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A STUDY OF THE

ALLYLIC SYSTEM OF DYPNONE

BY

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ALLYLIC SYSTEM OF DYPNONE

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THIS WORK IS DEDICATED TO MY

DEAR WIFE SOPHIE

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ABSTRACT

Trans- and cis-dyprone were prepared, and their reactivity towards different reagents was studied.

Trans-dyprone with p-nitrophenylhydrazine yielded the corresponding p-nitrophenylhydrazone, a new derivative.

Cis-dyprone with 2,4-dinitrophenylhydrazine gave two polymorphic forms of the cis-dyprone 2,4-dinitrophenylhydrazone.

Trans-dyprone with bromine failed to produce the dibromide; the difficulty of addition is attributable in part to the steric hindrance around the double bond. With chlorine the trans-dyprone yielded phenacyl chloride, possibly as the result of a reverse aldol reaction.

N-bromosuccinimide reacted with both trans- and cis-dyprone to produce trans- γ -bromodyprone, while in the presence of five mole per cent of benzoyl peroxide trans-dyprone yielded the γ -bromodyprone and 2,4-diphenyl furan. The identity of the reactions with trans- and cis-dyprones is no doubt due to the isomerization of the nonplanar and labile cis-isomer to the trans-form in the course of the reaction.

Trans- γ -bromodyprone reacted with aniline to yield 1,2,4-triphenylpyrrole, thus providing indirect evidence for the mechanism postulated by Fuson for the furanization of dyprone. The reaction shows promise as a synthetic method for substituted pyrroles.

The epoxidation reactions of both cis- and trans-dyprone were studied in conjunction with the House and Ro mechanism²²; both

compounds yield trans-dyprone oxide as the main product and cis-dyprone oxide as a minor product, which results lend weight to the mechanism.

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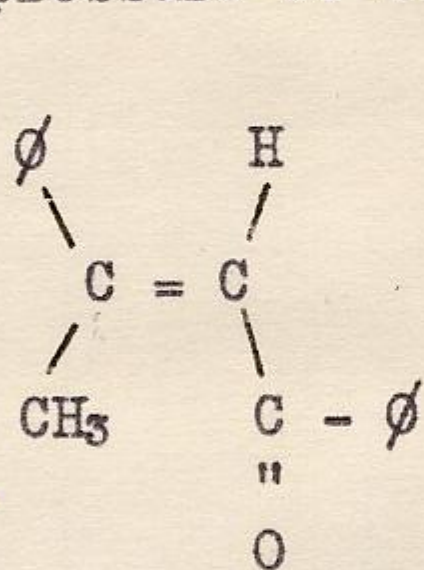
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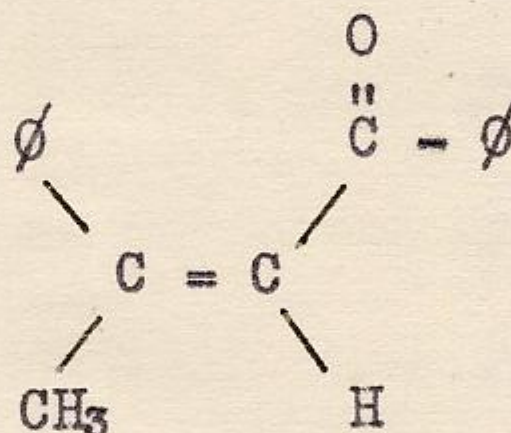
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INTRODUCTION

Trans-dypnone (I) is a yellow oil boiling at 145 - 151.5°C. under a pressure of 0.5 mm.



(I)



(II)

It is converted to its cis-isomer (II) by irradiation in sunlight in an ethanol or diethyl ether solution.

Since it is an α, β -unsaturated ketone, it exhibits many of the properties common to this class of compounds. The presence of the polarized $\beta - \overset{\beta}{\text{C}} = \overset{\alpha}{\text{C}} - \overset{\gamma}{\text{C}} = \overset{\delta}{\text{O}}$ system, disposed between two aromatic nuclei, results in a tendency for 1:4-addition, as well as 1:2-addition at the carbonyl group. Hence, the course of reactions usually observed on isolated double bonds, or on common saturated ketones, is altered in many cases.

The purpose of this research was to study some of those chemical peculiarities exhibited by dypnone, special attention being given to the reactions involving addition to the double bond and involving the allylic system.

Table 1

Melting Points of Trans-dypnone Derivatives

Derivative	Experimental M.P.	Literature M.P.
2,4-dinitrophenylhydrazone	166-167 ⁰	170 ⁰³ ; 173-174 ⁰⁴
Anti-phenyl oxime	129-131 ⁰	132-133 ⁰⁴ ; 134 ⁰³⁰
p-nitrophenylhydrazone	189-190 ⁰	--
Semicarbazone	--	150-151 ⁰⁴

The physical constants of trans-dypnone (the boiling point, the specific gravity, and the refractive index) were determined. The values are given in Table 2, together with the literature values.

Table 2

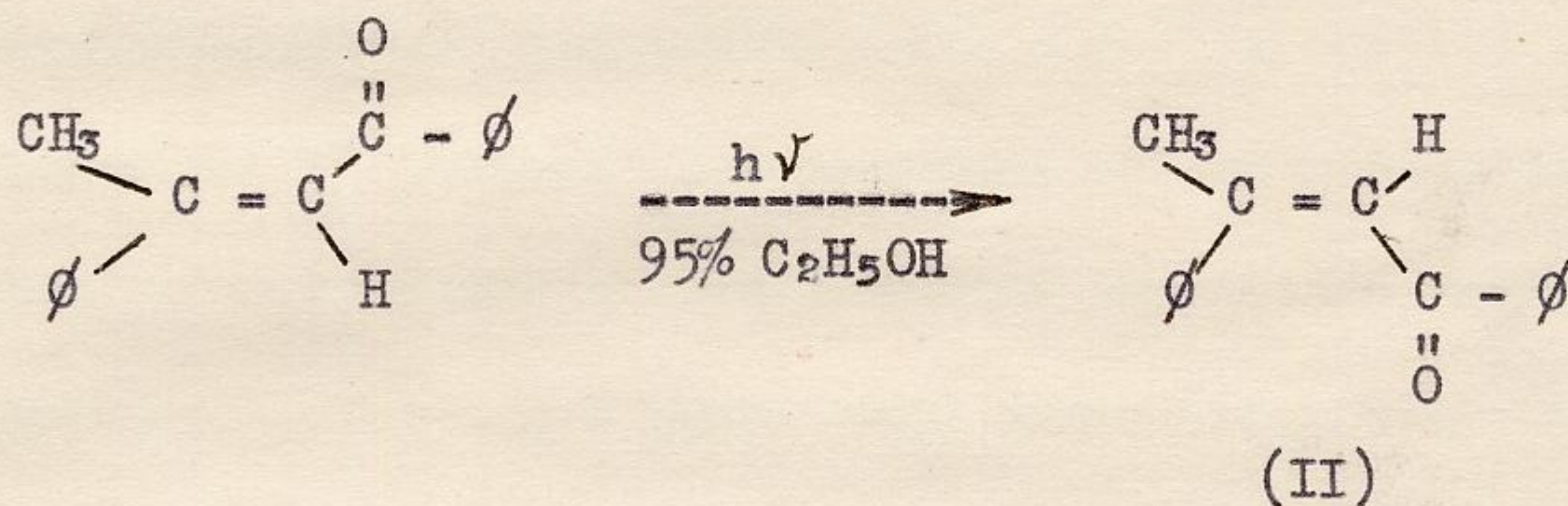
Physical Constants of Trans-dypnone

Physical Constant	Experimental Value	Literature Value
Boiling point	145-151.5 ⁰ /0.5 mm	154-157 ⁰ /0.3-0.5 mm ⁵ 150-155 ⁰ /1 mm ⁶
n_D^T	1.6347 18 ⁰ 1.6344 20 ⁰	1.6230 20 ⁰³ 1.6338 21.5 ⁰⁴ 1.6312 20 ⁰⁷ 1.6245 25 ⁰⁵ 1.6278 25 ⁰⁵
Specific refraction(r)	0.32778	0.32265 ⁴
Molar refraction(R)	72.83	71.72 ⁴ 71.17 ⁵
D_4^T	1.092 18 ⁰	1.087 20 ⁰³ 1.108 20 ⁰⁸

Having thus prepared and characterized the starting material, the following reactions were attempted:

II. Cis-dyprnone

The cis-dyprnone used in this investigation was prepared according to the directions given by Slade⁴. A solution of trans-dyprnone in 95% ethanol (4 gr dyprnone per 100 ml of ethanol) was irradiated by direct sunlight.



The progress of the conversion was followed spectrophotometrically. The irradiation was discontinued after forty eight hours in order to minimize the extent of polymerization. At that point the conversion was 88% complete, as shown by the mathematical ratio of the extinction coefficients for the two peaks in the ultraviolet spectrum, as compared to the ratio for pure cis-dyprnone⁴ (see experimental section of this thesis). The solvent was then removed under reduced pressure; and the remaining oil was spectroanalyzed again to ascertain that no reconversion to trans-dyprnone had taken place. It was found that reconversion had not taken place.

The resulting oil would require vacuum distillation for further purification, but this distillation was avoided due to the likelihood of reconversion⁴. It should be noted, however, that pure cis-dyprnone has been obtained in isolated instances where the vacuum distillation did not cause reconversion⁴; such pure samples of cis-dyprnone are the source of the mathematical ratio of the extinction

coefficients for the two peaks in the ultraviolet spectrum of cis-dyprone, mentioned just above.

