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Applications of Modified Wittig Reaction to Butatriene Synthesis

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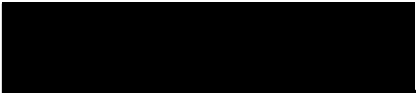
An Abstract of the Thesis of

___John Pearson___ for the ___M.S.___ in ___Chemistry___
      (Name)   (Degree)   (Major)

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Title: Applications of Modified Wittig Reaction
              to Butatriene Synthesis

Abstract approved ███████████████████ .
                    (Major Professor)

The preparation of allenes by the condensation of an acyl

chloride with a phosphonium ylid and subsequent elimination of an

acid salt and a phosphonium oxide has been established by Bestmann

and Hartung. It was felt that this process could be expanded to

include the synthesis of butatrienes. Butatrienes are stabilized

by aromatic substituents while aromatic substituents decrease the

nucleophilicity and reactivity of the phosphonium ylids to be used

in the synthesis of the butatrienes. The ylids employed were carbo-

methoxyphenylmethylenetriphenyl phosphorane, and a new compound,

carbethoxyphenylmethylenetriphenyl phosphorane, both of which

failed to form alkylated condensation products. Both ylids were

prepared by the "melt" method which gave better yields than compa-

rable processes in dry benzene.

The salt of a third ylid, carbethoxyphenylmethylenetrimethyl-phosphonium chloride - a new compound, was also prepared. However, the process for the preparation of this salt was not consistently reproducable and gave only low yields.

A previously unreported reaction involving the condensation of ethyl diethylphosphonoacetate and benzoyl chloride was carried out and led to the formation of ethyl phenylpropynoate as was proposed.

APPLICATIONS OF MODIFIED WITTIG REACTION

TO BUTATRIENE SYNTHESIS

by

JOHN PEARSON

A thesis submitted in partial fulfillment of the
requirements for the degree of

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in
CHEMISTRY

Portland State University
1968

TO THE OFFICE OF GRADUATE STUDIES AND RESEARCH:

The members of the Committee approve the thesis of

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I. INTRODUCTION

Ylids: Structure and Nomenclature

Ylids are a class of compounds that are dipolar in character, but differ from dipolar ions such as amino acids in two ways: 1) the heteroatom carrying a high degree of positive charge is attached directly to an anionic carbon atom, I, and 2) ylids are described as having an uncharged contributing form, II. Form I is often referred to as the ylid form and II as the ylene form; however, some workers

$$-\overset{..}{\underset{|}{C}}-\overset{+}{X} \longleftrightarrow \;>\!C \equiv X,$$

$$\text{I} \qquad\qquad\qquad \text{II}$$
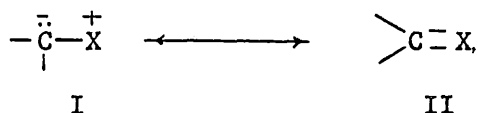
feel this differentiation is unnecessary (1).

The difference in opinion just mentioned underlines a problem in the nomenclature of ylids in general and phosphonium ylids in particular. For example, compound III has been named as triphenyl-phosphonium methylide (2), as triphenylphosphinemethylene (3), and as methylenetriphenylphosphorane (1). The system recommended by the

$$(C_6H_5)_3\overset{+}{P}\text{-}\overset{..}{C}H_2 \longleftrightarrow (C_6H_5)_3P\overset{-}{=}CH_2$$
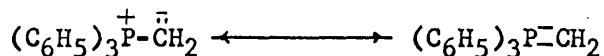
$$\text{III}$$

