytical Laboratories, Woodside, New York and Elek Microanalytical Laboratories, Harbor City, California.

2-Bromo-2'-methoxyacetophenone (VI). The procedure of Buckman et al.32 was followed. A yield of 80% of the bromoketone was thus obtained: bp 130° (1mm); ir (neat) 1680 cm⁻¹ (C=O); nmr (CCl₄) δ 7.3 (4H, m, ArH), 4.39 (2H, s, CH₂Br), and 3.96 (3H, s, OCH₃).

2-Azido-2'-methoxyacetophenone (VII). A solution of sodium azide (0.975 g, 15.0 mmole) in water (3 ml) was
added at once with stirring to the above bromoketone (3.00 g, 13.1 mmole) dissolved in ethanol (7.5 ml). Within thirty minutes there appeared a suspension of pale yellow oil which solidified on cooling. The solid was filtered and washed repeatedly with water until a silver nitrate test for bromide anion in the wash water was negative. After drying, 2.24 g (89%) of crude azide was recovered. It was recrystallized to constant melting point from methanol: mp 45-46°; ir (nujol) 2130 (strong, N\textsubscript{3}), 2210 (weak, N\textsubscript{3}), and 1675 cm\textsuperscript{-1} (C=O); nmr (CCl\textsubscript{4}) \delta 7.3 (4H, m, ArH), 4.32 (2H, s, CH\textsubscript{2}N\textsubscript{3}), and 3.95 (3H, s, OCH\textsubscript{3}).

Anal. Calcd for C\textsubscript{9}H\textsubscript{8}N\textsubscript{3}O\textsubscript{2}: C, 56.54; H, 4.74; N, 21.98. Found: C, 56.82; H, 4.93; N, 21.96.

2-Amino-2'-methoxyacetophenone hydrochloride (V). A suspension of 5% palladium on charcoal (0.375 g) in absolute ethanol (2 ml) was stirred under hydrogen at one atmosphere pressure and room temperature for ten minutes. A solution of azidoketone VII (1.00 g) in acidified ethanol (2.6 ml of 36% hydrochloric acid in 7.8 ml absolute ethanol) was admitted into the catalyst--ethanol mixture and allowed to react for 29 hr. The mixture was filtered and the catalyst was washed with three small portions of absolute ethanol, and the solution was concentrated on a rotary evaporator. Absolute ether was added until moderate precipitation of product occurred. After nine days of
refrigeration the solid was collected, washed with absolute ether, and dried to yield 0.763 g (72%) of the white, crystalline salt: mp (methanol--benzene) 165.0-165.6° (dec); ir (CCl₄) 2700 (NH₃⁺), 2580 (NH₃⁺), and 1665 cm⁻¹ (C=O); nmr (DMSO-d₆) 8.62 (3H, s, NH₃⁺), 7.4 (4H, m, ArH), 4.35 (2H, c, COCH₂), and 3.56 (3H, s, OCH₃).

2-Amino-1-(2-methoxyphenyl)-1-phenylethanol (II).
The Grignard reagent was prepared in flame-dried apparatus, and these procedures were carried out under an atmosphere of dry nitrogen. Phenylmagnesium bromide was prepared by reaction of dry bromobenzene (1.87 g, 11.9 mmole) with magnesium turnings (0.29 g, 12.1 mmole) in absolute ether (5 ml). The finely powdered amine salt from the previous procedure (0.402 g, 2.0 mmole) was added in small portions with stirring over 65 min, and the mixture was allowed to reflux gently in an oil bath for 4.5 hr. The reaction mixture was then poured into a solution of ammonium chloride (0.5 g) in water (10 ml plus one drop of concd ammonium hydroxide). After hydrolysis was complete, the layers were separated, the aqueous layer was extracted twice with ether, and the ether extracts were pooled with the original organic phase. After drying (MgSO₄), the solution was filtered, diluted with absolute ether (40 ml), and acidified with gaseous hydrogen chloride. A white precipitate formed at once, and after prolonged addition of hydrogen chloride a pink solid began to appear. At
This point addition of the gas was stopped and the flask was refrigerated for two days. The product was then filtered, washed with ether and allowed to dry. Yield 0.298 g (53%); mp 168-169°, lit. 175-176°.