At this point the 2,4-dinitrophenylhydrazone derivative was prepared according to the standard method². The resulting product was separated by fractional crystallization into two substances having different melting points (212 - 213°C. and 143 - 144°C.), but identical ultraviolet and infrared absorption spectra. Both substances on analysis showed the same percentage composition, within experimental error; this percentage composition corresponds to that of the cis-dyprone 2,4-dinitrophenylhydrazone.

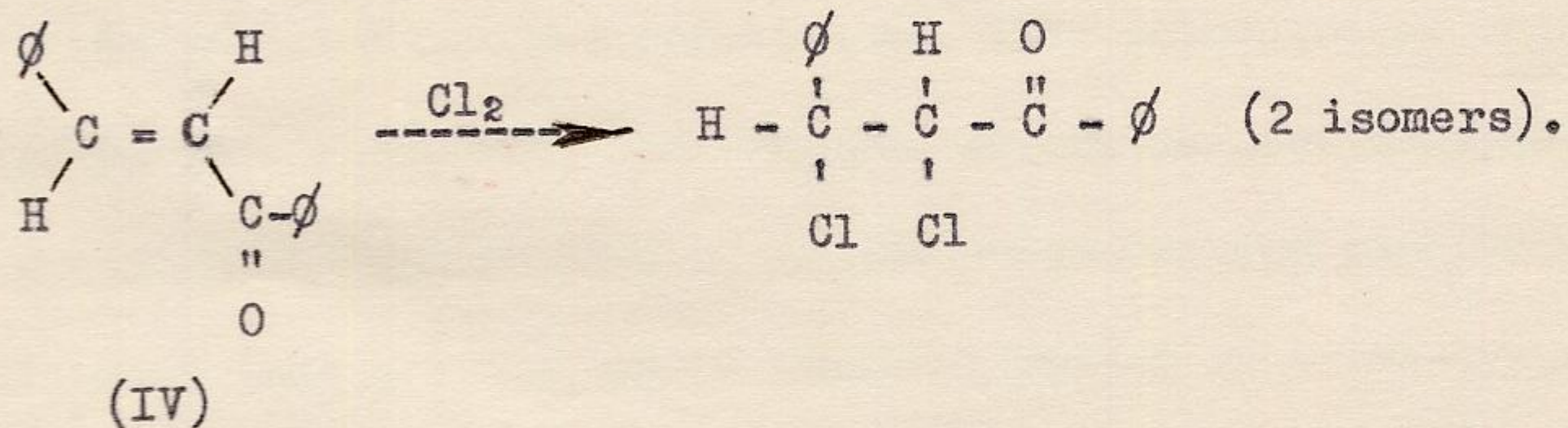
The interpretation of the above results is further complicated by the fact that the literature⁴ reports an analytically pure sample of the 2,4-dinitrophenylhydrazone of cis-dyprone with a melting point of 186 - 187°C. In view of these three samples, which differ only in melting point, polymorphism constitutes ^{a very} probable explanation of the situation.

The p-nitrophenylhydrazone was then attempted, following the modified procedure as used for the trans-isomer (see experimental section of this thesis). The product of the reaction was, however, identical to trans-dyprone-p-nitrophenylhydrazone, as indicated by the identity of melting points and of infrared absorption spectra. Also, the melting point of this product showed no depression after admixture of the product with a sample of trans-dyprone-p-nitrophenylhydrazone. Thus it is clear that the cis-configuration shifted to the trans-configuration under the conditions of the reaction.

A second modification of the procedure was then attempted, in the hope that by reducing the amount of sulfuric acid the extent of reconversion of the cis-isomer to trans-isomer would be reduced. The product had a distinctive melting point (147 - 148°C., as compared to the trans-dyprone-p-nitrophenylhydrazone: 189 - 190°C.), and gave an infrared absorption spectrum different from that of trans-dyprone-p-nitrophenylhydrazone, but its analysis did not correspond to that of the expected product. The compound obtained has not been identified.

III. Attempted Addition of Halogen to the Ethylene Linkage of trans-dyprone.

Halogens usually add to the double bond of α, β -unsaturated ketones in the normal manner. Abell and Siddall⁹, for example, obtained two isomeric dichlorides from trans-chalcone (IV). The structure of trans-chalcone is obviously very similar to that of trans-dyprone.



The trans-chalcone dibromides have also been reported in the literature.¹⁰

The literature, however, contains little on the action of halogens on dyprone. Delacre, in 1890¹¹ reported the bromination of dyprone; however, in the absence of any information on Delacre's method and on

the nature of his product, and in view of the difficulties experienced in attempts to synthesize the compound in the course of the present work (see below), it seems unlikely that he actually obtained dypnone dibromide. Slade¹² repeated this reaction, and the trans-dypnone dibromide was obtained and characterized. It was found necessary, however, to run the reaction at very low temperatures (-80°C .), since at higher temperatures trans-dypnone polymerized in the presence of bromine.

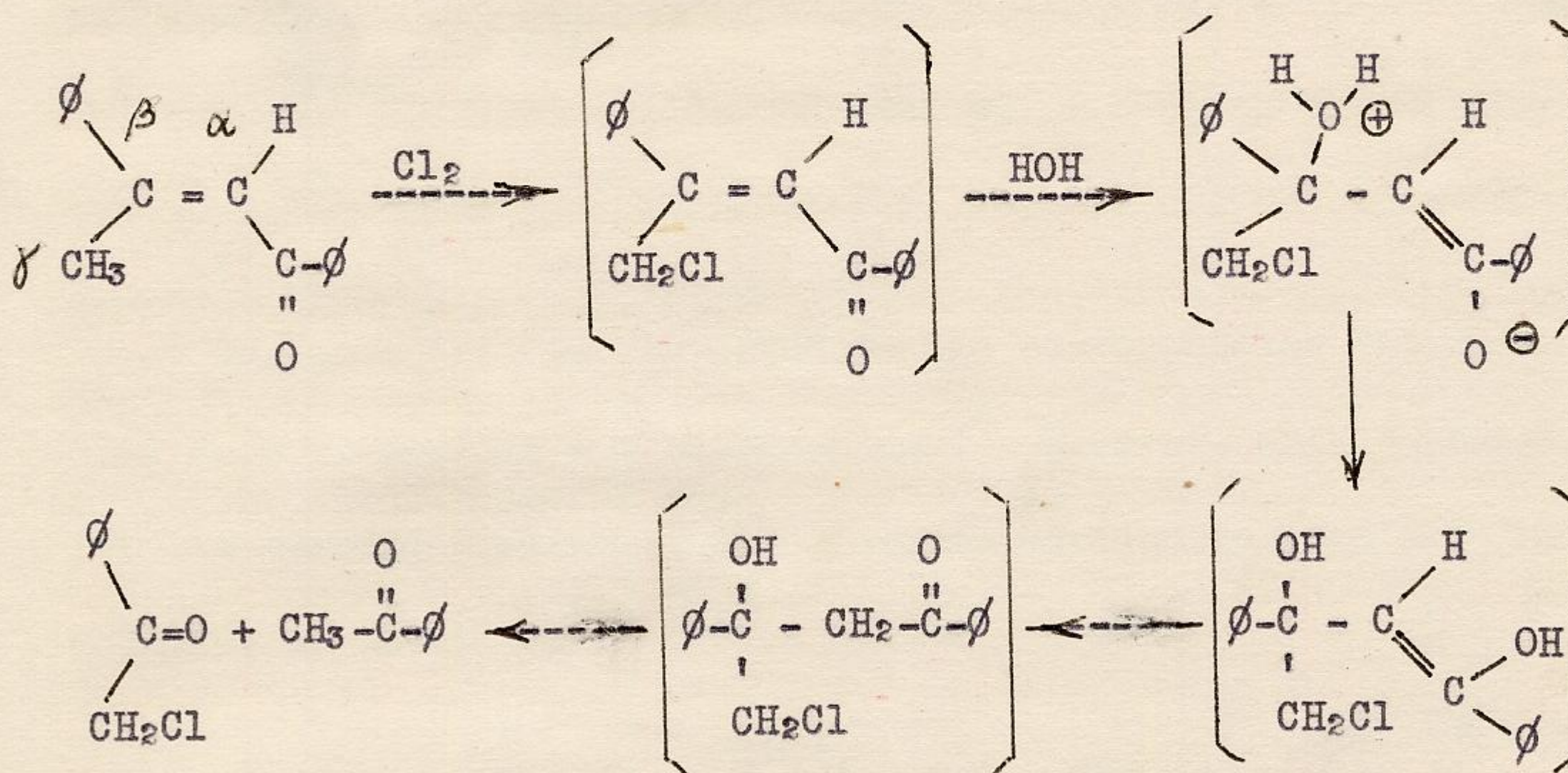
The reaction was repeated four times in the course of this research, varying the reaction temperature from -50° to -100°C ., without obtaining the desired product. The reasons for these unsuccessful attempts are not clear. The difficulty of addition is attributable in part to the steric hindrance around the double bond.

In this research, trans-dypnone was chlorinated according to the directions given by Abell and Siddall⁹ for the chlorination of chalcone.

A solution of trans-dypnone in chloroform was saturated with chlorine gas at 0°C . The solution was then concentrated under reduced pressure to a thick oil, the infrared absorption spectrum of which showed a strong absorption at $5.93\ \mu$, and no absorption at $6.00 - 6.20\ \mu$, indicating that the conjugated carbonyl system of trans-dypnone had been destroyed.

All methods employed for crystallizing the product were fruitless, and consequently the crude oil was used for the preparation of a 2,4-dinitrophenylhydrazone derivative. A crystalline product was obtained and microanalyzed, but it could not be identified.

and steric factors opposing simple addition, but the absence of a basic catalyst is an argument against the reverse aldol mechanism.