Editorial Report on Phosphorus Nomenclature in the Journal of the Chemical Society (4) favors the latter term, i.e., naming the compound as a substituted phosphorane. However, an alternate system is offered by A. W. Johnson that identifies the phosphoranyl group

as a substituent on a carbon skeleton (1). As an example, compound

IV named in the recommended manner would be (ethylmethylmethylene)-

triphenylphosphorane, but by the method of Johnson the same structure

$$(C_6H_5)_3\overset{+}{P}\text{-}\overset{CH_3}{\underset{\cdot\cdot}{C}}\text{-}CH_2CH_3 \longleftrightarrow (C_6H_5)_3P{=}C\overset{CH_3}{\underset{CH_2CH_3}{}}$$
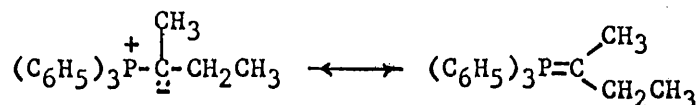
<center>IV</center>

becomes the less unwieldy 2-triphenylphosphoranylbutane. Johnson

indicates that his approach could easily be applied to the ylids of

sulfur and arsenic (1).

Role of Pentavalent Phosphorus in Structure of Phosphonium Ylids

The stability of phosphorus ylids is thought to arise from the

delocalization of the nonbonded electrons of the anionic carbon to

the phosphorus portion of the molecule. This delocalization would

require the formation of a pi bond, forming a pentavalent phosphorus

with sp^3d hybrid orbitals.

Evidence that discounts a strong inductive effect by the

phosphorus moeity and that points to participation of the empty 3d

orbitals of phosphorus comes from an examination of the pKa's of

several analogous compounds in the fluorene series. Treatment of

fluorene with butyllithium forms the fluorenyl anion, V. Fluorene

has a pKa of about 25 (5). By comparison, the conjugated acid of the

nitrogen ylid VI, has a pKa of about 24, indicating that V and VI

have approximately the same stability relative to their conjugate

acids. The similarity in the two pKa's indicates that the inductive

effect of the trimethylammonium group does not appreciably affect the
stability of the fluorenyl anion (7). The pKa of the conjugate acid
of the phosphonium ylid, VII, is approximately 10 (8). This latter

V	VI	VII
H	$+N(CH_3)_3$	$+P(C_6H_5)_3$
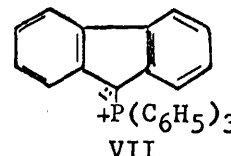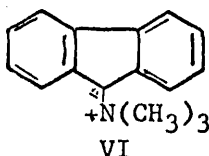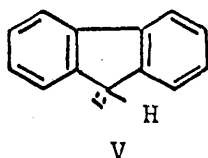
anion shows a stabilization too great to arise from simple inductive
effects, and its stability is therefore attributed to participation
of the empty 3d orbitals on the phosphorus.

Additional evidence for the expansion of the phosphorus valence
shell to include 3d orbitals arises from work on compounds such as
PCl_5 and $(C_6H_5)_5P$. Phosphorus pentachloride has been shown to be
a trigonal bipyramid in the liquid (8) and in the vapor phases (9).
The solid phase has been shown to consist of a salt of the tetra-
hedral cation PCl_4^+ and the octahedral anion PCl_6^-, the former being
an sp^3 hybrid the latter an sp^3d^2 hybrid (10). An X-ray crystallo-
graphic study of pentaphenylphosphorane shows it to be a trigonal
bipyramid structure - an sp^3d hybrid (11). Each of the above cases
demonstrates expansion of the phosphorus valence shell to include
3d orbitals in sigma bond formation.

To date, proof of the involvement of a 3d orbital of phospho-
rus in pi bond formation with another atom is based entirely on
experimental evidence. Calculations for a pπ - dπ system, a pi
bond involving a p-orbital on one atom and a d-orbital on another, in
phosphorus have not been offered, although several workers agree in

theory that such pi bonding is feasible (12,13).

