Amozonolysis of Cycloolefins

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Ozonization of five-membered cycloolefins emulsified in aqueous ammonia gave six-membered aromatic heterocyclic compounds. Larger ring olefins led to polymeric imines, which could be cleaved by hydrolysis to form dialdehydes. The ozonization of cyclohexene and cyclooctene in *t*-butylamine yielded cycloolefinic *t*-butylimines. These new reactions have been named "amozonolysis."

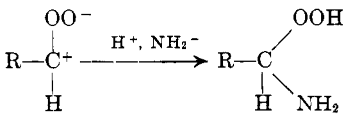
Ozonolysis of olefins in protonic solvents usually gives hydroperoxides and aldehydes or condensation products of the two; in aprotic solvents, monomeric or polymeric ozonides and peroxides result.[1]

In our laboratories, ammonia has been used as the protonic solvent. A series of seven cyclic olefins has been ozonized in aqueous ammonia, with results that are summarized in Table I. Two cycloolefins were also ozonized in *t*-butylamine. These reactions have been named "amozonolysis."

Discussion

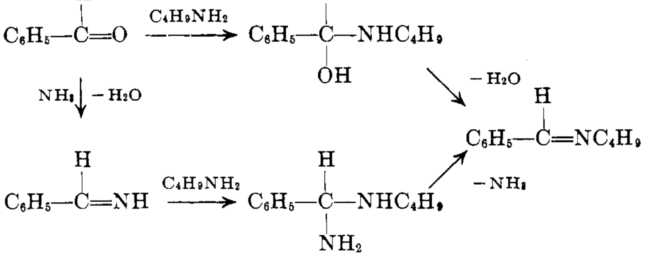
Ammonia proved to be relatively stable towards ozone[2] in presence of the more reactive olefins. At −30° the degree of dissociation of anhydrous liquid ammonia was high enough to yield sufficient H^+ and NH_2^- to add to the zwitterion (I) in the same manner as do the more common protonic solvents.

$$NH_3 \rightleftharpoons H^+ + NH_2^-$$

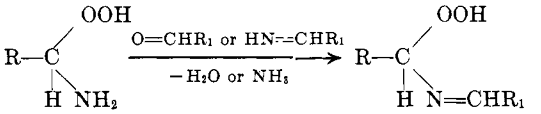


I

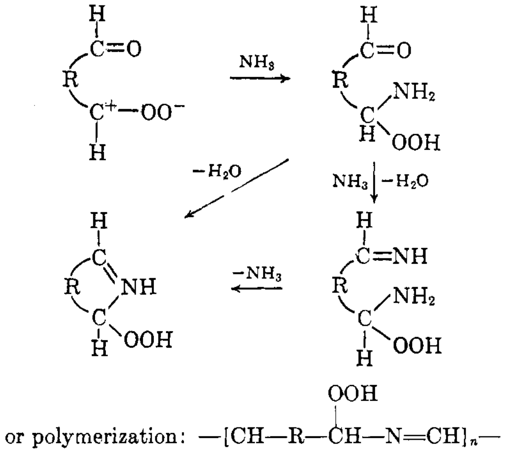
Besides this direct addition of ammonia, the carbonyl product of the ozonolysis condensed rapidly with ammonia and gave an imine. When present in the ammonia phase, alkyl amines reacted to give predominantly alkyl-substituted imino groups, in spite of excess ammonia. For example, benzaldehyde condensed with 1 mole equiv. of *n*-butylamine in an 80% aqueous ammonia emulsion to give N-butylbenzylidenimine in 91% yield. Whether the condensation proceeded directly with the carbonyl group or with the corresponding imino group formed by prior condensation of benzaldehyde with ammonia was not determined, because both paths lead to the same end product.



The higher affinity of the alkyl-substituted ammonia nitrogen towards the carbonyl group may be attributed to the increase of nucleophilic character of the amino nitrogen atom over that of unsubstituted ammonia. A similar property of the α-aminoalkylhydroperoxide led to the following condensation.



By amozonolysis of cycloolefins an analogous condensation gave cyclic or polymeric structures.

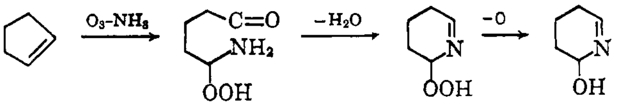


$$\text{or polymerization: } -[CH-R-\overset{OOH}{C}H-N=CH]_n-$$

The intra- or intermolecular condensation depended on the steric conditions of the olefinic starting material, which, for unbranched cycloolefins, was determined predominantly by the ring size. Thus, C_5 cycloolefins would be expected to favor intramolecular addition, yielding six-membered N-heterocyclic compounds, whereas higher cycloolefin homologs would mainly undergo polymerization.