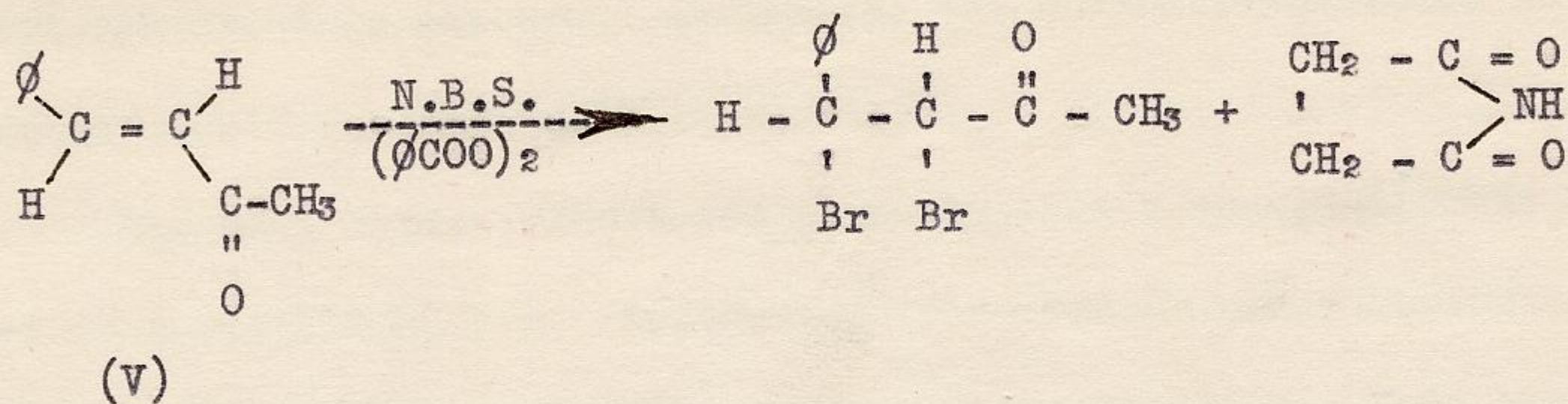


The acetophenone produced in the above mechanism was not detected in the actual case, but the small amount of acetophenone produced in conjunction with a 19.4% yield of phenacyl chloride could have been tied up with the crude solid in the condenser, it would thereafter have been lost on recrystallization.

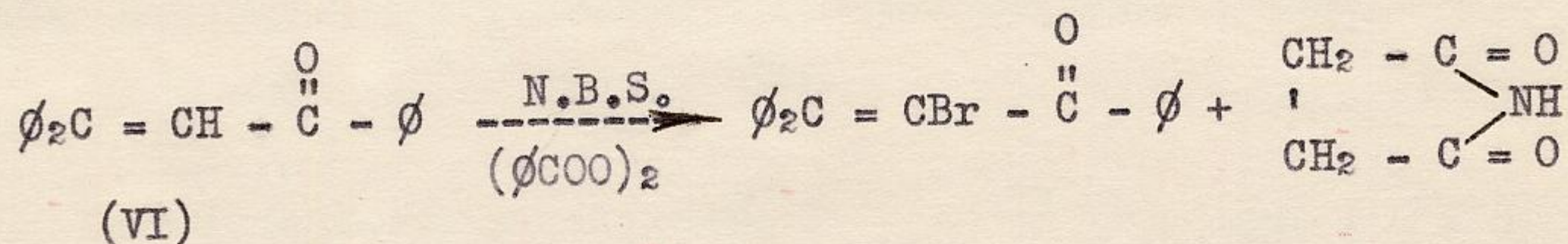
IV. Action of N-bromosuccinimide on Dypnone

The failure to obtain the dibromide addition product of trans-dypnone by direct bromination led to the use of another brominating agent, N-bromosuccinimide. Although N-bromosuccinimide is known to brominate the allylic position under most circumstances, cases have been reported where the reagent attacks the double bond of α, β-unsaturated ketones in the presence of five mole per cent of benzoyl peroxide.¹⁴ Thus, benzalacetone (V), when treated with N-bromosuccinimide in the presence of benzoyl peroxide, is converted

to benzalacetone dibromide in 46% yield.¹⁴:



Chalcone (IV) is converted to the corresponding dibromide (yield 57%) when treated in a similar manner.¹⁴ However, when β -phenyl chalcone (VI) is treated similarly, the α -bromo derivative, and not the dibromide, is obtained:¹⁴

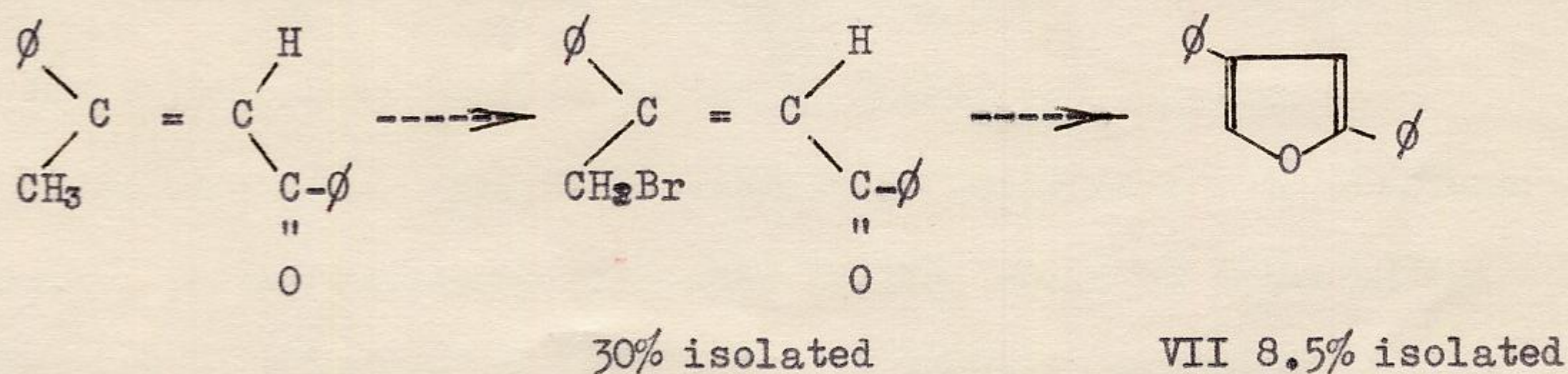


Unfortunately the mechanisms of the above reactions (especially for the addition reaction) have not yet been elucidated, although research^{14,15} has been conducted specifically for that purpose. The difficulty in the case of the addition reaction consists in discovering the source of the hydrogen required to replace the bromine of N-bromosuccinimide to yield succinimide.

In this research, trans-dyponone was first treated with N-bromosuccinimide in the absence of benzoyl peroxide. This reaction (Wohl - Ziegler reaction) is known to give the product of allylic bromination, γ -bromodyponone.¹⁶ A solution of dyponone in dry carbon tetrachloride was heated with N-bromosuccinimide at the reflux temperature of the solution. A 76.5% yield of succinimide and a 75% yield of trans- γ -bromodyponone were obtained. The trans- γ -bromodyponone, after recrystallization from ethanol, melted at 66.5 - 67.5°C. (Reported melting point

deduced from the infrared absorption spectrum of the solid, which did not show any absorption band characteristic of the carbonyl group. Also, microanalysis of an analytical sample revealed that bromine was absent and that the percentage composition was near to that of dyprnone. From the above considerations it was decided that the molecule might be a furan. The infrared absorption spectrum of the above solid was then found to be identical to the spectrum of 2,4-diphenylfuran (VII), the melting point of which is reported to be 109 - 110.5°C.¹⁷ The percentage composition of the compound obtained here satisfies the requirements of 2,4-diphenylfuran, thereby confirming its identity.

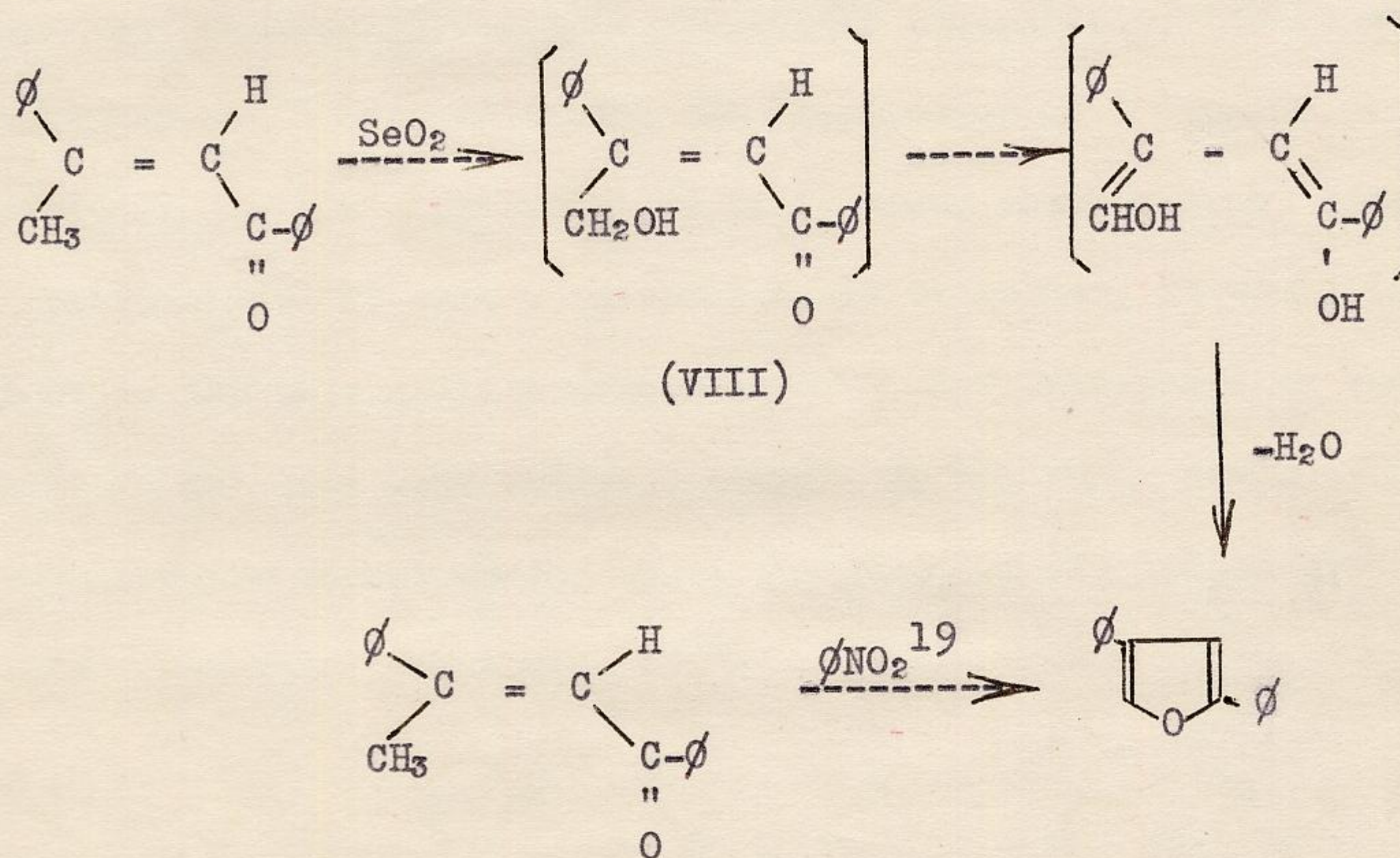
The above furanization can be explained in the light of earlier work¹², which has shown that γ -bromodyprnone can be converted to 2,4-diphenylfuran in the presence of a base, or on heating in the presence of moisture, or even on long standing at room temperature. It is likely, therefore, that dyprnone was first converted to γ -bromodyprnone (30% of which was actually isolated in the reaction mixture), which in turn was converted to the 2,4-diphenylfuran:



