THE SYNTHESIS AND WOLFF REARRANGEMENT
OF SOME DIAZOINDANONES

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By
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*****

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A. General Introduction

The hydrocarbon benzocyclobutene (IV) and several of its simple 1- and 1,2-substituted derivatives have been prepared recently in these laboratories.\(^1,2\) The rather severe strain which must be present in molecules possessing this ring system makes these compounds of considerable interest, and a study of compounds belonging to this series should provide valuable information concerning the effect of such strain on their chemical and physical properties. Obviously, such a study would be aided by the development of a general method of synthesis for compounds of this type.

\[
\begin{align*}
\text{II} & \xrightarrow{\text{NaI}} \text{Br} \\
\text{III} & \xrightarrow{\text{H}_2/\text{Pd}} \text{IV}
\end{align*}
\]

The key step in the preparation of the compounds so far described is the reaction, first carried out by Finkelstein\(^3\) in 1910, of \(\alpha,\alpha,\alpha',\alpha'\)-tetrabromo-o-xylene (I) with alcoholic sodium iodide.

---

\(^1\) M. P. Cava and D. R. Napier, J. Am. Chem. Soc., 78, 500 (1956); ibid., 72, 1701, 5606 (1957).

\(^2\) D. R. Napier, Ph. D. dissertation, The Ohio State University, 1957.

\(^3\) H. Finkelstein, Inaugural dissertation, Strasbourg, 1910.
yielding mainly 1,2-dibromobenzocyclobutene (II), Equation (1). This compound was converted by further treatment with sodium iodide and iodine into the corresponding diiodo compound III, which on catalytic reduction in the presence of base yielded the parent hydrocarbon (IV), Eq. (2). The extension of these reactions as a general method of synthesis of derivatives of IV bearing substituents in the benzene ring is limited by the inaccessibility of the requisite tetrabromo compounds (similar to I). No derivatives of IV substituted in the benzene ring have been described heretofore.

One approach to the synthesis of derivatives of benzocyclobutene would be to make use of derivatives of its higher ring-homolog, indan (V), which are, in general, readily available through standard cyclization procedures. If reactions leading to contraction of the five-membered ring could be carried out on appropriate compounds, then the ring system of IV would be formed. The high strain energy which must be overcome in passing from V to IV however, might be expected to impose a barrier too formidable for many reactions, and one might anticipate that some reactions which normally lead to ring contraction would take an altered course when applied to this system.

As an example of such behavior one may cite the acid-catalyzed rearrangement of substituted indenone oxides, a reaction which has been rather extensively investigated. The normal reaction for

4 E. Wietz and A. Scheffer, Ber., 54, 2234 (1921).
\(\alpha,\beta\)-epoxyketones involves rearrangement to a \(\beta\)-dicarbonyl system,\(^4\text{-7}\) Eq. (3), and House and Wasson observed\(^8\) that, as expected, ring contraction did occur in a cyclic case, Eq. (4). However, in the case of the indene oxide (VIII) the reaction took a different course, yielding not the benzocyclobutene (IX), Eq. (5), but isocoumarones (X), Eq. (6). With 2,3,5,6-tetraphenyldienone oxide (VIII, \(R_1 = R_2 = \phi\)),

a deep red product was obtained which was thought to be 2,4,5-triphenyl-
2-benzoylbenzoclobutenone (IX, R₁ = R₂ = $\emptyset$), but this was later shown not
to be the case.⁷

In choosing a possible reaction to investigate for this purpose
the following criteria would seem to be applicable: the reaction should
employ starting materials which one might expect to be reasonably acces-
sible; it should proceed via a high-energy intermediate; it should yield
products capable of convenient isolation and purification. A reaction
which meets these requirements is the Wolff rearrangement (see
discussion below).

The required intermediates for the Wolff rearrangement in this
system are the diazoindanones (XI) or (XII). Either of these on
rearrangement should yield the corresponding benzocyclobutene-1-car-
boxylic acid (XIII), Eqs. (7) and (8). No diazoindanones have as yet
been described.
B. The Wolff Rearrangement

The rearrangement of an $\alpha$-diazoketone with loss of nitrogen to form a carboxylic acid or derivative thereof, Eq. (9), is known, after its discoverer, as the Wolff rearrangement. As usually encountered

$$ R-C-C-R' \rightarrow R-C=CH-CO_2H $$  \hspace{1cm} (9)

$$ R-C-Cl \rightarrow R-C-C-H \rightarrow R-CH_2-CO_2H $$  \hspace{1cm} (10)

$$ R-C-C-R' \rightarrow R-C=CH-CO_2H $$  \hspace{1cm} (11)

it constitutes the second step in the well-known Arndt-Eistert procedure for acid homologation, Eq. (10). Mechanistically the reaction is formulated in three steps: the loss of nitrogen to produce a neutral, dicovalent carbon fragment (a "carbene"), migration of the group attached to the carbonyl to form a ketene, and reaction of the ketene with the solvent to give the observed product, Eq. (11). The

1 L. Wolff, Ann., 394, 25 (1912).
2 F. Arndt and B. Eistert, Ber., 68, 200 (1935).
4 G. Schroeter, Ber., 42, 2346 (1909).
5 It will be noticed that Schroeter's paper antedates that of Wolff. The discoveries were independent but Wolff is given credit since the reaction was described earlier in certain of his students' dissertations, e.g., Greulich, Jena, 1905. The reaction is infrequently called the Wolff-Schroeter rearrangement.
variation in products with reaction medium—acid, ester or amide from water, alcohol or amine, respectively—is strong presumptive evidence for the existence of the ketene as an intermediate. Indeed, if the rearrangement be carried out in an aprotic solvent the ketene can be isolated. Isotopic labelling experiments have shown that, as Eq. (11) requires, the carbonyl group in the diazoketone becomes the carbonyl group in the rearranged acid. Migration of R with its pair of electrons would imply retention of configuration, and such retention has been demonstrated.

In practice the rearrangement usually requires catalysis. The catalysts employed are varied, but usually contain silver in some form, e.g., finely divided silver or silver oxide, silver thiosulfate or ammoniacal silver nitrate. Less frequently platinum or copper has been used, but the latter can promote side reactions. In alcohol solutions a mixture of silver benzoate and triethylamine is particularly effective, but fails in some cases. None of these catalysts is generally applicable for all types of diazoketones and all solvent systems. The only truly general catalytic agent would appear to be ultraviolet light (vide infra).

One implication of the migration occurring in this rearrangement is, that if a cyclic diazoketone undergoes rearrangement, a ring contraction results, Eq. (12). Examples of such reactions have been reported only comparatively recently. In 1944, Süss\textsuperscript{12} reported the results of an investigation of the effect of ultraviolet light on solution of o-diazoöxides. This author showed, for example, that irradiation of solutions of the diazoöxide XIV\textsuperscript{13} derived from 1-amino-2-naphthol produced indene-1-carboxylic acid (XV), Eq. (13).

In other words a normal Wolff rearrangement had occurred. Similarly

\textsuperscript{12} O. Süss, åm., 556, 65, 85 (1944).

\textsuperscript{13} In accordance with common practice the diazoöxides are written here in the zwitter-ion form and the diazoketones are given covalent structures. It is to be realized, of course, that from the standpoint of resonance theory the actual molecular structure in each case is a hybrid of these (and other) canonical forms, e.g.:

\begin{align*}
\text{(a)} & \quad \text{(b)} & \quad \text{(c)} \\
\begin{array}{lll}
\text{-}\text{C} & \equiv & \text{C} \\
\text{N}^+ & \equiv & \text{N}^+ \\
\text{N}^- & \equiv & \text{N}^-
\end{array} & \quad \begin{array}{lll}
\text{-}\text{C} & \equiv & \text{C} \\
\text{N}^+ & \equiv & \text{N}^+ \\
\text{N}^- & \equiv & \text{N}^-
\end{array} & \quad \begin{array}{lll}
\text{-}\text{C} & \equiv & \text{C} \\
\text{O}^- & \equiv & \text{N}^+
\end{array}
\end{align*}

Structure (c) would be expected to contribute to a greater extent in the diazoöxides since in this form the conjugation of the aromatic ring is maintained.
the diazoamine XVI from o-aminophenol underwent rearrangement, Eq. (14); the actual isolated product in this case was the azo compound XVIII resulting from coupling of the starting material with the cyclopentadiene carboxylic acid (XVII) formed in the rearrangement, Eq. (15).

\[
\begin{align*}
\text{XVI} & \xrightarrow{\text{H}_2\text{O} / \text{hv}} \text{XVII} \\
\text{XVI} + \text{XVII} & \rightarrow \text{XVIII}
\end{align*}
\]

The results of Süss have been extended by Horner and co-workers\(^{14,15,16}\) who have studied the effect of ultraviolet light on diazoketones generally. These workers have found that a wide variety of diazoketones when irradiated under various conditions will undergo the Wolff rearrangement, and using this method have obtained some truly remarkable results.