The relatively insolubility of the cycloolefins in ammonia required the use of emulsions to obtain a sufficient interfacial contact between the olefin and ammonia. The suspended olefin droplet had to be mixed sufficiently well to allow the intermediate (I) to react instantly with the ammonia; otherwise inter- or intramolecular reactions within the aprotic environment of the droplet would lead to undesirable polyozonides and polyperoxides. Thus, selecting an emulsifier stable towards ozone and ammonia was of importance: polyoxyalkylene ethers of fatty alcohols such as Pronon and Brij were effective.

Cyclopentene should give the hydroperoxide (II). The stability of the hydroperoxidic group in ammonia proved to be low as might have been expected; the



II III

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(1) P. S. Bailey, *Chem. Rev.*, **58**, 1000 (1958).

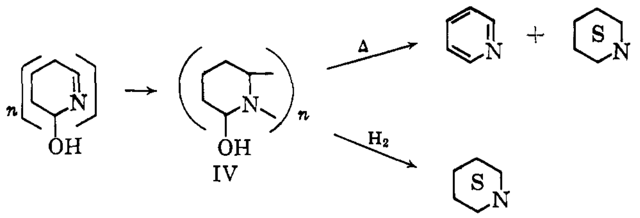
(2) I. J. Solomon, *J. Am. Chem. Soc.*, **84**, 34 (1962).

TABLE I

AMOZONOLYSIS OF CYCLOOLEFINS

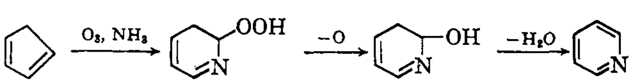
Cycloolefin	Mole	Ozone, mole	Product	Yield, mole %	Recovered starting material, mole	Product identification
Cyclopentene	0.73	0.65	Poly(2-hydroxypiperidine)	90	0.15	$[C_5H_9ON]_x$ Calcd.: C, 60.5; H, 9.2; N, 14.1. Found: C, 60.1; H, 9.0; N, 14.8.
Cyclopentadiene	0.91	0.45	Pyridine	18		Gas chromatography; mass spectroscopy
Indene	0.26	0.24	Isoquinoline	62	0.075	Mixture melting point of picrates; infrared
3-Methylindene	0.23	0.215	4-Methylisoquinoline	48	0.02	Mass spectroscopy; infrared
Indole	0.26	0.24	Quinazoline	9	0.045	Mixture melting point with authentic compound and picrates
Cyclohexene	0.37	0.33	Poly(hydroxytetramethylenimine)	80	0.049	$[C_6H_{11}ON]_x$ Calcd.: C, 63.7; H, 9.7; N, 12.4. Found: C, 64.2; H, 9.7; N, 12.9.
Cyclooctene	0.27	0.25	Poly(hydroxyhexamethylenimine)	80	0.02	$[C_8H_{15}ON]_x$ Calcd.: C, 69.0; H, 9.4; N, 10.1. Found: C, 68.5; H, 9.9; N, 11.0.

primary amozonolysis product had only 10 to 15% of the theoretical hydroperoxide content, indicating reduction by ammonia. The hydroperoxide was completely reduced by adding sulfite after amozonolysis. The 2-hydroxy-2,3,4,5-tetrahydropyridine (III) could not be isolated because of polymerization, probably by way of the —C═N double bond; it gave a resinous polymer of composition $[C_5H_9NO]_n$ (IV).

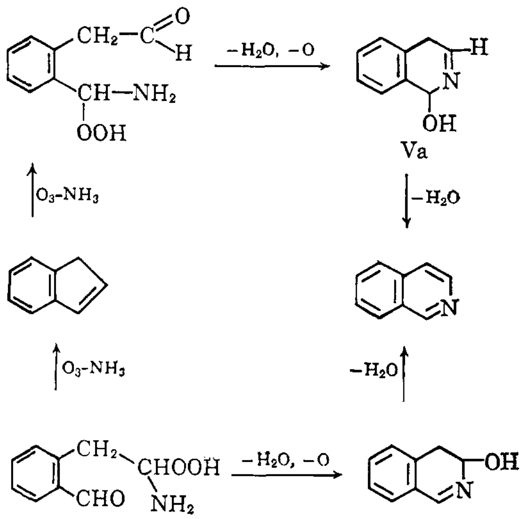


Pyrolysis of the polymer (IV) in an inert liquid gave a mixture of pyridine and piperidine in 12% yield, and minor amounts of methyl- and amino-substituted heterocyclic compounds. Attempts to hydrolyze and depolymerize IV in 5% hydrochloric acid were unsuccessful. Hydrogenation of IV in an aqueous solution at 120–130° and 600 p.s.i. of hydrogen gave 8% piperidine, as well as water-insoluble polymers.