V. Dypnone Furanizations

At this point, efforts to prepare dypnone dihalides were given up, and attention was turned to dypnone furanization.

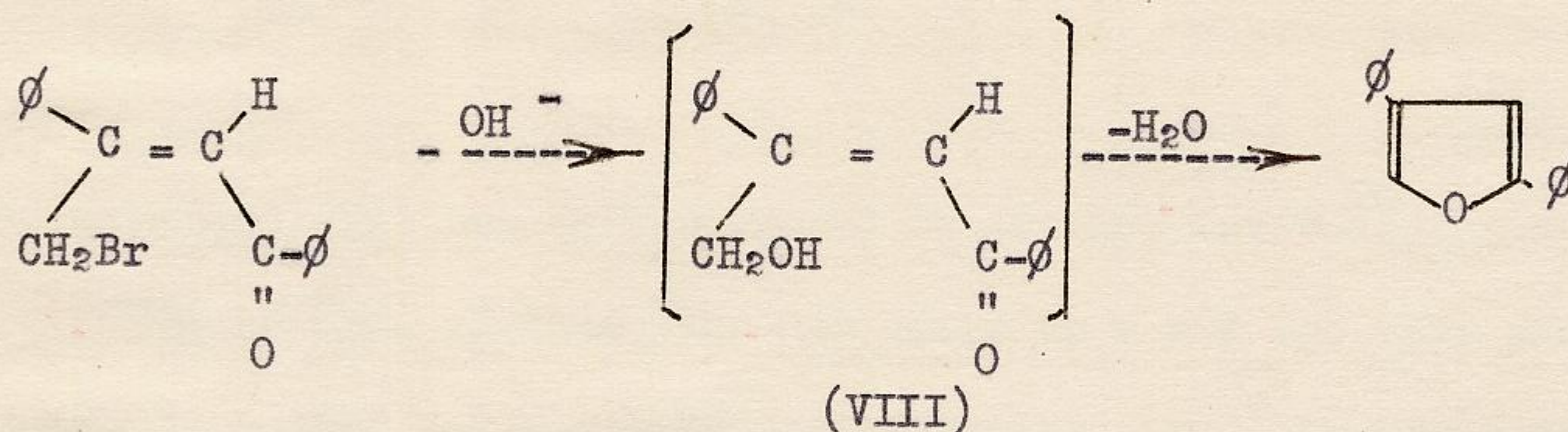
It had long been known that dypnone itself gave furan under oxidative conditions, but an actual mechanism for the oxidative furanization of dypnone to the 2,4-diphenylfuran was first proposed by Fuson, Fleming, and Johnson in 1938.¹⁸ The furanization was accomplished with selenium dioxide as the oxidizing agent. The proposed mechanism follows:



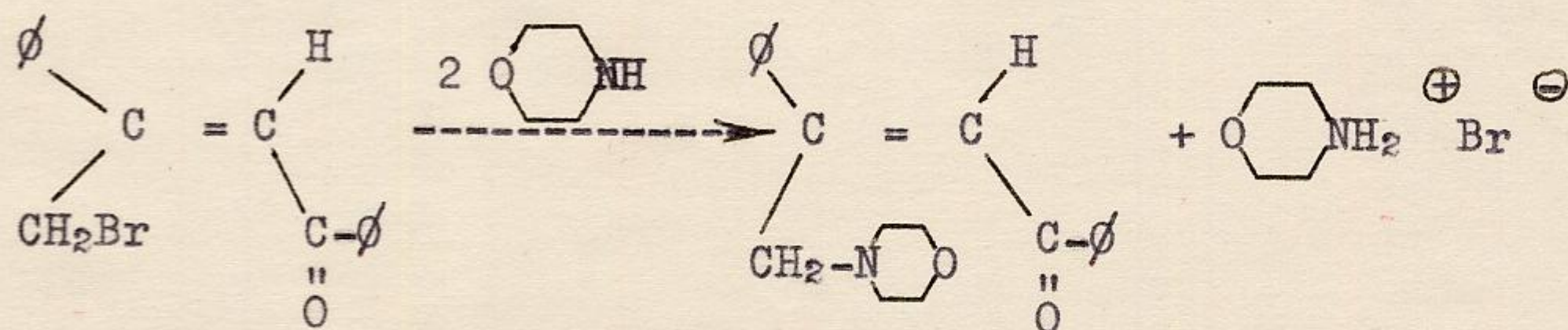
Fuson, Fleming, and Johnson postulate this same furan as the product of the oxidation of dypnone gotten by Engler and Dengler.¹⁹

Fuson and his coworkers advanced no evidence for this mechanism; however, if the γ -hydroxy compound, (VIII), could be isolated and then made to furanize, support would be given to the Fuson mechanism. Lutz and Slade¹² attempted to prepare this compound by reacting γ -bromodypnone with sodium hydroxide, but the γ -hydroxydypnone, if formed at all, existed only as an intermediate, the only isolable

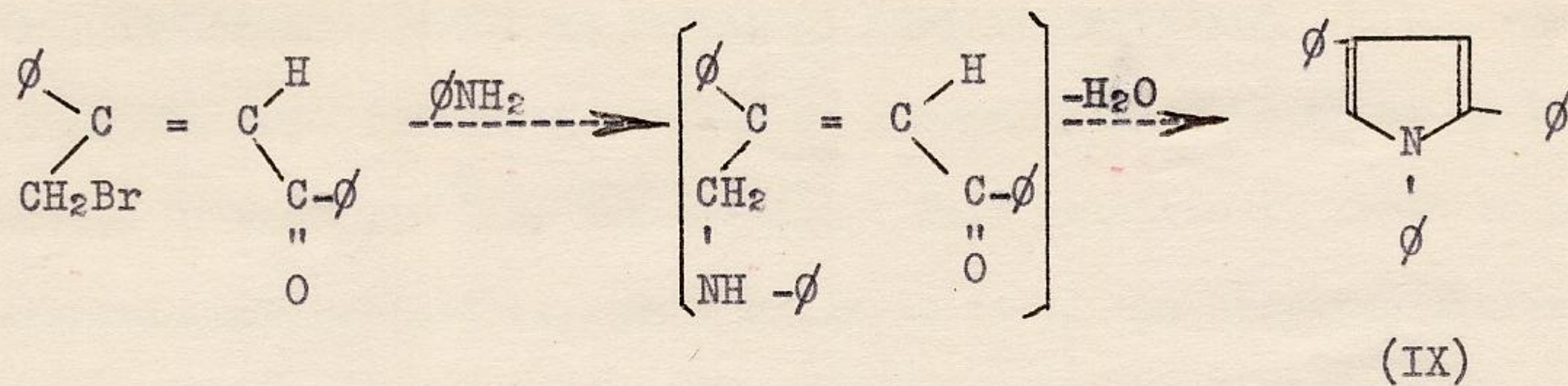
product was the furan. However, this reaction itself, with the likely intermediacy of the γ -hydroxydypnone, does lend some support to the Fuson mechanism.



Since the γ -hydroxydypnone is apparently incapable of stable existence, Lutz and Slade¹² next attempted the preparation of a dypnone compound containing, in the γ -position, a basic group which was not susceptible to cyclization. If such a compound could be gotten, it would lend weight to the intermediate existence of γ -hydroxydypnone in the above reaction, and thus lend indirect support to the Fuson mechanism. Morpholine was chosen as the base; the reaction did indeed give the stable γ -morpholinodypnone.