Of chief interest here are the results obtained by this group\(^{16}\) with diazocamphor (XIX). It has been known for many years that this

\(^{15}\) L. Horner and E. Spietschka, Ber., 85, 225 (1952).
\(^{16}\) L. Horner and E. Spietschka, Ber., 86, 934 (1955).
compound readily undergoes thermal decomposition, either alone,\textsuperscript{17} or in the presence of copper powder,\textsuperscript{18} to give the tricycle derivative, XX, Eq. (16). Irradiation of a solution of XIX in aqueous dioxane at 0°,

\[
\text{XIX} \xrightarrow{\Delta} \text{XX} \tag{16}
\]

however, produced normal rearrangement, yielding 1,6,6-trimethyl(1,1,2)-bicyclohexane-2-carboxylic acid (XXI), Eq. (17). In a similar manner,

\[
\text{XIX} \xrightarrow{\text{H}_2\text{O}, h\nu} \text{XXI} \tag{17}
\]

irradiation of XIX in the presence of ethanol, aniline, diethylamine or hydrazine afforded the ester XXII, anilide XXIII, diethylamide XXIV and the hydrazide XXV, respectively, Eq. (18).

\[
\text{XIX} \xrightarrow{\text{RH}, h\nu} \text{XXII}, \text{XXIII}, \text{XXIV, XXV} \tag{18}
\]

\[
\begin{align*}
\text{XXII, } R &= \text{OEt} \\
\text{XXIII, } R &= \text{NH-F} \\
\text{XXIV, } R &= \text{NET}_2 \\
\text{XXV, } R &= \text{NNHN}_2
\end{align*}
\]

\textsuperscript{17} R. Schiff, Ber., 14, 1375 (1881).

The formation of this highly-strained bicyclic system and the fact that good yields of each of the derivatives, as well as of the acid itself, were obtained indicate the power of this photolytic method. Other workers have successfully used this technique,\textsuperscript{9,19} which would certainly seem to be the method of choice in most instances.

Various side reactions can occur during a Wolff rearrangement. The most common of these involves reaction with the solvent without rearrangement to form \(\alpha\)-hydroxyketone derivatives, Eq. (19). By the use of proper catalysts this can be made the sole reaction.\textsuperscript{10,20} Another possible side reaction is the formation of diacylethylenes, Eq. (20).

\[
\begin{align*}
R-C-C-R' & \quad \xrightarrow{\text{OH}} \quad R-\overline{C}-OH-R' \\
& \quad \xrightarrow{\text{OR''}} \\
\end{align*}
\]

(19)

\[
\begin{align*}
2R-C-C-R' & \quad \xrightarrow{} \quad R-C-C-R' \\
& \quad \xrightarrow{\text{OR''}} \\
\end{align*}
\]

(20)

This reaction appears to be specifically catalyzed by copper oxide.\textsuperscript{21,22} The occurrence of a third important side reaction has very recently been demonstrated. Franzen\textsuperscript{23} has shown that diazoketones containing

\[\text{References}:
\begin{align*}
\text{\textsuperscript{19} A. Roedig and H. Lunk, Ber., \textit{57}, 971 (1954).} \\
\text{\textsuperscript{21} C. Grundmann, Ann., \textit{536}, 29 (1938).} \\
\text{\textsuperscript{22} I. Ernest, Coll. Czech. chem. comm., \textit{19}, 1179 (1954).} \\
\text{\textsuperscript{23} v. Franzen, Ann., \textit{602}, 199 (1957).}
\end{align*}\]
hydrogen atoms on the carbon adjacent to the diazo group yield large proportions of \( \alpha, \beta \)-unsaturated ketones in addition to the rearranged acids, Eq. (21). For the silver oxide-catalyzed reaction in aqueous dioxan, the ratio of the two products was found to be temperature dependent, with the proportion of acid increasing at higher temperatures. At comparable temperatures the photolytic reaction afforded a larger proportion of acid, but the effect of temperature on the photolysis was not investigated.

In the absence of a reacting solvent the ketene formed can react with unconverted diazoketone (or with the carbene therefrom). This explains the results of Wiberg and Hutton, who obtained \( \alpha, \gamma \)-di-\( t \)-butyl-\( \beta, \gamma \)-butenolide (XXVII) by photolysis of diazomethyl \( t \)-butylketone (XXVI) in the absence of solvent, Eq. (22).

\[
\begin{align*}
R - \overset{\text{I}}{\text{C}} - \overset{\text{II}}{\text{C}} - \overset{\text{III}}{\text{CH}_2 - R'} & \longrightarrow R - \overset{\text{II}}{\text{C}} - \overset{\text{III}}{\text{CH} = \text{CH} - R'} \\
\text{(21)}
\end{align*}
\]

\[
\begin{align*}
\text{Me}_3\text{C} \quad \overset{\text{III}}{\text{C}} - \overset{\text{II}}{\text{C}} - \overset{\text{I}}{\text{C}} - \overset{\text{III}}{\text{C}} - \overset{\text{II}}{\text{C}} - \overset{\text{I}}{\text{C}} & \longrightarrow \quad \text{Me}_3\text{C} \quad \overset{\text{III}}{\text{C}} - \overset{\text{II}}{\text{C}} - \overset{\text{I}}{\text{C}} - \overset{\text{III}}{\text{C}} \\
\text{XXVIII} & \end{align*}
\]

C. The Preparation of α-Diazoketones

Acyclic diazoketones bearing the diazo group on the terminal carbon atom (diazomethyl ketones) are readily prepared by the Arndt-Eistert method.1,2 This consists of adding an ethereal solution of the corresponding acid chloride to an ether solution containing (at least) two equivalents of diazomethane, Eq. (23) and (24). The mode of addition

$$R-\overset{\text{II}}{\text{C-Cl}} + CH_2=N_2 \longrightarrow R-\overset{\text{II}}{\text{C-C\text{\text{H}}}} + HCl \quad (23)$$

$$CH_2=N_2 + HCl \longrightarrow CH_3Cl + N_2 \quad (24)$$

and extra equivalent of diazomethane are required to suppress chloromethyl ketone formation, Eq. (25). In a useful modification, due to Newman and Beal,3 an organic base (triethylamine) replaces the second equivalent of diazomethane as the hydrogen chloride scavenger. The

---

1 F. Arndt and B. Eistert, Ber., 68, 200 (1935).
Armit-Eistert method has been extended to include the use of higher diazalkanes, but the results are much less favorable: non-crystalline products are usually obtained.\textsuperscript{4,5,6} Franzen\textsuperscript{7} noted that the triethylamine method was far superior in these cases. This general procedure is not applicable to the preparation of cyclic diazoketones.

Various methods applicable to cyclic as well as acyclic types have been developed. Chief among these is the oxidation of $\alpha$-keto-hydrazone, usually with mercuric oxide. Examples of this technique

\begin{align*}
\text{C}_{2}H_{5}\text{CO} & \overset{HgO}{\longrightarrow} \text{C}_{2}H_{5}\text{CON}_{2} \quad (26) \\
\text{XXVIII} \\
\text{C}_{2}H_{5}\text{CONHNH}_{2} & \quad (27) \\
\text{XIX} \\
\text{C}_{2}H_{5}\text{CONHNHN}_{2} & \quad (28) \\
\text{XXIX}
\end{align*}

\textsuperscript{7} V. Franzen, Ann., 602, 199 (1957).
are the preparation of azibenzil\textsuperscript{8,9} (XXVIII), Eq. (26); diazocamphor\textsuperscript{10} (XIX), Eq. (27); and diazoâœxindole\textsuperscript{11} (XXIX), Eq. (28). The oxidation of acenaphthenequinone monohydrazone (XXX) affords 7-diazo-8-acenaphthenone (XXXI) in very low yield,\textsuperscript{12} Eq. (29). Methods utilizing \(\alpha\)-aminoketones

\[
XXX \quad \rightarrow \quad XXXI
\]

include direct diazotization,\textsuperscript{13,14} e.g., Eq. (30), and decomposition of

\[
R \quad \begin{array}{c}
\text{CO} \\
\text{NH}_2
\end{array} \quad \text{HNO}_2 \quad \rightarrow \quad R \quad \begin{array}{c}
\text{CO} \\
\text{N}_2
\end{array}
\]

\(\alpha\)-(N-nitrosoacetamido) ketones,\textsuperscript{6} Eq. (31). A method which has received

\begin{footnotesize}
10 J. Bredt and W. Holz, J. prakt. Chem., \textsuperscript{[2]} 95, 133 (1917).
13 R. Shiff, Ber., 14, 1375 (1881).
14 A. Angeli, Gazz. chim. ital., \textit{23II}, 345 (1893).
\end{footnotesize}
little attention is due to Forster,\textsuperscript{15} and consists of treating the sodium salt of an $\alpha$-oximino ketone with an aqueous chloramine solution, Eq. (32); it has been used to prepare XIX and XXVIII.

\[
\begin{array}{c}
R-C-C-R' \\
\begin{array}{c}
\text{O} \\
N\rightarrow O^{-} \text{Na}^{+}
\end{array}
\end{array}
\xrightarrow{\text{NH}_2\text{Cl}}
\begin{array}{c}
R-C-C-R' \\
\begin{array}{c}
\text{O} \\
N_2
\end{array}
\end{array}
\]

(32)

D. Statement of the problem

The object of the present research was to devise a general method of synthesis of derivatives of benzocyclobutene; specifically, to investigate the synthesis and Wolff rearrangement of various diazooindanones.¹ ³

¹ During the course of this work a preliminary communication ² from the laboratories of Horner appeared, describing the synthesis and rearrangement of 2-diazoindanone. No experimental details or physical constants were reported therein, so a comparison of the properties of the compounds described here with those reported is not possible.