The bulk of the experimental evidence for such pi bonds is based primarily on cases where pi bonding is the only rational explanation. As an example, the following case predicates the involvement of a 3d orbital of another atom to form a pi bond. In systems where pi bonding is not possible, the basicity of phosphanes correlates with the sigma bonding ability of the phosphorus in the order $PR_3 \rangle P(OR)_3 \rangle PCl_3 \rangle PF_3$ (14). However, the bonding ability of these same phosphorus derivatives in complexes of metals with filled d-orbitals, such as $PtCl_2(PX_3)_2$ and $Ni(CO)_2(PX_3)_2$, was in exactly the opposite order (14,15). The explanation for this reversal is that the phosphorus shares its nonbonded electrons with the metal to form a sigma bond, and the filled d orbitals of the complexed metal overlap with the vacant d orbitals of the ligand to form a pi bond, the order of bond strength depending on the inductive effects of the substituent on the phosphorus. For example, PF_3 would be expected to form a weak sigma bond and a strong pi bond; the reverse would be expected for $P(CH_3)_3$ as was observed.

Another chemical approach, comparing the reactivity of vinyltrimethylammonium bromide, VIII, vinyltributylphosphorium bromide, IX, and vinyltriphenylphosphorium bromide, X, toward a Michael type addition to the carbon-carbon double bond, showed the vinylammonium ion to be inert to a variety of bases (16) while the

$$H_2C{=}CH\overset{+}{N}(CH_3)_3Br^- \qquad CH_2{=}CH\overset{+}{P}(\underline{n}{-}C_4H_9)_3Br^- \qquad CH_2{=}CH\overset{+}{P}(C_6H_5)_3Br^-$$
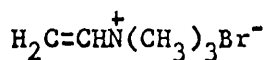
$$\text{VIII} \qquad\qquad\qquad \text{IX} \qquad\qquad\qquad \text{X}$$
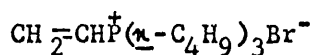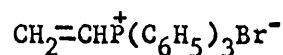
vinylphosphinium systems gave the expected addition products. The difference in reactivity is attributed to the ability of the phosphonium systems to stabilize carbanion intermediates of the addition through overlap of the filled $2\underline{p}$ orbital of the carbanion with the empty $3\underline{d}$ orbital of the phosphorus atom, Equation 1 (17,18). The same shell expansion by nitrogen appears to be prohibited since

$$B:^- + CH_2=CH\overset{+}{P}R_3 \longrightarrow \left[\overline{B}CH_2\overset{\cdot\cdot}{C}H\overset{+}{P}R_3 \longleftrightarrow BCH_2CH=PR_3 \right] \overset{H^+}{\longrightarrow} BCH_2CH_2\overset{+}{P}R_3$$

1

$$R= \underline{n}\text{-}C_4H_9, \ C_6H_5$$
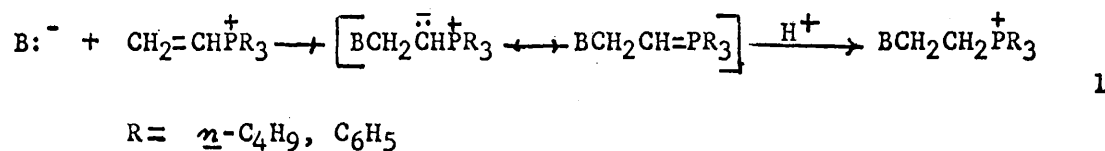
the next highest vacant orbital is the $3\underline{s}$ orbital which is described as being of too high energy for effective bonding (19). If only inductive effects were operational, one would expect that nitrogen would afford greater stabilization of the carbanion intermediate than the phosphorus. The carbon-phosphorus bond (1.87 Å) is considerably longer than the carbon-nitrogen bond (1.47 Å), which would mean that nitrogen should exert 30% more coulombic attraction than phosphorus. Since inductive effects can be discounted, the only rational explanation goes back to the $\underline{p}\pi$ - $\underline{d}\pi$ bonding between the carbanion carbon and the phosphorus.