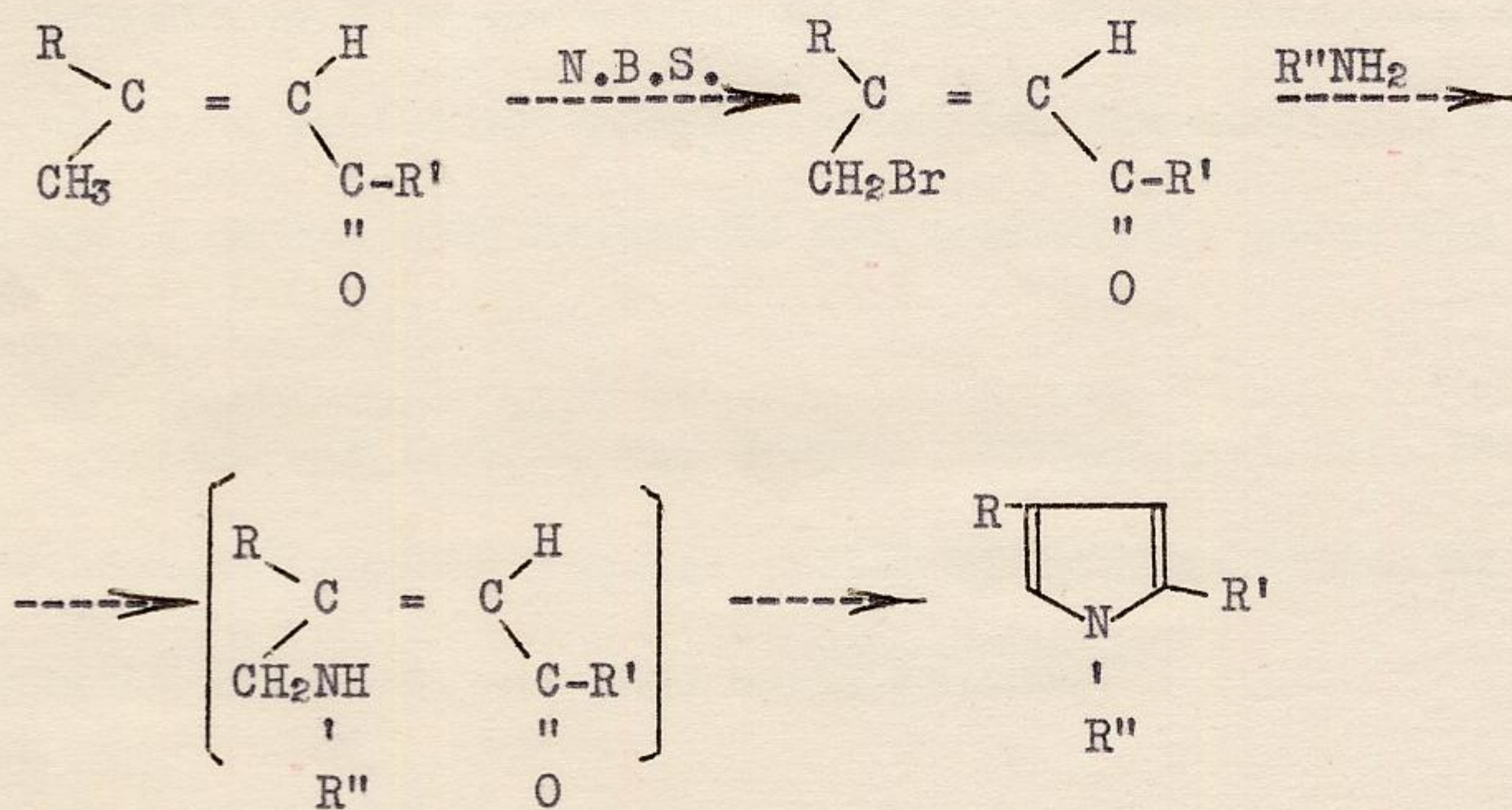


This present research has investigated the possibility of combining the principles of the above two reactions; i.e. if a primary amine be used as the base, cyclization should proceed to yield the pyrrole. The γ -bromodypnone was reacted with aniline to see specifically if a primary amine would cyclize the molecule. The 1,2,4-triphenylpyrrole (IX) was obtained in good yield.



The compound (IX) has been prepared by another route.²⁰

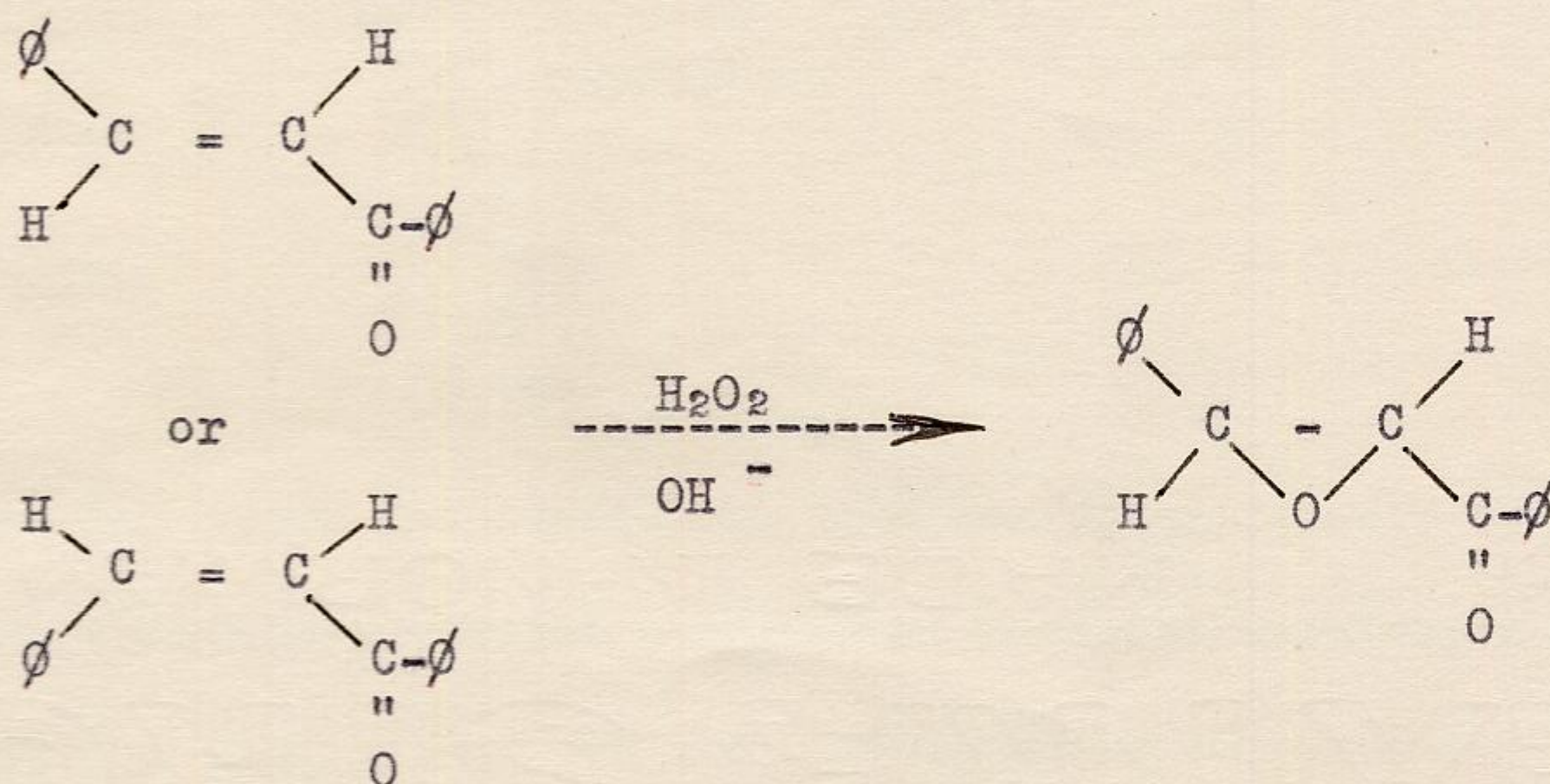
The success of this reaction opens up a new and very promising synthetic method for N-substituted pyrroles, involving only two steps from the appropriately substituted allyl ketone:



VI. Addition of Hydrogen Peroxide; Epoxide Formation

The epoxidation of olefins is generally brought about by the action of peracids²¹ on the olefins. This reaction is known to be stereospecific; that is, the configuration of the starting olefin is retained in the product. This method of epoxidation, however, is not suitable for α, β -unsaturated ketones, since the reaction with these compounds occurs very slowly, if at all.²² On the other hand, alkaline hydrogen peroxide, and sodium peroxide, which do not usually attack isolated double bonds, react well with α, β -unsaturated ketones to form epoxides. This mode of epoxidation, however, was found to be non-stereospecific; that is, the configuration of the starting unsaturated ketone is not necessarily preserved in the product.