³ A brief account of a portion of this work has been published: M. P. Cava and R. L. Little, Chemistry and Industry, 1957, 367.
DISCUSSION OF RESULTS

The first reaction investigated as a means of synthesis of a diazoindanone was the mercuric oxide oxidation of the monohydrazone of 4,7-dimethyl-1,2-indandione, prepared from the diketone (see p. 21 for the preparation of this compound) by reaction with hydrazine, Eq. (1). This latter reaction when carried out in methanol solution was capricious, yielding in some experiments deep red oils, in others, difficulty purified, discolored solids. The reason for this behavior is not clear, although the known sensitivity of the parent indandione to bases suggests one source of difficulty. Reduction of the diketone is another possibility—it is known that hydrazine will reduce phenanthraquinone. This difficulty was easily overcome, however, by carrying out the reaction in benzene. Upon addition of excess hydrazine to a solution of the dione in benzene an almost instantaneous reaction occurred, yielding an easily crystallized white product in 83% yield. Elementary analysis indicated that the product was the desired hydrazone (I).

The oxidation of I was carried out under conditions which have been

---

3 This compound is formulated as the 2-hydrazone rather than the isomeric 1-hydrazone for reasons discussed below (p. 22).
used successfully for the preparation of azibenzenil.\(^4\) Mercury oxide alone produced no visible reaction with the hydrazone; however, on addition of the recommended basic catalyst\(^4\) rapid development of color was observed. From these reaction mixtures it was possible to isolate, by chromatography on alumina, small amounts (5-10%) of a crude substance whose infrared spectrum showed an absorption band in the vicinity of 2070 cm\(^{-1}\), characteristic of a diazoketone.\(^5\) Variations in reaction time and in state of subdivision of the reactants did not appreciably alter the results. No pure material was obtained from these experiments, but comparison of the spectra of these products with the spectrum of the pure diazoketone later obtained showed that they consisted largely of the desired product.

The disappointing results obtained in these preliminary experiments led to the search for a better synthetic procedure. An attractive possibility was suggested by some recent work of Bamford and Stevens\(^6\) on the behavior of arylsulfonylhydrazones. These workers found that the p-toluenesulfonylhydrazones of various aldehydes and ketones when heated with alkali in ethylene glycol decomposed to nitrogen, p-toluenesulfinate ion and an olefin:

\[
R - C - CH_2 - R' \xrightarrow{\text{N}} N \Theta
\]

\[
R - CH = CH - R' + \text{N}_2 + \Theta \text{O}_{2}\text{S} \text{-CH}_3
\]


If the hydrazones possessed no α-hydrogens the products were the coupled olefins:

\[
2 \begin{array}{c}
C = N - N - \text{SO}_2 - \text{C}_6\text{H}_5 - \text{CH}_3 \\
\text{R} \\
\text{R}'
\end{array} \rightarrow \begin{array}{c}
C = C \\
\text{R} \\
\text{R}'
\end{array}
\]  

(3)

With some compounds, e.g. II, rearrangement was observed:

\[
\begin{array}{c}
\text{CH}_3 \\
\text{CH}_3
\end{array} - \begin{array}{c}
\text{C} - \text{C} - \text{C} - \text{C} - \text{C} - \text{C} - \text{CH}_3 \\
\text{CH}_3 \\
\text{N} - N - \text{SO}_2 - \text{C}_6\text{H}_5 - \text{CH}_3
\end{array} \rightarrow \begin{array}{c}
\text{CH}_3 \\
\text{CH}_3
\end{array} \begin{array}{c}
\text{C} - \text{C} - \text{C} - \text{C} - \text{C} - \text{C} - \text{CH}_3 \\
\text{CH}_3 \\
\text{N} - N - \text{SO}_2 - \text{C}_6\text{H}_5 - \text{CH}_3
\end{array}
\]  

II

Since the product in each of these cases corresponds to that which would be obtained by the decomposition of the corresponding diazo compound, Bamford and Stevens postulated that the diazo compound was an intermediate in the reaction, being formed by 1,1 elimination of p-toluenesulfinic acid from the hydrazone:

\[
\begin{array}{c}
\text{R} - \text{C} - \text{R}' \\
\text{N} - \text{SO}_2 - \text{C}_6\text{H}_5 - \text{CH}_3 \\
\text{N} - \text{SO}_2 - \text{C}_6\text{H}_5 - \text{CH}_3
\end{array} \rightarrow \begin{array}{c}
\text{R} \\
\text{C} - \text{R}'
\end{array}
\]  

(5)

Some support for this assumption was obtained by carrying out the elimination at lower temperatures. Under these conditions highly colored solutions were obtained which evolved nitrogen upon addition of acid, indicating that they contained the diazo compounds.

Analogous results were obtained by Carpino\(^7\) who studied the reactions of 1,1-dibenzyl-2-arylsulfonylhydrazines, and found that these compounds

---

\(^7\) L. A. Carpino, Abstracts of Papers Presented at the 130th Meeting of the A.C.S., 1956, p. 18-0.
were converted to dibenzyl by the action of base. If the dibenzylazamine is assumed to be the intermediate this reaction is seen to be similar to that above:

\[
\begin{align*}
\phi-CH_2 & \xrightarrow{\text{N—N—SO_2—CH_3}} \phi-CH_2 \\
\phi-CH_2 & \xrightarrow{\text{N—N—}} \phi-CH_2
\end{align*}
\]

The above results immediately suggest that the mono arylsulfonyl-hydrazone of α-diketones should, in the absence of any complicating factors, undergo a similar elimination with base to yield the corresponding α-diazoketones:

\[
\begin{align*}
R-C-C-R' & \xrightarrow{\text{N—SO_2—CH_3}} R-C-C-R' \\
N & \xrightarrow{\text{N—N—}} N_2
\end{align*}
\]

Examination of the literature disclosed that, in fact, a very similar reaction had been carried out. Borsche and Frank\(^8\) prepared the mono tosylhydrazone\(^9\) of p-benzoquinone (III), and found that the compound reacted rapidly with alkali, producing a solution of the unstable diazooxide (IV), previously prepared by diazotization of p-aminophenol (V):

\[
\begin{align*}
\text{III} & \xrightarrow{\text{OH}^-} \text{IV} & \text{IV} & \xleftarrow{\text{HNO}_2} \text{V}
\end{align*}
\]

---

\(^8\) W. Borsche and R. Frank, Ann., 450, 75 (1926).

\(^9\) "Tosyl" (abb. Ts) = "p-toluenesulfonyl".
In order to carry out the reaction indicated above three 1,2-indandiones were prepared, namely, the parent compound VIIIa, 4,7-dimethyl-1,2-indandione (VIIIb) and 4-methyl-7-chloro-1,2-indandione (VIIIc). The reactions employed were similar to those which have been used previously\(^1\) for the preparation of VIIIa, Eqs. (9) and (10). Treatment of the

\[
\text{VI}\ a,\ b,\ c \quad \text{→} \quad \text{VII}\ a,\ b,\ c
\]

(9)

\[
\text{VII}\ a,\ b,\ c \quad \text{→} \quad \text{VIII}\ a,\ b,\ c
\]

(10)

\[\begin{align*}
a(R^1 = R^2 = H); & \quad b(R^1 = R^2 = CH_3); & \quad c(R^1 = CH_3, R^2 = Cl).\end{align*}\]

1-indanones\(^{10}\) (VI) in methyl cellosolve solution with nitrous acid (generated \textit{in situ} from n-butyl nitrite and hydrochloric acid) produced the 2-oximinoindanones (VII) in good yield. The structures of compounds VIIb and VIIc, previously unreported, were inferred from their method of formation and correct elementary analyses, and their solubility in aqueous sodium hydroxide. These compounds, when hydrolyzed with aqueous hydrochloric acid in the presence of formaldehyde gave the corresponding diketones (VIII).