The free amine (II) was obtained by dissolving the hydrochloride (0.500 g) in water (5 ml) and adding 1 M sodium hydroxide (ca. 2 ml) dropwise. The resulting suspension was extracted with chloroform and the organic phase was dried (MgSO₄) and solvent was removed on a rotary evaporator. After recrystallization to constant melting point from chloroform--ether, the amine was obtained as white crystals: mp 104-106° (lit. mp 107-108°); ir (CDCl₃) 3485 cm⁻¹ (NH₂); nmr (CDCl₃) δ 7.0 (9H, m, ArH), 3.48 (3H, s, OCH₃), 3.37 (1H, d, J=13 Hz, CHNH₂), 3.09 (1H, d, J=13 Hz, CHNH₂), and 2.0 (3H, s, broad, NH₂ and OH).

2-Methoxydeoxybenzoin (XII). The reaction of 2-methoxybenzamide with benzylmagnesium bromide was carried out according to the procedure of Farooq et al. Purification of the product was effected by application of 15 g of the crude product to a column of 575 g of silica gel and elution with ether--pentane (1:4). Ir (neat) 1675 cm⁻¹ (C=O); nmr (CDCl₃) δ 7.2 (9H, m, ArH), 4.27 (2H, s, COCH₂), 3.83 (3H, s, OCH₃); uv λ max 207, 247, and 313 nm.

2-Methoxybenzil. By the procedure of Farooq et al., 2-methoxydeoxybenzoin (XII) (3.93 g, 17.4 mmole) was
oxidized\textsuperscript{65} by selenium dioxide (2.12 g, 19.1 mmole) in acetic anhydride (35 ml). Chromatography of the resulting oil on silica gel with petroleum ether--chboroform (1:1) provided 2.87 g (69\%) of nearly pure 2-methoxybenzil as a yellow oil which slowly crystallized, mp 67-68°, plus ca. 0.6 g of impure material.

The compound prepared as above was identical with another sample prepared by benzoin condensation between 2-methoxybenzaldehyde and benzaldehyde, followed by oxidation of the product with potassium permanganate, as described by Brass et al.\textsuperscript{66} Mp 70.1-70.7° (lit.\textsuperscript{66} 71-72°) ir (CCl\textsubscript{4}) 1655 and 1676 cm\textsuperscript{-1} (C=O); nmr (CDCl\textsubscript{3}) \delta 7.4 (9H, m, ArH) and 3.45 (3H, s, OCH\textsubscript{3}).

2-Hydroxybenzil. By following the procedure of Somin and Kuznetsov,\textsuperscript{67} an amber oil was obtained\textsuperscript{65} in 64\% yield which was only slightly impure as judged by thin layer chromatographic analysis on silica gel: ir (neat) 3350 (OH, very broad), 1720, 1675, and 1630 cm\textsuperscript{-1} (C=O); nmr (CDCl\textsubscript{3}) \delta 12.4 (1H, broad s, ArOH), and 7.6 (9H, m, ArH).

2'-Hydroxydeoxybenzoin. By the procedure of Specht\textsuperscript{68} 2'-hydroxydeoxybenzoin was obtained\textsuperscript{65} as a yellow solid. This solid was crystallized from ethanol--water to give tan flakes: mp 126-130° (lit.\textsuperscript{68} 110-120° (dec)); ir (CCl\textsubscript{4}) 3490 (OH) and 1675 cm\textsuperscript{-1} (C=O); nmr (acetone-d\textsubscript{6}) \delta 8.6 (1H, broad s, OH), 7.5 (9H, m, ArH), and 4.33 (2H, s, CH\textsubscript{2}).
2'-Methoxydeoxybenzoin (XIII). 2'-Hydroxydeoxybenzoin (0.734 g) in 2N sodium hydroxide (7.5 ml) was methylated by shaking with two 0.8-ml portions of dimethyl sulfate. The crystalline product was collected, washed with water, dried (MgSO₄), dissolved in ether and filtered through a short alumina column. Evaporation of solvent left XIII as a light yellow, crystalline solid (0.739 g, 94%); mp 56-58°. Crystallization from 2 ml of methanol raised the melting point to 58.5-59.5°; successive crystallizations of a portion of the solid from small quantities of methanol gave mp 60-61° (lit. 68.61.5-62°); ir (CCl₄) 1683 cm⁻¹ (C=O); nmr (CDCl₃) δ 7.4 (9H, m, ArH), 4.27 (2H, s, CH₂), and 3.74 (3H, s, OCH₃); uv λ max EtOH 204 and 243 nm.