Probably the most quantitative approach yet taken was by Doering and Hoffman in their study of deuterium uptake by tetramethylammonium iodide and tetramethylphosphonium iodide in a solution of deuterium oxide anion and deuterium oxide. They found that the phosphonium ion incorporated 73.9 atom per cent deuterium at 62°C in three hours but the ammonium salt at 100°C in 358 hours led

to only 1.13 atom per cent deuterium incorporation. The energy of

activation for the phosphonium case was 25.6 Kcal/mole while for the

ammonium case it was 32.2 Kcal/mole. Doering and Hoffman point out

that if electrostatic effects were the only factors functioning, the

phosphonium system would require a energy of activation of 41

Kcal/mole, which indicates that there is an effective stabilization

beyond inductive effects on the order of 15 Kcal/mole. They attribu-

ted this stabilization of the intermediate carbanion XI (Equation 2)

to valence shell expansion of the phosphorus atom by overlap of $3\underline{d}$ and

$$(CH_2)_3\overset{+}{P}CH_3 \xrightarrow{OD^-} \left[\begin{array}{c} (CH_3)_3\overset{+..}{P}CH_2 \\ \updownarrow \\ (CH_3)_3\overset{-}{P}CH_2 \end{array} \right] \xrightarrow{D_2O} (CH_3)_3\overset{+}{P}CH_2D \qquad 2$$
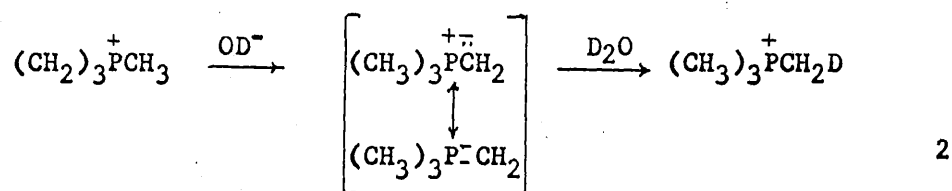
<center>XI</center>

$2\underline{p}$ orbitals (20).

Attempts to incorporate a phosphorus-carbon $3\underline{d}$-$2\underline{p}$ $\underline{pi}$ bond into

an aromatic $\underline{pi}$ system have so far been inconclusive. No overt

stabilization was noted for 1,1-diphenyl-3,4-dihydro-1-phosphanap-

thalene, XII, (21), nor for 1,1,2-triphenyl-1-phosphaindene, XIII,

(22). However, 1,1-diphenyl-1-phosphanaphthalene, XIV, demonstrated
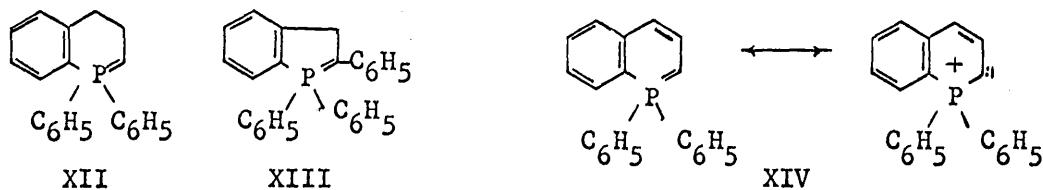
some reduction of nucleophilic character with respect to naphthalene

when alkylated with methyl iodide and exhibited maxima in the ultra-

violet at 362 mμ and 420 mμ (23).