\(^{10}\) The author is indebted to Prof. M. S. Newman of this Department for a generous gift of the indanones VIIb and VIIc.
These were yellow to orange crystalline solids whose infrared spectra showed two distinct carbonyl absorptions: one in the 1750 cm\(^{-1}\) region, characteristic of a cyclopentanone, and another near 1700 cm\(^{-1}\). This latter band has been observed in 1-indanones.

The monotosylhydrazones of these diketones were easily obtained by allowing them to react with one equivalent of tosylhydrazine in methanol solution, Eq. (11). The reactions proceeded rapidly, being essentially complete in one minute at the boiling point of methanol. Purer products were obtained however, by allowing the reactions to proceed at a lower temperature (ca. 40\(^{\circ}\)). Under these conditions the hydrazones slowly crystallized from the reaction mixture in very pure form. As evidence presented below will show, these products (IX) are the 2-hydrazones rather than the isomeric 1-hydrazones. This result is as anticipated, since one would expect the 1-carbonyl, as a consequence of its direct conjugation with the aromatic ring, to be less reactive toward carbonyl addition reactions than the 2-carbonyl which enjoys only cross-conjugation. In addition steric hindrance is greater at the 1-position, especially if \(R_2 \neq \text{H}\).

---


These tosylhydrazones were insoluble in water, but dissolved readily in an equivalent quantity of 0.1N sodium hydroxide to give bright yellow solutions. These solutions on standing at room temperature slowly deposited neutral material. The neutral products, which were readily purified by chromatography on alumina or by recrystallization, were bright yellow solids whose analyses and infrared spectra (intense band in 2070 cm\(^{-1}\) region) showed them to be the desired 2-diazoindanones (X). From the original aqueous filtrates it was possible to isolate an acidic product identical in all respects with authentic p-toluene-sulfinic acid. It is clear that the expected reaction had occurred:

\[ \text{IX} \begin{array}{ccc} R_1 & N-N-Ts \rightarrow & R_2 \\ R_3 & \end{array} \begin{array}{ccc} R_1 & N_2 \rightarrow & R_2 \end{array} \begin{array}{ccc} X \end{array} \begin{array}{ccc} R_3 & \end{array} \\\text{(12)} & \]

Reduction of the diazoketones with hydriodic acid\(^{13}\) produced the original indanones (VI):

\[ \text{X} \begin{array}{ccc} R_1 & N_2 \rightarrow & R_2 \\ R_3 & \end{array} \begin{array}{ccc} R_1 & N_2 \rightarrow & R_2 \end{array} \begin{array}{ccc} VI \end{array} \begin{array}{ccc} R_3 & \end{array} \\\text{(13)} & \]

The position of the diazo group (and hence of the tosylhydrazone group in IX) is thus definitely established.

In view of the results obtained by this method, it was of interest to ascertain whether it could be extended with equal success to some other readily available cyclic diketones.

Acenaphthenequinone (XIa), camphorquinone (XIIa) and isatin (XIIIa) each gave the corresponding monotosylhydrazones (Xlb, XIIb, XIIIb), although the yield of XIIb was rather low (56%). XIb and XIIb reacted smoothly with alkali yielding the diazoketones XIc and XIIc. The presence of the additional acidic hydrogen in XIIIb necessitated a slight modification in procedure. A solution of XIIIb in two equivalents of alkali was kept overnight, then saturated with carbon dioxide to liberate the

diazooxindole XIIIc. When phenanthraquinone (XIVa) was allowed to react with tosylhydrazine in refluxing methanol, the product isolated was not the expected tosylhydrazone (XIVb), but a neutral compound whose elementary analysis and infrared spectrum showed it to be the diazoketone (XIVc). A possible explanation for this behavior is that the initial product in this case is not the hydrazone XIVb but the tautomeric azophenol XV, in which the greater acidity of the hydrogen atom would
permit an easier elimination of p-toluenesulfonic acid:

\[
\begin{array}{c}
\text{XV} \\
\end{array} \rightarrow \begin{array}{c}
\text{XIVc}
\end{array}
\] (14)

The results obtained by this method are summarized in Table I (p. 26). It would appear that this procedure, with proper modification, should be capable of application to a variety of systems.

Since the preparation of the 1,2-indandiones required for the synthesis of the diazoindanones discussed above was carried out via the corresponding oximinoketones, a simpler route to the 2-diazoindanones seemed possible, namely, the method of Forster\(^\text{14}\) (see p. 15), which employs the oximinoketones directly. Forster's procedure involved addition of an aqueous chloramine solution (prepared by mixing equimolar quantities of ice-cold dilute ammonia and sodium hypochlorite solutions) to a cold alkaline solution of the oximinoketone. A more convenient procedure in the present cases involved generation of the chloramine \textit{in situ} by slow addition of hypochlorite solution to a cooled and well-stirred suspension of the sodium salt of the oximinoketone in aqueous ammonia. Under these conditions the corresponding diazoketones, identical in all respects with those obtained by the tosylhydrazone method, were

**TABLE I**

**YIELDS OF TOSYLHYDRAZONES AND DIAZOKETONES**

<table>
<thead>
<tr>
<th>Diketone ( (X = 0) )</th>
<th>Yield of Tosylhydrazone ( (X = \text{NNHTs}) )</th>
<th>Diazoketone ( (X = N_2) )</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Diketone" /></td>
<td>86%</td>
<td>58%</td>
</tr>
<tr>
<td><img src="image2" alt="Diketone" /></td>
<td>79%</td>
<td>93%</td>
</tr>
<tr>
<td><img src="image3" alt="Diketone" /></td>
<td>86%</td>
<td>90%</td>
</tr>
<tr>
<td><img src="image4" alt="Diketone" /></td>
<td>81%</td>
<td>65%</td>
</tr>
<tr>
<td><img src="image5" alt="Diketone" /></td>
<td>91%</td>
<td>93%</td>
</tr>
<tr>
<td><img src="image6" alt="Diketone" /></td>
<td>56%</td>
<td>76%</td>
</tr>
<tr>
<td><img src="image7" alt="Diketone" /></td>
<td>89%</td>
<td>73%</td>
</tr>
<tr>
<td><img src="image8" alt="Diketone" /></td>
<td>—</td>
<td>60%</td>
</tr>
</tbody>
</table>
produced:

\[
\begin{array}{c}
\text{VII}_a,c \\
\text{X}_a,c
\end{array}
\]

The yield in each case was near 60%, which is as good or better than the corresponding overall yield obtained in the tosylhydrazone procedure.

An interesting example of the complementary nature of these two reactions is provided by the results obtained with 3,3-diphenyl-1-indanone (XVI). This compound was converted to the known oximinoketone (XVII) and diketone (XVIII). In the latter compound the steric effect of the two phenyl groups is apparently sufficient to outweigh the effects of conjugation, since it is known that it is the 1-carbonyl in this compound which reacts with the usual carbonyl reagents. The tosylhydrzone obtained from (XVIII) would thus be expected to be the 1-isomer (XIX). In fact, decomposition of XIX with alkali afforded a red-orange diazo-ketone (XX), while treatment of XVII with chloramine gave the pale yellow isomeric compound (XXI):

\[
\begin{array}{c}
\text{XVII} \\
\text{XVIII} \\
\text{XIX} \\
\text{XX}
\end{array}
\]

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

B. The Rearrangements.

In view of the general applicability of the photolytic method, this technique was the one employed in the present investigation. The irradiations were conducted in an apparatus (described in the Experimental section) which permitted the measurement of evolved gas and control of temperature.

The preliminary experiments were carried out on the parent substance, 2-diazoindanone (Xa), since the expected product, benzocyclobutene-1-carboxylic acid (XXII), was known. This latter compound has recently been prepared by the following sequence of reactions:¹

\[
\text{XXII}
\]

Irradiation of a solution of Xa in aqueous tetrahydrofuran at \(-10^\circ\) until gas evolution had ceased followed by removal of the solvent produced a tarry residue from which it was possible to isolate a small amount (8%) of acidic product. The latter after crystallization and sublimation was obtained as a white crystalline compound which was identical in all

¹ D. R. Napier, Ph. D. dissertation, The Ohio State University, 1957.
respects with the acid prepared as described above. Thus the desired rearrangement had occurred:

\[
\begin{align*}
\text{XXI} & \quad \text{H}_2\text{O} \quad h\nu \\
\text{CO}_2\text{H} & 
\end{align*}
\]  

(18)

The infrared spectrum of the neutral material showed no absorption at 2070 cm\(^{-1}\) indicating complete conversion of the diazoketone.