3-Phenylbenzofuran (XIV). The procedure of Davies and Middleton was followed. Bp 115° (1mm) (lit. 110° (0.3 mm)); nD²⁵ = 1.6308 (lit. nD²⁵ = 1.6296); ir (neat) 860 cm⁻¹ (furan band); nmr δ 7.4 (m); uv λ max EtOH 205 and 270 nm.

Deamination of II. The aminoethanol II (199.6 mg) was dissolved in 50% aq acetic acid and the solution was placed in an ice bath. A solution of sodium nitrite (284 mg, a fivefold excess) in water (2 ml) was added dropwise with stirring over five minutes, and the mixture was allowed to stir for 24 hr at 0°. At the end of this period, the reaction was quenched by adding a 10% aq sulfamic acid solution dropwise until the solution no
longer gave a positive test with starch-iodine paper. The reaction mixture was transferred to a continuous extractor, diluted with water (21 ml), and subjected to continuous extraction with petroleum ether for approximately 8 hr. The extract was stirred with anhydrous potassium carbonate until the solution was neutral; then it was filtered and the potassium carbonate residue was dissolved in water and extracted with chloroform. These extracts were dried (MgSO₄) and combined with the original organic phase. After removal of the solvent on a rotary evaporator, the crude product weighed 160.5 mg. This mixture was dissolved in 5 ml of ether and filtered through 2 g of neutral alumina. The nonpolymeric products were readily eluted with ca. 20 ml of ether; removal of solvent left 151.6 mg of an oil. This mixture was subjected to the analysis described below; results are recorded in Table 1.

A similar run was carried out with 200.2 mg of II in an oil bath at 30±1° for four hours. After continuous extraction the crude product weighed 162.4 mg; after elution through alumina, 133.0 mg of mixture was recovered. This was subjected to the analyses described below and the results are recorded in Table 1.

The 3-phenylbenzofuran could be separated from the deoxybenzoins by chromatography on silica gel (100-200 mesh). Product XIV was eluted with either--petroleum ether (2:98), and XII and XIII were eluted with ether.
Determination of the ratio of XIV to XII and XIII in the deamination products. A mixture of known composition was prepared from XIV and the deoxybenzoins separated on column chromatography; this was dissolved in ether and analyzed by glpc to determine detector response to each of the two peaks in the chromatogram. The retention time for XIV was 6.3 min, and that of the deoxybenzoin mixture was 12.1 min. Then the product mixtures from the previous procedure were analyzed by glpc with appropriate detector-response corrections applied to the measured peak areas (planimeter).

Determination of proportions of XII and XIII in the deamination products. Standard mixtures of the deoxybenzoins XII and XIII were prepared such that each mixture weighed ca.50 mg. These mixtures were 75.8, 79.6 and 83.6% in XII. Each of these deoxybenzoin mixtures was dissolved in 0.3 ml of CDCl₃ and its nmr spectrum recorded. The methoxy proton peaks of the two compounds differ in chemical shift by 6.4 Hz in this solvent and at this concentration, and expansion of the sweep to 120 Hz separates the two signals. The integrations of the expanded methoxy peaks of the standards were used for comparison with those of the deamination samples. Peak-height ratios of these signals in the standard mixtures, determined at both 600- and 120-sweep widths, were also determined and plotted against composition. The ratio of
XII to XIII in the alumina-filtered deamination mixture was determined by the nmr integration and by comparison with the peak-height ratio plots. Agreement between the values determined by the three methods was within 1%. It was demonstrated that presence of XIV in the deamination samples had no effect on this analysis.