The monocyclic ylid 1,1-diphenyl-1-phosphabenzene, XVI, was

obtained by treatment of XV with NaOH (Equation 3). The noncyclic

analog could not be isolated by this method, indicating some stabili-

$$
\begin{array}{ccc}
\underset{\substack{\\ \text{XV}}}{\overset{\displaystyle}{\underset{C_6H_5 \quad C_6H_5}{\overset{+}{P}}}} ClO_4^- & \overset{OH^-}{\underset{HClO_4}{\rightleftharpoons}} & \underset{\substack{\\ \text{XVI}}}{\underset{C_6H_5 \quad C_6H_5}{P}}
\end{array}
\qquad 3
$$
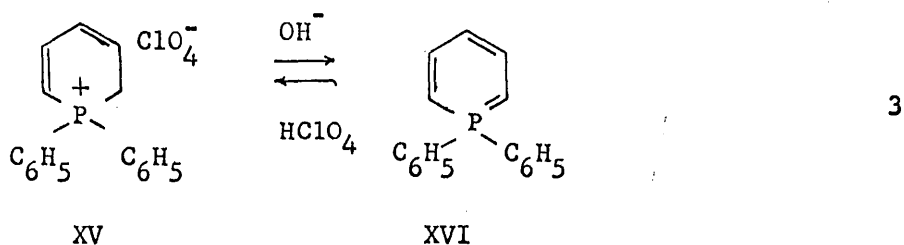
zation and incorporation of the $\underline{p}\pi$ - $\underline{d}\pi$ bond into the benzoid

system (23).

Finally, to add some confusion, NMR work on ^{31}P chemical shifts

in a series of ylids and their conjugate acids showed nearly identical

shielding in both cases, Table I (24). This implies that electron

Table I

NMR Chemical Shifts of β-Ketophosphonium Ylids
and Conjugate Acids

R	^{31}P Shift of $(C_6H_5)_3\overset{+}{P}CH_2COR$ (ppm)	^{31}P Shift of $(C_6H_5)_3P{=}CHCOR$ (ppm)
C_6H_5	-16.9	-21.6
C_2H_5O	-19.7	-19.1

density on the phosphorus is nearly the same in both instances and

that there is little delocalization of electron density from the car-

banion portion of the molecule to the phosphorus in these ylids. On

the other hand, NMR results from the study of difluoromethylenetris-

(dimethylamino)phosphorane, XVII, showed a ^{31}P chemical shift of

65.5 ppm while the diethylamino analog has a shift of 58 ppm (25).

$$\left[(CH_3)_2N \right]_3 \, -P\!=\!CF_2$$
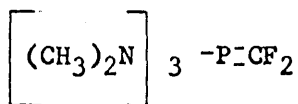
XVII

This high shielding of phosphorus is taken to indicate a high degree

of $\underline{p}\pi$ - $\underline{d}\pi$ overlap between the anionic carbon and the phosphorus.

It should be noted that most workers accept the concept of

$\underline{p}\pi$ - $\underline{d}\pi$ bonding and valence shell expansion in phosphonium ylids,

and the observed chemistry seems to bear them out. Until pertinent

calculations or spectroscopic evidence is provided to show otherwise,

the approach is assumed to be valid (26,27).

Structural Effects on the Chemistry of Phosphonium Ylids

Ylids are generally used in condensation processes, such as

the Wittig condensation-elimination reaction. The rate of such con-

densations is dependent on the nucleophilicity of the ylid, i.e.,

of the contribution of form I (page 1). The nucleophilicity of the

ylid is, in turn, dependent on the substituents on the phosphorus and

alkylidene portions of the molecule.

With respect to the substituents on the alkylidene portion,

it can be seen that electron-withdrawing substituents will stabilize

the ylid form by charge dispersal with a concommitant loss in

nucleophilicity and reactivity. For example, the following series

of triphenylphosphoranes indicates a pronounced effect by alkylidene

substituents on stability and reactivity.

a) methylenetriphenylphosphorane, III (page 1): absorbs oxygen rapidly, reacts with aldehydes, ketones, water, acid, halides, and esters (28).

b) formylmethylenetriphenylphosphorane, XVIII: reacts with benzaldehyde but not with cyclohexanone under similar conditions and has a carbonyl stretching frequency in the infra-red of 6.15 mμ (29,30).

c) diphenylmethylenetriphenylphosphorane, XIX: unreactive with aldehydes and ketones (31).

d) fluorenylidenetriphenylphosphorane, VII (page 2): considered by some workers as having no value in the Wittig reaction due to inherent stabilization (32) and as having limited applications by others (33,34).