Similar treatment of 2-diazo-4-methyl-7-chloro-1-indanone (Xc) afforded in the same yield an easily purified, beautifully crystalline acid whose elementary analysis corresponded to the desired product and whose infrared spectrum showed OH and CO absorptions identical with those of XXII. This acid is accordingly formulated as XXIII:

\[
\begin{align*}
\text{Xc} & \quad \text{CO}_2\text{H} \\
\text{XXIII} & 
\end{align*}
\]  

(19)

In view of the greater ease of purification of this acid compared to XXII, it was decided to use Xc for further experiments on the effects of reaction conditions on the yield of acid.

In the reaction under consideration here two side reactions suggest themselves as major sources of difficulty. The first of these is the competing H-migration observed by Franzen (see p. 10). This reaction might be particularly favored in the present cases since it
offers an alternate to formation of the highly strained ring system:

$$\text{(20)}$$

If the favorable effect of higher temperature on rearrangement observed by Franzen is operable in the case of the diazoindanones then higher temperatures should decrease the importance of this reaction.

The second possible side reaction considered was the reaction of the acid formed with the diazoketone to form an ester:

$$\text{XXII} + Xa \rightarrow \text{ester} \quad \text{(21)}$$

Although no authenticated case of the occurrence of this reaction during a Wolff rearrangement has been recorded it would seem to be probable since it is known that diazoketones yield esters when treated with acids.

If this is indeed a significant side reaction, it could be eliminated by carrying out the rearrangement in the presence of a base, which would convert the acid to its salt as it was formed.

---

2 Note that this is not the case with diazocamphor since H-migration would lead to a bridge-head double bond:

$$\text{(22)}$$

The effect of temperature and added base was accordingly investigated. Solutions of Xc in aqueous THF were irradiated under the desired conditions, and worked up in an identical manner to determine the yield of acid. The results are summarized in Table II.

### Table II

**EFFECT OF TEMPERATURE AND BASE ON YIELD OF REARRANGED ACID**

<table>
<thead>
<tr>
<th>Diazoketone</th>
<th>Added Base</th>
<th>Temperature(^a)</th>
<th>Yield of acid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NaHCO(_3)</td>
<td>50</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>NaHCO(_3)</td>
<td>15</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>NaHCO(_3)</td>
<td>50</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>NaHCO(_3)</td>
<td>65</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>Et(_3)N</td>
<td>50</td>
<td>0</td>
</tr>
</tbody>
</table>

\(^a\) Temperatures below 50\(^\circ\) are bath temperatures; the temperature of the reaction mixture would be somewhat higher.
It is seen from these results that raising temperature alone produces no effect on the yield of acid. The addition of sodium bicarbonate however, results in a substantial increase in yield, and this effect is essentially independent of temperature. It thus appears that the presence of free acid is detrimental to the reaction. When the bicarbonate was replaced by triethylamine no acid could be isolated. This result is surprising in view of the work of Wilds and Meader\(^4\) who found that the thermal rearrangement of various diazoethyl ketones is favored by the presence of tertiary amines. On the other hand, it has been shown\(^5,6\) that simple diazo compounds react with tertiary amines to give a variety of products, and this reaction may be intervening in the present instance. An attempt to carry out the rearrangement in the presence of hydrazine was unsuccessful since this reagent reacted with Xc under the conditions used.

The neutral materials from these photolyses were red gums from which no crystalline material could be isolated. These were not examined further, although the infrared spectrum of each was determined. The absence of the band in the 2080 cm\(^{-1}\) region indicated that complete conversion of the diazoketone had occurred.

Under the best conditions thus determined, the rearrangement of Xa was repeated and the acid XXII obtained in 21 \% yield. Similarly,

Xb afforded a 22% yield of crystalline acid formulated as 3,6-dimethyl-benzocyclobutene-1-carboxylic acid (XXIV):

![Chemical Structure](image)

The low yields obtained in the final step notwithstanding, the reactions described here would appear to constitute a convenient and general route to the benzocyclobutene carboxylic acids, and, through the latter, to a variety of functional derivatives.
EXPERIMENTAL

All melting points were taken on a Fisher melting point block, and are uncorrected. Analyses were by Galbraith Microanalytical Laboratories, Knoxville, Tennessee. The infrared spectra were taken on a Perkin-Elmer Model 21 or a Baird Associates Model B recording spectrophotometer.

Starting materials and reagents

1-Indanone — commercial sample (Aldrich Chem. Co.).
4-Methyl-7-chloro-1-indanone — a distilled sample\(^1\) was recrystallized from benzene to give pale yellow prisms, m.p. 127-128° (reported:\(^2\) 128°).
4,7-Dimethyl-1-indanone — a sample\(^1\) melting at 77-78° was used without further purification. Reported\(^3\) m.p. 78-79°.
n-Butyl nitrite — prepared by the method of Miller and Audrieth, Inorg. Syn., II, 139 (1946); the undistilled product was used. This material when stored in a tightly stoppered bottle at -5° could be kept up to 8 months without apparent deterioration.
Tosylhydrazine — prepared by the method of Frendenberg and Blummel, Ann., 440, 51 (1924); m.p. 112° as reported by these authors.

Other materials were prepared as described below or were ordinary commercial samples.

\(^1\) Gift of Prof. M. S. Newman.
The Photolysis Apparatus

The photolysis apparatus consisted of a pyrex tube 2 in. in diameter and 14 in. in length bearing a 45/50 female standard taper joint into which fit the U-shaped quartz ultraviolet lamp. Below this joint a side arm was attached which was connected via 24/40 standard-taper joints to a Friederichs Condenser and thence to a water reservoir from which water was displaced by the evolved gas. The ultraviolet lamp was a low-pressure argon-filled mercury discharge tube, operated with voltage supplied from the secondary of a commercial neon sign transformer (500:1 step-up). The primary voltage (60 v.) was regulated by a variable transformer. The pyrex tube was placed in a Dewar flask containing the appropriate ice-salt water mixture or water cooled by a copper coil through which cold water circulated. With no cooling the equilibrium temperature of the reaction mixtures was 50 ± 2°.

2-Oximino-4-methyl-7-chloro-1-indanone (VIIe). To a solution of 20 g. (0.11 mole) of ketone in 400 ml. methyl cellosolve and 50 ml. conc. HCl was added, with stirring, 16 ml. (16 g., 0.16 mole) n-butyl nitrite. The mixture was allowed to stand for 45 minutes, when it was a mush of white crystals, then poured with stirring into 1000 ml. cold water. The product was filtered with suction, washed with water until free of the odor of butanol, and allowed to dry in air. Yield: 21.3 g. (92%) powdery, off-white crystals. This material was suitable for use in succeeding reactions.

Two recrystallizations from methanol/water produced an analytical sample: tiny white needles, dec. 245-250°.

Analyzed for C_{10}H_{8}NO_{2}Cl: C, 57.29; H, 3.85; N, 6.68; Cl, 16.91

Found: C, 57.47; H, 3.97; N, 6.49; Cl, 16.71
4-Methyl-7-chloro-1,2-indandione (VIIIc). A suspension of oximino ketone (33 g., 0.16 mole) in 250 ml. water, 250 ml. 36% formaldehyde and 125 ml. conc. HCl was heated on the steam bath with intermittent stirring for 35 minutes, cooled to room temperature and diluted to 1000 ml. with cold water. The product was filtered with suction, washed with cold water until free of formaldehyde and sucked dry. Yield: 24 g. (78%) bright yellow powder.

An analytical sample was obtained by recrystallization from ethyl acetate/pet. ether (30-60°) as orange needles, m.p. 195-200°. Anal. Calcd. for C_{10}H_{7}O_{2}Cl: C, 61.70; H, 3.63; Cl, 18.23

Found: C, 61.74; H, 3.73; Cl, 18.45

The infrared absorption spectrum (solution in methylene chloride, 50 mg./ml.) showed intense bands at 1724 cm^{-1} and 1768 cm^{-1}.

Tosylhydrazone of 4-methyl-7-chloro-1,2-indandione (IXc). Twenty grams (0.103 mole) of the diketone was dissolved in 425 ml. warm methanol, and the orange solution filtered from a trace of insoluble material. The solution was warmed to ca. 50°, removed from heat, and 20 g. (0.107 mole) tosylhydrazine added with stirring. When all the latter had dissolved, the solution was allowed to stand; solid began separating after one minute. After four hours the product was filtered off, washed with a little cold methanol, sucked partially dry, and dried in air overnight. Yield: 31 g. (83%) tiny, pale yellow needles, m.p. 176-177° dec.