Those C_5 cycloolefins that could form stable cycloimines after dehydration of the reduced amozonolysis product gave considerably better yields of heterocyclic compounds. Thus, cyclopentadiene gave pyridine.



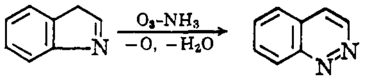
To minimize ozonolysis of the second double bond, an excesss of 1 mole equiv. of cyclopentadiene was used for the reaction. The yield of pyridine was 18%. This was due to the side reaction, polymerization of cyclopentadiene. Such polymerization almost disappeared when the double bond was conjugated with a benzene ring, as in indene. Ozonolysis of indene in ammonia gave isoquinoline in 62% yield. The collapse of the indene molozonide and subsequent amozonolysis probably gave a mixture of Va or Vb which, upon dehydration, formed isoquinoline.



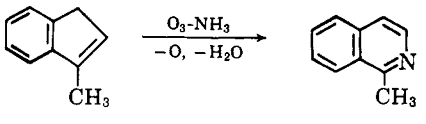
Va

Vb

Amozonolysis of 3-methylindene gave 4-methylisoquinoline in 48% yield.

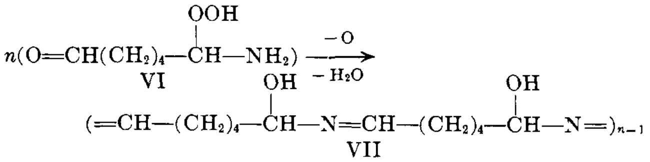


The amozonolysis of indole gave quinazoline by similar ring expansion. The low yield of 9% was



probably due to a considerable amount of ozone-catalyzed oxidation of the indole nitrogen which led partially to indigo and partially to resinous oxidation products.[3]

Cyclohexene gave the aldehyde (VI), which polymerized to form polymers. As the ammonia phase was



$$n(\mathrm{O{=}CH(CH_2)_4{-}\overset{\overset{OOH}{|}}{C}H{-}NH_2}) \xrightarrow[-\mathrm{H_2O}]{-\mathrm{O}} (\mathrm{{=}CH{-}(CH_2)_4{-}\overset{\overset{OH}{|}}{C}H{-}N{=}CH{-}(CH_2)_4{-}\overset{\overset{OH}{|}}{C}H{-}N{=}})_{n-1}$$

VI

VII

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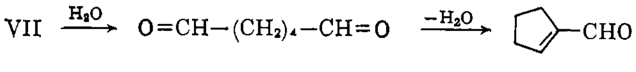
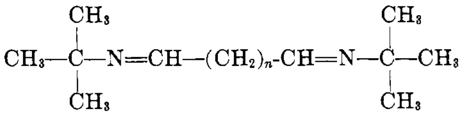
[3] C. Egler and R. Janecke, *Chem. Ber.*, **9**, 1415 (1876).

gradually displaced by water as solvent, the product precipitated as an insoluble polymer, suggesting cross linking through polyaddition of the imino groups of the linear polyimine (VII). The polymer corresponding to the formula $[-CH-(CH_2)_4-CH(OH)-N]_n$ was obtained in 80% yield. It was insoluble in common solvents and decomposed without melting at 320°. Dilute mineral acids dissolve the polymer readily, probably by salt formation, as it was reprecipitated unchanged by base. Attempted hydrogenation at high pressure and temperature failed; however, steam distillation with superheated steam gave cyclopentene-1-carboxaldehyde (VIII) in 18% yield. This indicated hydrolysis of the polymer chains to form adipic dialdehyde, which then condensed to cyclopentene-1-carboxaldehyde.