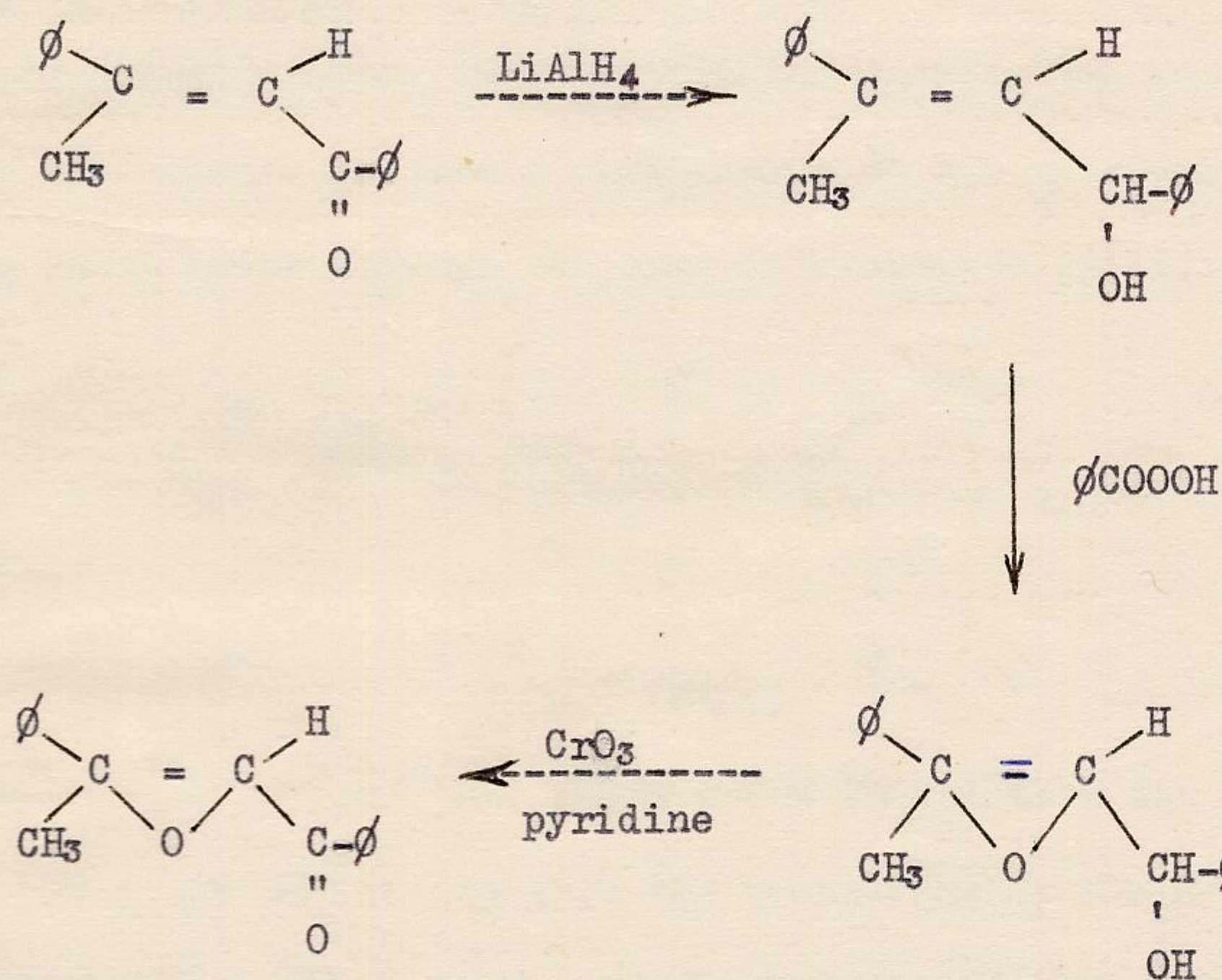
Black and Lutz²³, for example, showed that both the cis- and the trans-isomer of chalcone yield, after epoxidation with alkaline hydrogen peroxide, the same epoxy ketone.



Wasserman and his coworkers^{24,25} prepared, by the same method, two isomeric dypnone epoxides from the trans-isomer of dypnone.

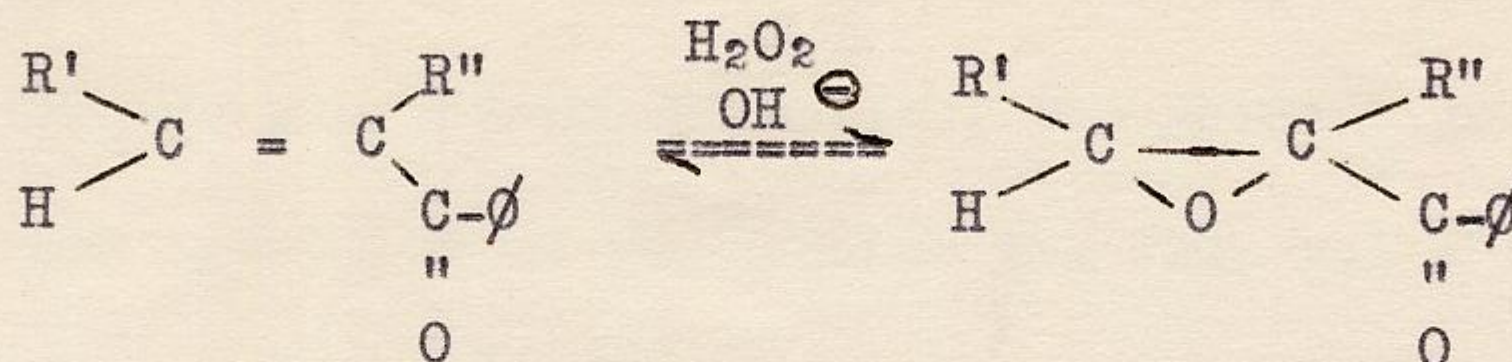
the trans-configuration to isomer (X), while the cis-configuration was reserved for isomer (XI).

In order to prove the truth of this argument, Wasserman and Aubrey²⁵ in 1955 prepared trans-dyprnone epoxide by a series of stereospecific reactions and found that the product was identical to isomer (X) obtained from the direct epoxidation of trans-dyprnone. The stereospecific preparation of trans-dyprnone epoxide is outlined as follows:



The kinetics of the epoxidation reaction by alkaline hydrogen peroxide were first studied by Bunton and Minkoff²⁷ in 1949. On the basis of those studies, House and Ro²² proposed that the mechanism of base-catalyzed epoxidation of α, β -unsaturated ketones proceeds as shown (using trans-dyprnone as an example):





the products of which are not capable of base-catalyzed epimerization because of the presence of the R'' - groups on the α -carbon atoms. The fact that α -substituted unsaturated ketones of this type did indeed give non-stereospecific products is evidence that the above mechanism of House and Ro is probably correct.

As has been noted above, the trans-dyprnone epoxide was obtained with a yield of 62%. The same preference for the trans-isomer was observed by Stevens and coworkers.¹⁶ The explanation for the higher yield of the trans-dyprnone epoxide as compared to the cis-dyprnone epoxide was suggested independently by many authors,^{23,24,28} but their suggestions were unified in an article by Zimmerman, Singer and Thyagarajan in 1959²⁹. They pointed out that the trans-isomer offered less steric hindrance. Actually most of the epoxides of α, β -unsaturated ketones reported in the literature are in the trans-configuration, wherein the acyl or benzoyl group is least hindered.

If the House and Ro mechanism is to be correct, then the configuration of the starting α, β -unsaturated ketone should have little or no effect on the nature and relative yields of the products. This conclusion could be tested (and evidence thus adduced for or against the House and Ro mechanism) by attempting the epoxidation of cis-dyprnone and comparing the results obtained with those gotten on epoxidation of trans-dyprnone. The experiments were carried out in

the research leading to this thesis, and the experimental results of this research support the mechanism; the percentage yield of the trans-dyprnone epoxide from cis-dyprnone was 42%, while that of the cis-isomer was only 9.3%. These results are to be compared with those obtained from the epoxidation of trans-dyprnone in this research; again the trans-epoxide was the favored compound, being formed in 56% yield, while the cis-dyprnone oxide was isolated in 12% yield.

EXPERIMENTAL

The ultraviolet absorption spectra were determined in 95% ethanol (unless otherwise indicated) using a Beckmann model D.U. Spectrophotometer.

All infrared spectroanalyses were performed on a Perkin-Elmer "Infracord" Infrared Spectrophotometer.

All melting points are corrected.

Preparation of Trans-Dyprone

The trans-dyprone was synthesized by the method of Calloway and Green.¹ In a five-liter round-bottomed three-necked flask, equipped with a stirrer and a reflux condenser protected by a calcium chloride tube, were placed 453 gr (3.4 mole) of aluminum chloride and 3,400 ml of carbon disulfide. Acetophenone (816 gr, 6.8 mole) was then added dropwise through a dropping funnel while the mixture was being stirred and cooled in a water bath. Stirring was continued for five hours after completion of the addition of acetophenone. The stirrer was then removed and the mixture was allowed to stand at room temperature for seven days. During this period the lower part of the mixture solidified, and the color of the supernatant liquid became dark brown.

The reaction product was hydrolyzed by mixing it thoroughly with 6,000 gr of cracked ice; the resulting layers were separated by means of a four-liter separatory funnel.

The aqueous layer was extracted twice with 250 ml portions of carbon disulfide, the washings being added to the original carbon disulfide

solution, while the water layer was discarded.

The carbon disulfide solution was then washed twice with 300 ml portions of water and once with a 10% solution of sodium bicarbonate, and finally dried overnight over sodium sulfate.

The mixture was then filtered, and the solvent was removed by distillation. The distillation was continued under reduced pressure, whereby 398 gr (48%) of unreacted acetophenone, b.p. $56 - 62^{\circ}$ / 1 mm, was recovered. Impure dypnone of boiling range $140 - 180^{\circ}$ / 1 mm was then obtained; this oil on redistillation yielded 317 gr (42% yield) of dypnone of boiling range $145 - 151.5^{\circ}$ / 1 mm.

Absorption maxima: μ , 228.5, $\epsilon = 9,990$; 295, $\epsilon = 15,400$.

μ , 3.40M, 6.12S, 6.35S, 6.78W, 6.99S, 7.34M,

7.47M, 7.92S, 8.58M, 9.37W, 9.62M, 9.82M, 10.05W,

10.58S, 11.58M, 11.72M.

The specific gravity of trans-dypnone, determined with a Fisher-Davidson Gravitometer, was found to be 1.092 gr/ml at 18° (average of two determinations), (see Discussion for literature values).

The refractive index determined with an Abbe refractometer was 1.6347 at 18° (average of two readings) and 1.6344 at 20° (average of two readings). The specific refraction was calculate to be 0.32778; the molar refraction was calculated to be 72.83. (See Discussion for literature values).