Recrystallization from abs. ethanol afforded an analytical sample as fine white needles, m.p. 177-178° dec.
Anal. Calcd. for $C_{17}H_{15}N_2O_4Cl$: C, 56.27; H, 4.17; N, 7.72; Cl, 9.77; S, 8.82

Found: C, 56.28; H, 4.15; N, 7.90; Cl, 9.77; S, 9.02

2-Diazo-4-methyl-7-chloro-1-indanone (Xc).

A. By the action of base on the tosylhydrazone: A solution of the tosylhydrazone (10.9 g., 0.030 mole) in 305 ml. 0.1N NaOH (0.0305 mole) was allowed to stand at room temperature. After 8 hours the tan solid which had separated was filtered off, washed well with water and sucked dry. Yield: 6.0 g. (97%).

Recrystallization from 95% ethanol afforded (2 crops) 5.6 g. (90%) long, pale yellow needles. An additional recrystallization from 95% ethanol gave an analytical sample, m.p. 170-176° dec.

Anal. Calcd. for $C_{10}H_{11}N_2OCl$: C, 58.13; H, 3.42; N, 13.70; Cl, 17.18

Found: C, 57.91; H, 3.56; N, 13.88; Cl, 17.21

The infrared absorption spectrum (solution in methylene chloride; 50 mg./ml.) showed intense bands at 2075 and 1666 cm$^{-1}$.

The alkaline aqueous filtrate was extracted with ether and the ether layer discarded. The aqueous layer was acidified and extracted with ether. Evaporation of the dried ether layer gave a white crystalline solid, identical in melting point and infrared spectrum p-toluenesulfinic acid.

B. By treating the oximinoketone with chloramine: In a one liter, three-necked flask equipped with mechanical stirrer, dropping funnel and thermometer, and cooled in an ice bath was placed a solution of oximinoketone (6.3 g., 0.03 mole) in 30 ml. 1N NaOH (0.03 mole) and 200 ml. H$_2$O. Stirring was commenced, and as the solution cooled a portion of the sodium salt separated as a fine mushy precipitate. When the temperature
reached 2°, 4 ml. 15N H$_2$OH (0.60 mole) was added, followed by 100 ml. 5.25% NaOCl solution (5.3 g., 0.071 mole) added dropwise over 20 minutes. After an hour the ice bath was removed and stirring continued for 5 hours. The brown solid was filtered off, washed well with water and sucked dry. The crude product (4.4 g.) was taken up in methylene chloride and the deep red solution treated with activated charcoal until orange in color. Concentration and chilling afforded fine yellow needles (3.9 g., 63%), m.p. 173-180° dec. The infrared spectrum of the product was identical with that obtained in part A above.

Reduction of the diazoketone with HI. A solution of the diazoketone (0.50 g.) in 25 ml. methylene chloride was shaken with 4 ml. 47% HI. After the initial copious evolution of nitrogen had ceased, the mixture was allowed to stand with intermittent shaking for 15 minutes. The mixture was diluted with water and the methylene chloride layer removed, washed twice with sodium thiosulfate solution, twice with water and dried. Removal of the solvent left a yellow solid residue which was sublimed at 115°/4 mm. to yield 0.3 g. (theory requires 0.47 g.) pale yellow prisms, m.p. 128-129° alone or admixed with 4-methyl-7-chloro-1-indanone.

2-Oximino-1-indanone (VIIa). To a solution of 10 g. (0.076 mole) indanone in 60 ml. methyl cellosolve and 20 ml. conc. HCl was added with stirring 5 ml. n-butyl nitrite. When solid began separating (ca. 30 seconds) an additional 5 ml. (total: 10 g., 0.097 mole) n-butyl nitrite was added. After standing for 30 minutes the mixture was poured into 1000 ml. cold water. The crude product was filtered off, washed well
with water, sucked nearly dry and recrystallized from methanol, yielding 8.7 g. (71%) long white needles, dec. 190-215°. A small sample was recrystallized from methanol/water to give glistening colorless needles sintering 190-200°, dec. 210-220°; reported: dec. 200° (218-220°); 4 shrinking 200°, dec. 215°. 5

1,2-Indandione (VIIa). A suspension of oximinoketone (10 g., 0.62 mole) in 20 ml. 35% formaldehyde and 40 ml. conc. HCl was stirred at room temperature for 20 minutes, diluted to 300 ml. with cold water and filtered. The yellow powder was washed with cold water until free of formaldehyde, and sucked dry (5 g.). The filtrate on standing deposited 4 g. crystalline starting material (identity proved by mixed m.p.). Conversion: 55%; Yield: 92%.

Recrystallization from ether afforded bright yellow platelets, m.p. 95-112°; reported: 5 95-115°.

Tosylhydrazone of 1,2-indandione (IXa). A solution of diketone (10.0 g., 0.0685 mole) and tosylhydrazine (12.8 g., 0.069 mole) in 300 ml. methanol was kept overnight at room temperature. The product was filtered off, washed with a little cold methanol and sucked dry. Yield: 18.3 g. (86%) buff needles, m.p. 175-177° dec.

Recrystallization from abs. ethanol afforded an analytical sample as tiny prisms, m.p. 173-179° dec.

Anal. Calcd. for C_{16}H_{14}N_{2}O_{3}: C, 61.13; H, 4.49; N, 8.91

Found: C, 61.30; H, 4.56; N, 9.02


2-Diazo-1-indanone (Xa).

A. By the action of base on the tosylhydrazone. A solution of tosylhydrazone (5 g., 0.016 mole) in 100 ml. 0.162N NaOH (0.0162 mole) was mixed with 50 ml. methylene chloride and the mixture allowed to stand for 2.5 hours. The yellow color gradually transferred from the aqueous to the organic layer. The methylene chloride layer was removed, washed with water, dried over sodium sulfate and evaporated to give 2 g. brown-yellow solid. This was taken up in boiling cyclohexane, the solution decanted from a trace of insoluble oil and chilled, when yellow needles (1.08 g.) separated. The mother liquor was diluted with petroleum ether (30-60°) and chilled, yielding a second crop (0.38 g.). Total yield: 1.46 g. (58%), m.p. 86-88°.

Sublimation at 78°/0.5 mm. afforded bright yellow prisms, m.p. 87-88°.

Anal. Calcd. for C₉H₆N₂O: C, 68.37; H, 3.82; N, 17.71
Found: C, 68.38; H, 3.99; N, 17.60

The infrared spectrum (methylene chloride solution, 40 mg./ml.) showed strong absorption at 2075 cm⁻¹ and 1667 cm⁻¹.

B. By the action of chloramine on the oximinoketone. In a three-necked, round bottom flask equipped with mechanical stirrer, dropping funnel and thermometer and cooled in an ice bath was placed a solution of 5 g. (0.031 mole) oximinoketone in 100 ml. 0.32N NaOH (0.032 mole). Stirring was commenced and when the temperature reached 2°, four ml. 15N NH₄OH (0.06 mole) was added, followed by 100 ml. 5.25% NaCl solution (5.3 g., .071 mole) added dropwise during 30 minutes. After an additional 30 minutes the ice bath was removed and stirring continued for 2 hours. At the end of this time the solid was filtered off, washed with water,
dried over magnesium sulfate and evaporated under reduced pressure. The yellow crystalline residue (2.85 g., 58%) was identical in all respects with the product obtained in part A above.

**Reduction of the diazoketone with HI.** A solution of the diazoketone (0.50 g.) in 15 ml. methylene chloride was shaken with 4 ml. 47% HI. After the initial copious evolution of nitrogen the mixture was allowed to stand for 15 min. with intermittent shaking. The mixture was diluted with water, and the methylene chloride layer separated, washed twice with sodium thiosulfate solution, twice with water, and dried. Removal of the solvent left an oil which when treated with a solution of 1 g. 2,4-dinitrophenylhydrazine in 40 ml. 70% ethanol and 5 ml. conc. H$_2$SO$_4$ afforded a bright red-orange precipitate. This after drying weighed 0.92 g. (theory: 0.97 g.) and melted at 260° undepressed by the 2,4-dinitrophenylhydrazone prepared from 1-indanone.

**2-Oximino-4,7-dimethyl-1-indanone (VIIb).** To a solution of 10 g. (0.063 mole) of the ketone in 150 ml. methyl cellosolve and 35 ml. conc. HCl was added, with stirring, 8 ml. (8 g., 0.078 mole) n-butyl nitrite. The mixture was allowed to stand for 90 minutes, when it was a mush of white crystals, then poured with stirring into 800 ml. cold H$_2$O. The product was filtered with suction, washed with water until free of the odor of butanol, and dried in air. Yield: 10.5 g. (90%) white crystals, suitable for use in succeeding reactions.