**Deamination control experiment.** Compound XIII (50 mg) was subjected to the deamination conditions described above. Similar work-up followed by continuous extraction recovered 44 mg of crystalline material; this was filtered through alumina and then analyzed by glpc. The material was indicated to be pure XIII.

**2-Methoxybenzophenone.** The synthesis of a 2-methoxybenzhydrol was carried out according to the procedure of Stoermer and Friderici; the crude, tan colored product was obtained in 85% yield.

An oxidizing solution, which was prepared by dissolving sodium dichromate dihydrate (87 g) in a mixture of acetic acid (65 ml), sulfuric acid (118 ml) and water (384 ml), was chilled to 10° and added dropwise over the course of 45 minutes to a solution of crude, chilled 2-methoxybenzhydrol (50 g) in benzene (400 ml). The progress of the reaction was monitored by thin layer chromatography (silica gel G developed in acetic acid--acetone--petroleum ether, 1:4:20 and visualized by ultraviolet light and ceric nitrate spray). After stirring at
room temperature for 8 days, the phases of the reaction mixture were separated, and the aqueous layer extracted with ether until the ether extract was colorless. The pooled organic phases were washed with 5% sodium bicarbonate until the aqueous wash was basic. The organic phase was filtered, washed once with water, and dried (MgSO₄). After filtration the ether was removed from the bright yellow solution on a rotary evaporator, and the crude, brown product, which weighed 46 g, was distilled under reduced pressure. The fraction boiling at 162-168° (4 mm) (lit. 210° (27 mm)) was used in subsequent reactions: yield, 25.3 g (51%); mp 34.5-37.5° (lit. 39°); nmr (CDCl₃) δ 7.3 (9H, m, ArH) and 3.58 (3H, s, OCH₃); ir (neat) 1660 (C=O) and 1250 cm⁻¹ (ArOCH₃).

2,2'-Dimethoxybenzopinacol. The classical photo-reduction of Bachmann was applied to 2-methoxybenzophenone. In a borosilicate glass flask was dissolved 2-methoxybenzophenone (6.00 g) in isopropyl alcohol (34 ml) which was acidified with one drop of dilute acetic acid solution (one drop glacial acetic acid in 17 ml isopropyl alcohol). The flask was corked tightly and clamped in the inverted position on the roof where it could be exposed to bright sunlight. The white crust of product which formed on the walls of the flask was shaken down from time to time better to allow penetration of sunlight. After 19 days the product was filtered, washed twice with isopropyl alcohol
and dried in vacuo: yield 4.78 g (79%); mp 173-176° (lit.\textsuperscript{2a} 168-169°); ir (nujol) 3480 (OH) and 1235 cm\textsuperscript{-1}(ArOCH\textsubscript{3}); nmr \delta (CDCl\textsubscript{3}) 7.0 (18H, m, ArH); 6.10 and 5.44 (2H, 2 s, OH), and 3.33 and 3.20 (6H, 2 s, OCH\textsubscript{3}).

Following Matsumoto\textsuperscript{7a} the product (0.500 g) was subjected to column chromatography on silica gel (100-200 mesh). Despite slow elution (benzene--hexane, 3:2), only the first product obtained from the column (identified by Matsumoto as the meso diatereomer) could be obtained pure.

2,2'Dimethoxybenzopinacol sulfite (III). The pyridine used was dried over molecular sieves. A fresh bottle of thionyl chloride was used without further purification. To a stirred solution of 2,2'-dimethoxybenzopinacol (3.99 g, 9.36 mmoles) dissolved in pyridine (19 ml) was added at once thionyl chloride (2.46 g, 20.7 mmoles). The reaction flask was immediately cooled to room temperature in an ice bath and allowed to stir overnight. After most of the pyridine was removed on a rotary evaporator, the residue was dissolved in chloroform and extracted three times with water. The pooled water extracts were extracted once with chloroform, and all organic phases were pooled and dried (MgSO\textsubscript{4}). After removal of the solvent, 4.00 g (90%) of pale yellow, glassy solid remained. Attempted recrystallizations from polar solvents invariably gave substantial amounts of the epoxide (IX), as evidenced by the typical rhombic crystals and by the characteristic signal in the
nmr spectrum. Crystallization from hexane gave pure, colorless, tetragonal prisms, mp 115-120°C (dec); ir (CCl₄) 1260 (ArOCH₃) and 1210 cm⁻¹ (ν=0₄₆); nmr (CDCl₃) δ 7.0 (18H, m, ArH), and 3.28 (6H, s, OCH₃).