Derivatives of Trans-Dypnone

2,4-dinitrophenylhydrazone: This derivative was prepared by the general method of Shriner, Fuson, and Curtin.²

Dypnone (1 gr) was dissolved in 40 ml of 95% ethanol. 2,4-dinitrophenylhydrazine (0.8 gr) was dissolved in four ml. of concentrated sulfuric acid, and water was added dropwise until solution was complete. To this warm solution 10 ml of ethanol was added. The two solutions were then mixed together, and the resulting mixture was allowed to stand at room temperature for about 15 minutes. The product was recrystallized from an ethanol-ethyl acetate mixture; melting point 166 - 167° (Literature, 170⁰³, 173 - 174⁰⁴). The yield was 55.5%. Absorption maxima: μ , 385, ϵ = 9,900.

μ , 3.18W, 3.45W, 6.25S, 6.34S, 6.72S, 7.09M, 7.55S, 7.68S, 8.82S,
9.02M, 9.80W, 10.85W, 12.00M.

p-Nitrophenylhydrazone: (New derivative). A mixture of 1 gr of p-nitrophenylhydrazine, 1 gr of dypnone, and 15 ml of ethanol was heated to boiling, and 4 ml of concentrated sulfuric acid were added. The mixture was allowed to stand at room temperature until crystallization occurred. The product was recrystallized from ethanol; melting point 189 - 190°. The yield was 62.5%.

Analysis calculated for C₂₂H₁₉N₃O₂: C, 74.00; H, 5.36; N, 11.77.

Found: C, 74.39; H, 5.45; N, 11.87.

Absorption maxima: μ , 230, ϵ = 11,350.

μ , 3.45W, 6.36S, 6.78S, 7.00W, 7.25M, 7.72S,
8.51W, 9.02S, 9.24M, 9.45W, 10.01W, 11.92M.

Anti-phenyl oxime: This compound was prepared by the general method of Shriner, Fuson, and Curtin.² A mixture of 1 gr of dypnone, 1 gr of hydroxylamine hydrochloride, 5 ml of pyridine, and 5 ml of absolute ethanol was heated under reflux for two hours on a water bath. The solvent was then evaporated, and the residue was treated with 5 ml of cold water.

The solid which separated was recrystallized from an ethanol-water mixture; melting point 129 - 131° (Reported, 132 - 133⁰⁴, 134⁰³¹).

Absorption maxima: μ , 250, $\epsilon = 17,500$.

μ , 2.98W, 3.20S, 6.24M, 6.78M, 7.00S, 7.31W,
7.58M, 9.12W, 9.35W, 9.75W, 10.26S, 10.70S,
11.52M.

Semicarbazone: The procedure followed is the standard procedure for water insoluble compounds described by Shriner, Fuson, and Curtin.² The derivative, however, failed to precipitate.

Preparation of Cis-Dyprone

A solution of 40 gr of trans-dyprone in 1000 ml of diethyl ether (or 95% ethanol) in a pyrex round-bottomed flask was exposed to direct sunlight for approximately 48 hours, after which time the absorption maxima of the photoequilibrium mixture showed that the conversion was 88% complete. The solvent was then removed under reduced pressure using a water aspirator, the use of heat being avoided to minimize reconversion of cis-dyprone to the trans-isomer. The oil remaining after solvent removal was again, U.V. spectroanalyzed, to ascertain whether any reconversion to trans-dyprone had taken place during solvent removal; no such reconversion had occurred. Experimental absorption maxima:

μ , 255, $\epsilon_1 = 12,560$; 285, $\epsilon_2 = 12,198$. Reported absorption maxima of pure cis-dyprone⁴: μ , 255, $\epsilon_1 = 13,500$; 287.5, $\epsilon_2 = 11,500$. Experimental ratio, $\frac{\epsilon_1}{\epsilon_2} = 1.03$, reported ratio $\frac{\epsilon_1}{\epsilon_2} = 1.17$. These ratios correspond to 88% conversion.

Derivatives of Cis-Dypnone

2,4-dinitrophenylhydrazone: The procedure was that of Shriner, Fuson, and Curtin² and hence is identical to the one described for the preparation of trans-dypnone 2,4-dinitrophenylhydrazone.

The crude product had a melting point of 139 - 166^o and was not completely soluble in a 50% ethanol-ethyl acetate mixture. The insoluble fraction was then separated by filtration and recrystallized from ethyl acetate; melting point 212 - 213^oC.

Analysis Calculated for C₂₂H₁₈N₄O₄: C, 65.68; H, 4.47.

Found: C, 65.63; H, 4.76.

Absorption maxima: μ , 387, ϵ = 13,600.

μ , 3.10W, 3.38W, 6.21S, 6.31M, 6.63M, 7.09W,
7.53S, 7.67M, 8.84M.

The melting point of the ethanol-soluble fraction was 143 - 144^oC.

Analysis Calculated for C₂₂H₁₈N₄O₄: C, 65.68; H, 4.47; N, 13.93.

Found: C, 65.69; H, 4.66; N, 14.12.

Absorption maxima: μ , 386, ϵ = 12,900.

μ , 3.10W, 3.38W, 6.21S, 6.31M, 6.64M, 7.08W,
7.52S, 7.68M, 8.82M.

Literature⁴ reports an analytically pure sample of m.p. 186 - 187^oC.

Attempted preparation of cis-dypnone p-nitrophenylhydrazone: The procedure was identical to that followed for the preparation of trans-dypnone p-nitrophenylhydrazone. The product obtained was again trans-dypnone p-nitrophenylhydrazone. This fact was confirmed by a mixed melting point determination on a mixture composed of the product of this reaction and a known sample of trans-dypnone p-nitrophenylhydrazone (189 - 190^o)

and by comparison of the infrared absorption spectra of the two samples, which proved to be identical.

The above preparative procedure was repeated, employing five drops of concentrated sulfuric acid instead of four ml of the acid. The product after recrystallization from ethanol had a melting point of 147 - 148°C.

Analysis Calculated for $C_{22}H_{18}N_3O_2$: C, 74.00; H, 5.35; N, 11.77.

Found: C, 57.32; H, 6.31; N, 19.49.

Absorption maxima: μ , 3.05W, 3.92W, 6.35S, 6.75M, 7.63S, 7.93W,
8.05M, 9.05S, 11.85M.

The product was not identified.

Attempted Bromination of trans-dypnone

In a 500-ml three-necked round-bottomed flask, equipped with a mechanical stirrer, a reflux condenser, and a dropping funnel, was placed a solution of 22.2 gr (0.1 mole) of dypnone in 100 ml of dry diethyl ether. The flask was immersed in an acetone-liquid air bath (-80°C.), and 16 gr (0.1 mole) of bromine were allowed to drip slowly through the dropping funnel into the reaction mixture. Stirring was continued for about two hours after the addition of bromine was completed, the temperature of -80°C. being maintained. The solution was then concentrated under reduced pressure to a thick yellow oil. The product was successively dissolved in absolute ethanol, benzene, and petroleum ether without success in bringing about crystallization. An attempt to vacuum distil the oil was equally unsuccessful; the oil decomposed completely.

The above reaction was repeated three more times at temperatures of -50°, -70°, and -100°C. In all cases the same oily product was obtained.

Absorption maxima: μ , 3.41W, 5.98S, 6.33M, 6.40W, 6.68M, 6.77W,
6.99S, 7.35M, 7.60M, 7.75W, 8.10S, 9.65M,
10.18M.

Attempted Chlorination of Trans-Dyprone

A cold solution of 11.1 gr (0.05 mole) of dyprone in 90 ml of chloroform was saturated for 30 minutes with chlorine gas. The solvent was then removed under reduced pressure, and 14.8 gr of an oil was obtained. The product was treated successively with chloroform, ethanol, benzene, and light petroleum ether, but no solid crystallized out.

Derivatives were then attempted from the crude oil. The oxime and the p-nitrophenylhydrazone failed to precipitate. The action of 2,4-dinitrophenylhydrazine on the oil yielded yellow crystals, melting point 123-124°C.

Analysis Calculated for $C_{22}H_{18}N_4O_4Cl_2$ (dyprone dichloride 2,4-dinitrophenylhydrazone): C, 55.83; H, 3.82; N, 11.84.

Found: C, 44.83; H, 4.39; N, 22.70.

Absorption maxima: μ , 3.10W, 6.22S, 6.32S, 6.65S, 7.09M, 7.53S,
7.78S, 8.05W, 8.85M, 9.10M, 9.95W, 10.90M,
12.00M.

Vacuum distillation of the crude oil yielded 1.5 gr of phenacyl chloride, which distilled at 100°/ 4 mm and solidified in the condenser; the rest of the oil decomposed in the distillation flask. The melting point of the solid after recrystallization from petroleum ether was 48 - 52°C. (Reported, 54°C.¹³) Yield (based on dyprone) was 19.4%.

Analysis Calculated for C_8H_7OCl : C, 62.14; H, 4.56; Cl, 22.96.

Found: C, 61.46; H, 4.66; Cl, 23.24.

The infrared absorption spectra of the above solid and an authentic sample of phenacyl chloride proved to be identical.

The phenacyl chloride 2,4-dinitrophenylhydrazone was prepared following the standard method of Shriner, Fuson, and Curtin.² Yellow needles were obtained; melting point 208 - 210^od. (Reported melting point 212^oC.²).

Analysis Calculated for C₁₄H₁₁N₄O₄Cl: C, 50.24; H, 3.31; N, 16.76; Cl, 10.60.

Found: C, 50.55; H, 3.54; N, 17.63; Cl, 11.31.

Preparation of Trans- γ -bromodypnone

The procedure was that of Wasserman, Aubrey, and Zimmerman²⁴, with some modifications.