Two recrystallizations from abs. ethanol afforded an analytical sample as silken white needles, dec. 215-218°.
Anal. Calcd. for C_{11}H_{11}NO_{2}: C, 69.83; H, 5.86; N, 7.40
Found: C, 69.78; H, 5.87; N, 7.28

4.7-Dimethyl-1,2-indandione (VIIIb). A suspension of 10 g. (0.053 mole) oximinoketone in 70 ml. water, 50 ml. 36% formaldehyde, and 25 ml. conc. HCl was heated on the steam bath with intermittent stirring for 30 minutes, cooled to room temperature and diluted to 1000 ml. with water. The crude product was filtered off, washed with water until free of formaldehyde, and sucked dry. The yellow powder was taken up in a minimum amount of benzene, and the solution poured with stirring into 500 ml. petroleum ether (30-60°); the product precipitated as tiny, bright yellow crystals (7 g.). A second crop (1.2 g.) was obtained by chilling the mother liquor. Yield: 89%.

Recrystallization from cyclohexane/ethyl acetate afforded long, golden needles, m.p. 134-135°.

Anal. Calcd. for C_{11}H_{10}O_{2}: C, 75.84; H, 5.79
Found: C, 75.81; H, 5.76

The infrared spectrum showed bands at 1775 and 1721 cm^{-1}.

Tosylhydrazone of 4.7-dimethyl-1,2-indandione (IXb). Crude diketone (3.5 g., 0.02 mole) was dissolved in 100 ml. warm methanol, and the solution filtered to remove a trace of insoluble material. The clear, orange filtrate was heated on the steam bath and a solution of tosylhydrazine (3.8 g., 0.02 mole) in 30 ml. warm methanol added. The mixture was removed from the heat and allowed to cool to room temperature. After two minutes solid began separating copiously. After an hour the product was filtered off, washed with a little cold methanol and dried.
in air. Yield: 5.4 g. (79%) off-white needles, m.p. 163-169.5° dec.

An analytical sample was obtained by recrystallization from abs. ethanol: glistening white needles, m.p. 170-171° dec.

Anal. Calcd. for C₈H₁₈N₂O₂S: C, 63.14; H, 5.30; N, 8.18; S, 9.36
Found: C, 63.38; H, 5.45; N, 8.11; S, 9.35

2-Diazo-4,7-dimethyl-1-indanone (Xb). To a solution of 3.4 g. (0.0099 mole) of tosylhydrazone in 100 ml. 0.1N NaOH (0.01 mole) was added 50 ml. methylene chloride. The mixture was kept at room temperature for two hours, when the yellow color was all in the organic layer. The latter separated, washed with water and dried over sodium sulfate. Evaporation of the solvent left an orange crystalline residue (1.75 g., 93%). Recrystallization from cyclohexane afforded long golden needles (1.23 g., 66%). After an additional recrystallization from cyclohexane the compound melted at 120-122°.

Anal. Calcd. for C₁₁H₁₀N₂O: C, 70.95; H, 5.41; N, 15.05
Found: C, 70.81; H, 5.50; N, 15.09

The infrared spectrum (methylen chloride solution showed strong absorption at 2088 and 1667 cm⁻¹.

Ethyldrazone of 4,7-dimethyl-1,2-indandione (I). To a solution of 2.0 g. (0.011 mole) of the diketone in 20 ml. benzene was added drop-wise 0.5 ml. anhydrous hydrazine. The mixture set to a gel-like mass of solid in 30 seconds. The mixture was diluted with petroleum ether and filtered. Recrystallization of the crude product from aqueous methanol afforded 1.8 g. (67%) long, white silken needles, dec. 165-173°.
An additional recrystallization from methanol/water gave an analytical sample, dec. 166-175°.

*Anal.* Calcd. for \( \text{C}_{11} \text{H}_{12} \text{N}_2 \text{O} \): C, 70.18; H, 6.43; N, 14.88

Found: C, 70.32; H, 6.48; N, 14.88

**Oxidation of the hydrazone (I) with mercuric oxide.** An intimate mixture of 1.9 g. (0.01 mole) of the hydrazone, 4.5 g. (0.021 mole) of freshly prepared yellow mercuric oxide and 2 g. anhydrous sodium sulfate was covered with 100 ml. of anhydrous ether and the mixture shaken mechanically at room temperature. After five minutes no apparent change had occurred. A few drops of 10% ethanolic KOH were added and shaking continued, whereupon the mixture turned successively orange, green and purple. After 25 minutes the mixture was filtered and the solid residue washed with ether until the washings were colorless. The combined filtrates were evaporated to dryness. The purple solid residue was taken up in a small amount of methylene chloride and placed on a column of alumina. Elution of the alumina with methylene chloride produced an orange solution, which on evaporation gave 0.056 g. small brown-yellow needles, m.p. 110-115°. Yield: 7.5%.

The infrared spectrum of this product showed the band at 2088 cm\(^{-1}\), and closely resembled that of the tosylhydrazone product.

Similar runs in which the reactants were finely ground together in a mortar, and in which the shaking time was decreased to 15 minutes or increased to 40 minutes gave yields of from 3-10 percent.
Tosylhydrazone of acenaphthenequinone (XIIb). To a suspension of the quinone (5.0 g., 0.0276 mole) in 50 ml. boiling methanol was added 5.5 g. (0.0296 mole) tosylhydrazine, and the mixture refluxed on the steam bath. After one minute all material had dissolved and after an additional 30 seconds, solid separated copiously. The mixture was removed from the heat and allowed to cool to room temperature. The product was filtered off, washed with a small amount of cold methanol and sucked dry. Yield: 8.5 g. (83%) fluffy yellow needles.

Recrystallization from isopropyl alcohol/chloroform gave fine, pale yellow needles, darkening 175°, melting 179° dec.

Anal. Calcd. for C_{19}H_{14}N_{2}O_{S}: C, 65.12; H, 4.03; N, 8.00; S, 9.15

Found: C, 65.05; H, 4.08; N, 8.06; S, 9.24

10-Diazo-9-acenaphthone (XIc). A solution of the tosylhydrazone (7.0 g., 0.02 mole) in 100 ml. methylene chloride was stirred mechanically with 200 ml. 0.1N NaOH (0.02 mole) for three hours. The organic layer was separated, washed with water, dried over sodium sulfate, concentrated to 20 ml. and placed on a column of alumina. Elution of the column with 50:50 (vol.) methylene chloride/petroleum ether (30–60°) and evaporation of the orange eluate gave an orange solid which crystallized from petroleum ether in bright orange needles, m.p. 94°; reported 92–94°.

Yield: 2.9 g. (73%).

Infrared absorption bands at 2070 and 1666 cm\(^{-1}\) (solution in methylene chloride, 50 mg./ml.).

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Tosylhydrazone of camphorquinone (XXb). A solution of the quinone (5.3 g., 0.032 mole) and tosyldiyldrazine (60 g., 0.0322 mole) in 50 ml. boiling methanol was refluxed on the steam bath for one hour. The cooled, pale yellow solution was diluted with water when a thick yellow oil separated. The oil was taken up in methylene chloride, and the solution washed with water and dried over Na₂SO₄. The solution was concentrated to a small volume and petroleum ether (30-60°) added in portions with stirring whereupon solid separated. When further additions of petroleum ether gave no additional solid the product was filtered off, washed with petroleum ether and sucked dry. Yield: 6.0 g. (56%) powdery, faintly yellow crystals, m.p. 110-113°.

Anal. Calcd. for C₁₇₂₂₂₂₅:S: C, 61.05; H, 6.63; N, 8.38; Found : C, 59.56; H, 7.09; N, 8.28

3-Diazocamphor (XIIe). A solution of the tosylhydrazone (3.3 g. 0.01 mole) in 100 ml. 0.1N NaOH (0.01 mole) was covered with 50 ml. petroleum ether (30-60°) and the mixture stirred mechanically at room temperature. The pale yellow color gradually transferred from the aqueous to the organic layer. After two hours the petroleum ether layer was removed and evaporated under reduced pressure, yielding bright yellow crystals (1.03 g.). The aqueous layer was again covered with 50 ml. petroleum ether and the mixture stirred for 12 hours. Treating as before gave 0.33 g. of crystals. Total yield: 1.36 g. (76%) yellow prisms m.p. 70-74°. A small portion was sublimed at 50°/2 mm. to give fine yellow prisms m.p. 75°; reported: 75°.  