Anal. Calcd for C₂₈H₂₄O₅S: C, 71.16; H, 5.12; S, 6.78. Found: C, 70.95; H, 5.01; S, 6.52.

**Benzopinacol.** Zinc amalgam was prepared by rinsing 20 mesh zinc (60 g) with hydrochloric acid (0.1 M) and treating the cleaned metal with mercuric chloride (4.5 g in 3 ml conc hydrochloric acid and 75 ml water) according to the procedure given by Vogel. The amalgam was washed once with water, three times with 95% ethanol and twice with absolute ethanol. Benzophenone (36.4 g, 0.2 moles), which was dissolved in absolute ethanol (70 ml), was combined with the zinc amalgam in a round-bottomed flask. To the stirred mixture was added hydrogen chloride (dried by passage through sulfuric acid). After three hours the white precipitate was collected by filtration and washed with ethanol. After recrystallizing twice from acetone-water and once from benzene-hexane, the melting point was 176.5-182.0°C (lit. 182-183); ir 3420 cm⁻¹ (OH).

**Benzopinacol sulfite (IV).** This sulfite was prepared exactly the same way as III, and the crude product was recovered in 92% yield. The product was crystallized repeatedly to give apparently pure, white, block-like crystals: mp 119-122°C (dec); ir (nujol) 1235 cm⁻¹ (very strong,
Anal. Calcd for C_{26}H_{20}O_{3}S: C, 75.70; H, 4.89; S, 7.77. Found: C, 75.95; H, 4.94; S, 7.72.

Pyrolysis of benzopinacol sulfite (IV). Pyrolyses were carried out in new borosilicate culture tubes heated in an oil bath maintained at 137°. Quantitative runs were conducted under a gentle stream of dry nitrogen in new, scrupulously cleaned culture tubes which had been rinsed with ammonium hydroxide and well dried before pyrolysis. These precautions made no noticeable difference in estimated product proportions. Solutions for pyrolysis were prepared by dissolving ca. one mg of the sulfite in 100 microliters of an organic solvent (nitrobenzene, dimethylformamide, diglyme, or tetralin). After the pyrolysis the solution was evaporated to dryness in vacuo.

Analysis of sulfite pyrolysis products. The pyrolysis products were dissolved in a known volume of tetrahydrofuran and spotted, by means of a syringe, onto an 8" x 8" glass plate coated to a thickness of 0.25 mm with silica gel GF 254. The plate was developed in chloroform--hexane (1:2) and visualized under a short wave ultraviolet lamp.

For quantitative runs, product standards were spotted on the same plate. A pure sample of each product to be quantitated was spotted in three different amounts which encompassed the anticipated yield of that product after pyrolysis. After development each spot was removed from
the plate by means of a vacuum cleaning apparatus\textsuperscript{75} and eluted with 2.00 ml of 95\% ethanol. Ultraviolet absorbances were measured on a Cary 14 spectrophotometer, and a blank reading was subtracted from the measured value. The ultraviolet absorbance wavelengths used for this quantitation were 253 (benzpinacolone, X), 233 (epoxide IX), and 241 nm (tetraphenylethylene). Concentrations of the various products were determined by interpolating the absorbance vs. concentration graphs prepared from the standards. This method was found to be in error by less than seven percent of the estimated value (an error of at least five percent is expected for this method\textsuperscript{75}).
REFERENCES


65. This reaction was kindly carried out by Dr. Francis Harris.