The apparatus was protected from moisture by a calcium chloride tube, and the carbon tetrachloride used as solvent was dried over phosphorus pentoxide and distilled.

To a solution of 22.2 gr (0.1 mole) of trans-dypnone, dissolved in 100 ml of carbon tetrachloride was added (0.1 mole) 17.8 gr N-bromosuccinimide. The mixture was refluxed for three hours, at the end of which time a crust of yellow solid was formed at the surface of the solution. The mixture was allowed to cool, and the solid was separated by filtration. The solid was washed twice with 10 ml portions of carbon tetrachloride, the washings being added to the solution, after which the solid was dissolved in boiling water. The water was then evaporated, and the residue was recrystallized from ethanol, yielding 76.5% succinimide, melting point 123^oC. (literature melting point of succinimide is 125^oC.²).

The carbon tetrachloride solution obtained from the filtration was

then concentrated under reduced pressure until a yellowish oil remained. This oil was dissolved in absolute ethanol, and the solution was left overnight in the refrigerator, where crystallization took place. The product was recrystallized from ethanol; melting point $66.5 - 67.5^{\circ}\text{C}$. (Reported: $66 - 67^{\circ}\text{C}$.¹⁶). The yield was 75%.

Absorption maxima: μ , 298, $\epsilon = 15,600$.

μ , 3.40W, 6.12S, 6.33S, 6.43M, 6.80W, 6.99M, 7.10W,
7.45M, 7.84M, 8.20W, 8.55M, 9.33W, 9.59M, 9.71W,
9.79W, 9.99M, 10.11M, 11.43W, 11.80M.

Reaction of cis-dyprone with N-Bromosuccinimide: Cis-dyprone was treated as described above. The product obtained was again trans- γ -bromodyprone; melting point, and mixed melting point with a known sample of trans- γ -bromodyprone, were $66 - 68^{\circ}\text{C}$. (Literature, $66 - 67^{\circ}\text{C}$.¹⁶). The yield was 41%. The identity of the product of this reaction with trans- γ -bromodyprone was further shown by the identity of their ultraviolet spectra and the identity of their infrared spectra.

Reaction of Trans-Dyprone with N-Bromosuccinimide and Benzoyl Peroxide

2,4-diphenylfuran: A mixture of 22.2 gr (0.1 mole) of dyprone, 17.8 gr (0.1 mole) of N-bromosuccinimide, 1.2 gr (0.005 mole) of benzoyl peroxide, and 100 ml of carbon tetrachloride was heated for three hours. The solution became red brown in color during this period, and a red brown solid separated on the surface of the solution. After separating the solid from the solution by filtration, the solid was treated with boiling water. Concentration of the aqueous solution yielded succinimide which, following recrystallization from ethanol, melted at 123°C . (Litera-

ture, $125^{\circ}\text{C}.$ ²). The yield was 48%.

The carbon tetrachloride solution, which had turned brown during the heating period, was now divided into two equal portions and treated separately. The first portion was concentrated under reduced pressure to a thick green oil which was subsequently dissolved in light petroleum ether. The solution was allowed to stand at room temperature overnight, yielding γ -bromodypnone; melting point, and mixed melting point with a known sample, $67 - 68^{\circ}\text{C}.$ (Literature, $66 - 67^{\circ}\text{C}.$ ¹⁶). The yield was 30%. No other pure substance could be isolated from this portion of the reaction mixture; a green polymer was obtained.

The second portion was placed on a column of neutral alumina prepared in light petroleum ether. The column was eluted with light petroleum ether (boiling point $50 - 70^{\circ}\text{C}.$), and fifteen 25 ml fractions were collected. Crystalline material, melting point $105 - 111^{\circ}\text{C}.$, was obtained on evaporation of the first ten fractions. Recrystallization from ethanol yielded 950 mg of white flakes, melting point $109 - 110^{\circ}\text{C}.$ (Literature, $109 - 110.5^{\circ}\text{C}.$ ¹⁷). The yield was 8.5%, calculated as 2,4-diphenylfuran.

Analysis Calculated for $\text{C}_{16}\text{H}_{12}\text{O}$: C, 87.27; H, 5.45.

Found: C, 87.70; H, 5.43.

Absorption maxima: μ , 3.40W, 6.25W, 6.35W, 6.75S, 6.95M, 8.80S,
10.78M, 10.95S.

The infrared absorption spectrum was found to be identical to the known spectrum of 2,4-diphenylfuran.

Reaction of Trans- γ -bromodypnone with Aniline

Preparation of 1,2,4-triphenylpyrrole: To a solution of 5 gr (0.017 mole) of γ -bromodypnone in 200 ml of dry diethyl ether was added 5 ml (0.054 mole) of aniline, in a dropwise manner. The mixture was shaken for five minutes, until no more anilinehydrobromide crystallized, and was allowed to stand overnight at room temperature. The solvent was then removed under reduced pressure, and the solid cake which remained was broken and shaken with 100 ml of water. The water insoluble fraction was then filtered and recrystallized from absolute ethyl alcohol; melting point 151 - 152°C. (Reported, 150 - 151°C.²⁰). The yield was 58%.

Analysis Calculated for C₂₂H₁₇N: C, 89.45; H, 5.80; N, 4.75.

Found: C, 89.37; H, 5.84; N, 4.76.

Absorption maxima: μ , 231, ϵ = 6,265; 259, ϵ = 26,470; 280, ϵ = 21,050.

μ , 3.39M, 6.27S, 6.42W, 6.60W, 6.70S, 6.82W,
6.92M, 7.20M, 7.86W, 7.55W, 8.15M, 8.45W,
9.32M, 9.73W, 10.40W, 10.98W, 12.34M.

Epoxidation of Trans-Dypnone

The procedure is that of Wasserman, Aubrey, and Zimmerman.²⁴ A solution of 10 gr (0.045 mole) of trans-dypnone in 100 ml of methanol was treated with a mixture of 12 ml of 25% hydrogen peroxide and 10 ml of 10% sodium hydroxide. The reaction mixture was then cooled and shaken for about an hour, after which water was added, and the white solid which separated was filtered off. The solid was then dissolved in a large quantity of ethanol (300 ml) and allowed to crystallize slowly. White needles of cis-dypnone oxide, (1.3 gr; 12% yield) were obtained, the melting point of which was

159 - 161.5°C. (Reported, 163 - 164°C.²⁴). Upon dilution of the filtrate with water, 6.0 gr (56% yield) of white plates of trans-dyprnone oxide were collected, melting point 90.5 - 92.5°C. (Reported, 94 - 95°C.²⁴). The overall yield was 68%.

Absorption maxima

Cis-dyprnone oxide: $m\mu$, 249, $\epsilon = 13,500$.

μ , 3.40W, 5.98S, 6.31W, 6.39W, 6.75W, 6.96M,
7.22M, 7.39W, 7.63W, 8.20M, 8.55W, 9.25W,
9.78W, 10.00W, 10.23S, 11.15W, 11.78M.

Trans-dyprnone oxide: $m\mu$, 250.5, $\epsilon = 17,110$.

μ , 2.90W, 3.04W, 3.38M, 4.15W, 5.14W, 5.30W,
5.56W, 5.92S, 6.29S, 6.35M, 6.72M, 6.92S,
7.25S, 7.62M, 7.70M, 7.81S, 8.15S, 8.52M,
8.68W, 9.04M, 9.12W, 9.28M, 9.64M, 9.79S,
10.00W, 10.42S, 10.28W, 11.40W, 11.80S,
12.15M.

Epoxidation of Cis-Dyprnone

A solution of cis-dyprnone was treated as described above. From this reaction mixture were obtained 1.0 gr (9.3% yield) of cis-dyprnone oxide, melting point 158.5 - 160.5°C. (Reported values above) and 4.5 gr (42% yield) of trans-dyprnone oxide, melting point 90.5 - 92.5°C. (Reported values above). The overall yield was 51.3%. Mixture melting points with the compounds of corresponding melting point obtained from the epoxidation of trans-dyprnone showed no depression, and the infrared and ultraviolet absorption spectra of the corresponding compounds were identical.

SUMMARY

Trans-dyprnone was prepared and identified fully by means of its physical constants and its chemical derivatives. A new derivative, the p-nitrophenylhydrazone, was prepared by a slight modification of the standard procedure.

Cis-dyprnone was prepared and identified spectrophotometrically. The 2,4-dinitrophenylhydrazone of cis-dyprnone was prepared, and two products of different melting point, but identical composition (within experimental error), identical infrared spectra, and identical ultraviolet spectra (again within experimental error) were isolated. Since this derivative is reported in the literature with still another melting point, it is concluded that cis-dyprnone 2,4-dinitrophenylhydrazone exhibits polymorphism.

Attempted bromination of trans-dyprnone failed to produce the dibromide, while the chlorination reaction yielded phenacyl chloride, possibly as a result of a reverse aldol reaction in the presence of traces of water. The absence of a basic catalyst renders this postulation questionable, however.

N-bromosuccinimide reacted with both trans- and cis-dyprnone to produce trans- γ -bromodyprnone, while in the presence of five mole per cent of benzoyl peroxide trans-dyprnone yielded the γ -bromodyprnone and some 2,4-diphenylfuran. The fact that trans- and cis-dyprnone gave the same products, indicating conversion of cis-dyprnone to the trans-isomer during reaction, is not surprising in view of the nonplanarity and consequent instability of the cis-isomer.

Trans- γ -bromodyprnone reacted with aniline to yield 1,2,4-triphenylpyrrole, thus lending indirect support to Fuson's¹⁸ mechanism for the

oxidative furanization of dypnone; this reaction also opens up a new synthetic method for N-substituted pyrroles.

The epoxidation reactions of both trans- and cis-dypnone were studied in conjunction with the House and Ro²² mechanism; the reactions proceeded according to expectations and thus lend support to the mechanism.

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