Tosylhydrazone of isatin (XIIIb). To a solution of isatin (10.0 g., 0.063 mole) in 250 ml. warm methanol was added, with stirring, 12.8 g. (0.069 mole) tosylhydrazine. When all the latter had dissolved the solution was allowed to stand; solid began separating after one minute. After two hours the product was filtered off, washed with a little cold methanol and sucked dry. Yield: 19.4 g. (91%) golden yellow platelets. Recrystallization from methanol afforded small bright yellow prisms, dec. 190-200°.

Anal. Calcd. for C₁₉H₁₃N₂O₂S: C, 57.13; N, 13.33; H, 4.16
Found: C, 57.50; N, 13.17; H, 4.31

Diazoxindole (XIIIc). The tosylhydrazone (6.3 g., 0.02 mole) was dissolved in 200 ml. 0.2N NaOH (0.04 mole) and the deep red solution was allowed to stand overnight. The solution was saturated with carbon dioxide and the precipitate filtered off, washed well with water and sucked dry. Yield: 3.0 g. (94%) orange powder. Recrystallization from benzene afforded blood-red crystals, m.p. 168° dec.; reported 8 168° dec.

The infrared spectrum showed intense bands at 2090 and 1704 cm⁻¹ (saturated solution in methylene chloride).

3,3,3-Triphenylpropanoic acid. The following procedure is adapted from that of Gagnon.⁹ A mixture of triphenylcarbinol (60 g., 0.23 mole), malonic acid (50 g., 0.29 mole) and acetic anhydride (24 g.,

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0.235 mole) was kept at 175° in an oil bath for 1.5 hours. At the end of this time the melt was poured into a metal pan and allowed to solidify overnight. The cake of brown crystals was broken up, triturated with petroleum ether (60-80°), and filtered. Recrystallization of the crude product from acetic acid yielded 58 g. (84%) faintly yellow prisms, m.p. 178°; reported 9 178-179°.

3,3-Diphenyl-1-indanone (XVI). This compound was prepared by the method of Gagnon. 9 Twenty grams 3,3,3-triphenylpropanoic acid yielded 12 g. (64%) recrystallized product, m.p. 127-130°; reported 9 131-132°.

2-Oximino-3,3-diphenyl-1-indanone (XVII). To a solution of the ketone (10 g., 0.034 mole) in 300 ml. of methyl cellosolve and 20 ml. conc. HCl was added 6 ml. n-butyl nitrite (0.06 mole). The solution was allowed to stand at room temperature for three hours, then poured with stirring into one liter of crushed ice. The precipitated product was filtered off, washed well with water and sucked dry. Yield: 9.0 g. (80%) yellow powder, m.p. 203-206°, reported 10 205-9°. This material was used without further purification.

3,3-Diphenyl-1,2-indandione (XVIII). This compound was prepared by the method of Koelsch and LeClaire. 10 From 6.5 g. oxime there was obtained 5.6 g. diketone, m.p. 145-50°; reported 10 150-151°.

Tosylhydrazone of 3,3-diphenyl-1,2-indandione (XIX). To a solution of the diketone (3.0 g., 0.01 mole) in 150 ml. boiling methanol was added 1.9 g. (0.01 mole) tosylhydrazine. The solution was allowed to stand overnight without further heating. At the end of this time the solid was filtered off and sucked dry. Yield: 2.8 g. large yellow prisms. Concentration of the filtrate and cooling afforded a second crop (0.6 g.). Total yield: 3.4 g. (72%).

Recrystallization from abs. ethanol afforded fine yellow prisms, m.p. 183-190° dec.

Anal. Calcd. for C_{28}H_{22}N_{2}O_{3}: C, 72.08; H, 4.75; N, 6.01
Found : C, 72.03; H, 4.93; N, 6.11

1-Diazo-3,3-diphenyl-2-indanone (XX). A solution of 1.5 g. (0.0032 mole) tosylhydrazone in 30 ml. methylene chloride was shaken with 45 ml. 0.1N NaOH for four hours. The orange organic layer was removed, washed with water, dried and placed on a column of alumina. Elution of the column with 50/50 (vol.) methylene chloride/petroleum ether gave an orange eluate. Evaporation of the solvent left 0.65 g. (65%) tiny orange prisms.

Recrystallization from cyclohexane afforded red rods, m.p. 162-164° dec.

Anal. Calcd. for C_{21}H_{14}N_{2}O: C, 81.27; H, 4.55; N, 9.03
Found : C, 81.46; H, 4.57; N, 8.89

Infrared absorption bands were observed at 2080 and 1690 cm\(^{-1}\) (solution in methylene chloride, 40 mg./ml.).
2-Diazo-3,3-diphenyl-1-indanone (XXI). A solution of 1.6 g. (0.005 mole) oxime in 5 ml. 1.2N NaOH and 150 ml. of H₂O was cooled to 4° and 1.5 ml. 15N NH₄OH added, followed by 20 ml. 5.25% NaOCl solution added dropwise with stirring over ten minutes. Stirring was continued for three hours. At the end of this time the yellow product was taken up in methylene chloride, and the solution washed well with water and dried. Removal of the solvent left a yellow oil which soon crystallized. The product was triturated with ligroin and filtered. Yield: 1.0 g. (65%) tiny pale yellow crystals.

Recrystallization from ethyl acetate/petroleum ether afforded yellow platelets, m.p. 179-180°.

Anal. Calcd. for C₂₁H₁₄N₂O: C, 81.27; H, 4.55; N, 9.03

Found : C, 80.65; H, 4.48; N, 9.16

Infrared absorption bands at 2030 and 1667 cm⁻¹.

3-Methyl-6-chlorobenzocyclobutene-1-carboxylic acid (XXIII). A solution of diazoketone (2.0 g., 0.0097 mole) in 170 ml. THF and 30 ml. water containing 2 g. NaHCO₃ was irradiated at 50° until gas evolution had ceased (9 hours). The orange solution was diluted with 50 ml. water and distilled until free of THF. The tarry aqueous residue was extracted repeatedly with methylene chloride, and the aqueous layer acidified to yield a tan solid (0.42 g.). The crude acid was taken up in 100 ml. boiling water and the hot solution filtered from a trace of brown tar. The filtrate on cooling deposited white needles (0.36 g.), m.p. 144-145°. Yield: 13%.

An analytical sample was obtained by sublimation at 95°/0.5 mm. as fine white needles, m.p. 143-144°.
Anal. Calcd. for C\textsubscript{18}H\textsubscript{9}O\textsubscript{5}Cl: C, 61.11; H, 4.62; Cl, 18.05

Found : C, 61.38; H, 4.87; Cl, 17.84

The results of similar experiments under various conditions are recorded in Table II (p. 31).

**Benzocyclobutene-1-carboxylic acid (VI).** A solution of 2.0 g. (0.0126 mole) 2-diazo-1-indanone in 200 ml. tetrahydrofuran and 100 ml. water containing 2.0 g. Na\textsubscript{2}CO\textsubscript{3} was irradiated at the boiling point for 10 hours. Removal of the THF by distillation left a tarry residue. After repeated extraction with methylene chloride, the aqueous layer was acidified and extracted with ether. The ether layer was washed with water, dried over sodium sulfate and evaporated, leaving a light brown solid residue. Sublimation of the crude acid at 90°/2mm. yielded small white prisms (0.400 g., 21%) m.p. 71-74°.

Recrystallization from petroleum ether afforded fine white needles m.p. 74-75°, undepressed on admixture with an authentic sample.\textsuperscript{11}

The infrared spectrum was identical with that of Napier's acid.

**3,6-Dimethylbenzocyclobutene-1-carboxylic acid (XXIV).** A solution of 1.0 g. (0.0054 mole) diazoketone in 170 ml. THF and 30 ml. water containing 1.0 g. sodium bicarbonate was irradiated at 50° for 16 hours. The solution was distilled until free of THF and the tarry aqueous layer extracted with methylene chloride. The aqueous layer was acidified and

\textsuperscript{11} D. Napier, Ph. D. dissertation. The Ohio State University, 1957.
extracted with ether. Evaporation of the ether gave a yellow waxy residue which was sublimed at 78°/0.5 mm. to give 0.21 g. (22%) tiny white prisms, m.p. 107-109°.

Anal. Calcd. for C_{11}H_{12}O_2: C, 75.02; H, 6.87

Found: C, 75.12; H, 6.97
AUTOBIOGRAPHY

I, Robert Lloyd Little, was born in Ironton, Ohio, on June 5, 1931. My elementary and secondary education were obtained in the public schools of that city. In 1949, I entered Capital University, Columbus, Ohio, where I received the degree Bachelor of Science in 1953. In the same year I enrolled in the Graduate School at Ohio State University, where I served as an Assistant in the General and Organic Divisions of the Department of Chemistry. During my final quarter of residence I was the recipient of a Du Pont grant.