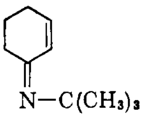
VIII

To avoid polyimine formation and possible cross linking, we used a primary amine that contained a bulky alkyl group instead of ammonia. Ozonolysis of cyclohexene in *t*-butylamine was expected to give tetramethylenedi(*t*-butylimine) (IX). However, this amozonolysis gave a mono-*t*-butylimine (41%) to which the structure XI was assigned by mass, ultraviolet, and infrared spectroscopy; it hydrogenated to N-cyclohexyl-*t*-butylamine. No polymer was formed. XI probably formed by way of 2-cyclohexen-1-one from 2-cyclohexene-1-hydroperoxide, which resulted from oxidation of cyclohexene with the O_3–O_2 gas mixture.

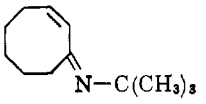


$$CH_3-C(CH_3)_2-N=CH-(CH_2)_n-CH=N-C(CH_3)_2-CH_3$$

IX, $n = 4$
X, $n = 6$



XI



XII

Amozonolysis of cyclooctene gave results similar to those for cyclohexene. Thus the reaction in ammonia led to cross-linked polyimines which were hydrolyzed by steam distillation to give suberic aldehyde in 26% yield. Ozonization in *t*-butylamine gave cyclooctene-3-*t*-butylimine (XII) in a 49% yield; it was hydrogenated to the corresponding N-cyclooctyl-*t*-butylamine. Additionally, 5% of hexamethylene-1,6-di(*t*-butylimine) (X) was formed and identified by mass spectroscopy. It indicated, in contrast to the behavior of cyclohexene, the occurrence of the "normal" amozonolysis with cyclooctene.

Amozonolysis of five-membered cycloolefins provides a novel synthetic method whereby ozone effects ring enlargement by a nitrogen atom to yield an aromatic, heterocyclic system. The method is not limited to five-membered cycloolefins, but can be extended to many other cyclic and linear olefins. With these, however, intramolecular condensation to give heterocyclic derivatives is less favorable than intermolecular addition, and polymerization by intermolecular addition is favored. Thus, six- and eight-membered cycloolefins, as well as linear terminal olefins, such as octene-1, undergo predominantly polymerization.

Experimental

The general procedure for the amozonolysis comprised emulsification of about 5% cycloolefins in the liquid ammonia phase. The cycloolefin contained 0.5% Pronon 523 (polyoxyethylene tridecyl alcohol from Process Chemicals Co.) as emulsifier. Ozonization was run at −35 to −60° in a vessel provided with a thermometer, gas vent, and a vibromixer blade (Chem. Ap. Zürich) which was attached to a hollow shaft through which the ozone–oxygen gas mixture was introduced at the bottom of the reactor. The vertical high-frequency vibration caused excellent contact among ozone, olefin, and ammonia. The reaction vessel was partially immersed in a Dry Ice–acetone bath. After introduction of the calculated amount of ozone, most of the ammonia was evaporated by being gradually warmed to room temperature; water or an organic solvent was added to keep the reaction product in solution. In some cases the incomplete reduction of the hydroperoxides by ammonia necessitated the addition of potassium sulfite. The reaction product was isolated either by extraction or by water evaporation *in vacuo*, and purified.

The same reaction products and results were obtained when liquid anhydrous ammonia was substituted by 100 wt. % aqueous ammonia. The aqueous ammonia was easier to handle and was generally used except for cyclopentene and cyclopentadiene. These cycloolefins have a low boiling point, requiring an amozonolysis temperature of −50°, at which aqueous systems freeze. The 100 wt. % aqueous ammonia solution was prepared by cooling an emulsion of 30% aqueous ammonium hydroxide and the cycloolefin to −35° in the reactor, followed by condensation of the calculated amount of ammonia. Pronon 523 worked well as emulsifier for the cycloolefins in liquid as well as aqueous ammonia. It proved inert towards ozone and oxygen and gave stable emulsions at temperatures as low as −35°. Other commercial nonionic detergents that were condensation products of ethylene oxide with fatty alcohols were also effective.

Ozone was generated by a Welsbach T 23 ozonator. Its concentration in oxygen, which served also as a carrier gas, averaged 2.8–3.0 wt. %. The ozone output of the generator was determined by passing the O_3–O_2 mixture through a 2% potassium iodide solution within a timed period, the amount of liberated I_2 being titrated with thiosulfate. The generator was calibrated for a fixed gas-flow rate, pressure, and discharge voltage on *n* g. of O_3/hr.

Cyclopentene, cyclopentadiene, indene, 3-methylindene,[3] indole, cyclohexene, and cyclooctene (all except 3-methylindene were purchased from Eastman) were treated under the described conditions. Both cyclopentene and cyclopentadiene were amozonolyzed at −50° in anhydrous ammonia to minimize the loss by evaporation by the oxygen stream. The reaction with cyclopentene gave a clear ammonia solution from which the polyimine was obtained after evaporation of ammonia. Hydrogenation of 10 g. of polyimine in 100 ml. of water with 1 g. of 5% palladium on charcoal and 0.5 g. of platinum oxide at 600 p.s.i. of hydrogen and 120–130° gave 0.8 g. of crude piperidine (10%) and 8 g. of water-insoluble polymer after 10 hr. For the pyrolysis, a solution of 10 g. of polyimine in 50 ml. of methanol was slowly added to dinonyl phthalate at 250° with stirring for 80 min. Methanol distilled with the pyrolysis products. The major component was pyridine, *ca.* 95% pure, obtained in 10% yield. With the same technique, when glycerol was used as pyrolysis medium, the polyimine unexpectedly gave piperidine as the major product along with pyridine; the total yield was 12%.

In the amozonolysis of cyclopentadiene, a 50% excess of the diolefin was used. To minimize polymerization, it was added during the reaction at such a rate that a continuous excess over the ozonized diolefin was maintained.

Indole, m.p. 52°, was dissolved in 30 g. of dimethoxyethane and this solution was emulsified. After ozonization, reduction, and refluxing, the aqueous reaction solution contained unchanged indole and other water-insoluble products which were removed by filtration. The filtrate was evaporated to dryness in a Rinco at 30° and 10 mm. The crystalline residue was leached with anhydrous ethanol to extract the reaction product from the inorganic salts; the product was distilled *in vacuo* to isolate quinazoline.

The polymers from the cyclohexene and cyclooctene amozonolysis were insoluble in all solvents except organic and mineral acids from which they could be precipitated by base. These polymers were hydrolyzed by adding a 50% aqueous acetic acid solution to vigorously stirred water at 100° through which superheated steam (120°) was passed. The aldehydes were collected in the steam distillates and either precipitated with semicarbazide or extracted with ether. Cyclopentene-1-carboxaldehyde (15–20%) was identified as its semicarbazone, m.p. 209°, lit.[4] m.p. 208°. Suberic aldehyde (26%) gave the disemicarbazone, m.p. 183°, lit.[5,6] m.p. 183–185°.

The ozonizations of cyclohexene and cyclooctene in *t*-butylamine (500 ml.) were carried out as described with ammonia. The hydrocarbons were soluble in the butylamine and needed no emulsifier. After amozonolysis, about three-fourths of the solvent was distilled off, 200 ml. of water was added, and the reaction products were isolated by extraction with ether. Vacuum distillation gave, in the case of cyclohexene, cyclohexene-3-*t*-butylimine, 30 g. (41%), b.p. 150°. It was identified by infrared and mass spectra (parent peak at 151). As the imine was relatively unstable, it was immediately hydrogenated: 10 g. of distillate were dissolved in 100 ml. of methanol and hydrogenated at atmospheric pressure with platinum oxide catalyst, giving 7 g. of N-cyclohexyl-*t*-butylamine, b.p. 87° (37 mm.), picrate m.p. 187°.

Anal. of picrate. Calcd. for $C_{16}H_{24}N_4O_7$: C, 50.0; H, 6.3; N, 14.6. Found: C, 50.3; H, 6.5; N, 14.7.

Mass and infrared spectra were consistent with the proposed structure.

Cyclooctene gave cyclooctene-3-*t*-butylimine, 3 g. (49%), b.p. 75° (18 mm.), which was identified by the mass spectrum (parent peak at 179) and infrared. Hydrogenation of the flash distillate from the crude reaction product at 15 mm. gave N-cyclooctyl-*t*-butylamine, b.p. 59° (4 mm.), picrate m.p. 198°.

Anal. of picrate. Calcd. for $C_{18}H_{28}N_4O_7$: C, 52.4; H, 6.9; N, 13.6. Found: C, 52.2; H, 7.0; N, 13.7.

A higher boiling fraction (b.p. 102°) solidified and was identified as octamethylene-1,8-di(*t*-butylamine), m.p. 55°, by its mass spectrum (parent peak at 256) and infrared; yield 6%.

Pure *t*-butylamine reacted readily with ozone to yield 2-methyl-2-nitrosopropane. In the presence of olefins, however, oxidation of the amine was a minor reaction, owing to faster ozonolysis of the more reactive carbon–carbon double bonds.

In a competitive reaction of butylamine and ammonia with benzaldehyde, N-butylbenzylidenimine was formed by dropwise addition of 10 g. of distilled benzaldehyde together with 0.1 g. of Pronon 523 as emulsifier to a solution of 7 g. of *n*-butylamine in 100 ml. of 80% aqueous ammonia at −20° with vigorous stirring. After 4 hr. the ammonia was evaporated and the reaction product was isolated by ether extraction and distillation. N-butylbenzylidenimine, b.p. 123°, was obtained in 91–92% yield (14.2 g.). It was identified by mass and infrared spectroscopy.

To determine if hydroperoxide was reduced by ammonia, 10 g. of 2-hydroperoxyoctane[7] was emulsified in 120 ml. of 100% aqueous ammonia at −35° and stirred for 6 hr. After evaporation of ammonia, the reaction product was isolated by ether extraction and dried with anhydrous magnesium sulfate. The content of hydroperoxide in 5 g. of the reaction mixture was iodometrically titrated, showing 2.3 g. of unchanged starting material. The infrared spectrum was identical with a 1:1 mixture of authentic 2-hydroperoxyoctane and octanol-2. No carbonyl band was observed.

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[4] L. Ruzicka and E. Peyer, *Helv. Chim. Acta*, **18**, 676 (1935).

[5] O. Wallach, *Ann.*, **347**, 327 (1906).

[6] K. W. Rosemund and F. Zetzsche, *Chem. Ber.*, **54**, 2889 (1921).

[7] C. Walling and S. A. Buckler, *J. Am. Chem. Soc.*, **77**, 6032 (1955).

A New Synthesis of Diaryl- and Alkylaryl-Substituted Acetylenes from α-Diketones and Triethyl Phosphite

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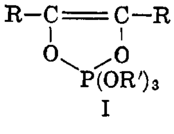
A novel method for the preparation of diaryl- and alkylaryl-substituted acetylenes from α-diketones and triethyl phosphite has been studied. When 1 mole of α-diketones was heated with 2 moles of triethyl phosphite at 215°, corresponding diaryl- and alkylaryl-substituted acetylenes were obtained in the yields ranging from 24 to 60%. Diaryl- and alkylaryl-substituted acetylenes were obtained in good yields by treating 1:1 adducts of triethyl phosphite and α-diketones in the presence of excess triethyl phosphite at 215°.

It has been recently found[1] that diphenylketene reacts with triethyl phosphite to form a 2:1 addition compound which, when pyrolyzed, is converted into diphenylacetylene, a deoxygenated product, and triethyl phosphate in fairly good yields.

$$2(C_6H_5)_2C{=}C{=}O + (C_2H_5O)_3P \longrightarrow [\text{adduct}] \xrightarrow{\Delta} C_6H_5C{\equiv}CC_6H_5 + (C_2H_5O)_3PO + \text{diphenylketene dimer}$$

Further, it has been shown that when the 2:1 adduct was heated in the presence of 1 mole of triethyl phosphite, diphenylacetylene and triethyl phosphate were obtained in good yields along with a small amount of diphenylketene dimer.

On the other hand, Ramirez[2] and Kukhtin[3] reported that tertiary phosphite esters react with α-diketones to form cyclic 1:1 adducts (I).



I

$R{=}R'{=}$ CH_3 or C_6H_5
$R{=}C_6H_5$, $R'{=}CH_3$

In the present experiment, the decomposition of the 1:1 adduct of benzil and triethyl phosphite in the presence of 1 mole of triethyl phosphite was tried first under the assumption that it would yield diphenylacetylene, a deoxygenated product, and 2 moles of triethyl phosphate.

Indeed, when a mixture of 2 moles of triethyl phosphite and 1 mole of benzil was heated at 215° for 2.5 hr. under nitrogen, diphenylacetylene and triethyl phosphate were obtained in 60 and 88% yields, respectively, along with the diphenylketene dimer (24%).

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[1] T. Mukaiyama, H. Nambu, and M. Okamoto, *J. Org. Chem.*, **27**, 3651 (1962).

[2] (a) F. Ramirez, R. B. Mitra, and N. B. Desai, *J. Am. Chem. Soc.*, **82**, 2651 (1960); (b) F. Ramirez and N. B. Desai, *ibid.*, **82**, 2652 (1960).

[3] (a) V. A. Kukhtin, *Dokl. Akad. Nauk SSSR*, **121**, 466 (1958); *Chem. Abstr.*, **53**, 1105*b* (1959); (b) V. A. Kukhtin, K. M. Kirillora, and R. R. Shagidullin, *J. Gen. Chem. USSR*, **32**, 640 (1962).