$$(C_6H_5)_3P{=}CHCHO \qquad\qquad (C_6H_5)_3P{=}C(C_6H_5)_2$$
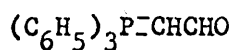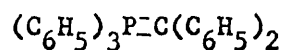
XVIII   XIX

It should be mentioned that acyl ylids are quite stable, not only due to inductive effects but also to resonance effects involving an enolate form. X-ray crystallographic studies on α-halophenacylidenetriphenylphosphoranes indicate that the ylids have a planar skeleton and contain a trigonally hybridized ylidic carbon with the carbonyl oxygen and phosphorus groups in a cis orientation, XX. The analysis by Stephens, Table II, indicates that the length of the ylid bond is between that of the phosphorus-carbon single bond length (1.87 Å) and the double bond length (1.67 Å). The length of the carbon-carbon bond of the C-CO group approximates the carbon-carbon

double bond length (1.33 Å), and the length of the carbonyl bond is
longer than the normal carbon-oxygen double bond length of 1.23 Å (35),
indicating that the enolate form XX makes an important contribution.

Table II

Bond Lengths for α-Halophenacylidenetriphenylphosphoranes
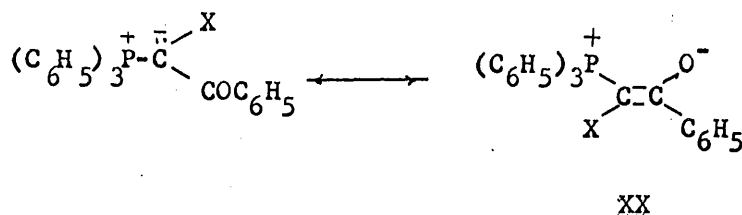
Bond	X $=$ I	X $=$ Cl
P-C	1.71 Å	1.74 Å
P-C_6H_5	1.77-1.82 Å	1.80-1.82 Å
C-CO	1.35 Å	1.36 Å
C-O	1.28 Å	1.30 Å

The anionic carbonyl stretching frequency of phenacyltriphenyl-
phosphonium salts occurs in the infra-red at 6.15 mμ, but the same
band in the corresponding ylid occurs at about 6.7 mμ (30). This
shift has been noted in other carbonyl ylids and is interpreted to
mean that there is considerable single bond character in the carbon-
oxygen bond due to delocalization of the carbanion electrons into
the carbonyl function (24,30,36,37). Additional evidence for an
enolate structure in acyl ylids stems from the fact that replace-
ment of R $=$ H by R $=$ CH_3 in ylids of the form $(C_6H_5)_3P=C(R)CO_2CH_3$
leads to a decrease in the carbonyl stretching frequency (38).

Many attempts to alkylate acyl ylids have led to exclusive O-alkylation products, again showing that in ylids of this type the primary electron density may be located on the oxygen atom (39). There is some confusion on this point, however, as many acyl ylids undergo normal alkylations (40,41).

The substituents on phosphorus also exert a powerful effect on the reactivity of ylids. As mentioned (page 3), one would expect PF_3 to favor a stronger pi bond in metal complexes than $P(CH_3)_3$. Carrying these observed inductive effects into ylid chemistry, one would expect that electron-withdrawing substituents on the phosphorus to favor the ylene characteristics, by increasing d orbital resonance. On the other hand, if electron-releasing functions are present on the phosphorus atom, one could expect an increase in reactivity by decreasing the level of d orbital participation and a favoring of the ylid characteristics of the molecule. These assumptions are borne out by the fact that carbomethoxymethylenetricyclohexylphosphorane is a stronger base than carbomethoxymethylenetriphenylphosphorane and, unlike the latter, is sensitive to water (42).

Another enlightening example is the reaction of fluorenylidene phosphoranes with aldehydes and ketones, Table III. When the phosphorus has three phenyl substituents, only activated aldehydes give substantial yields of olefin in the listed reaction (Equation 4). On the other hand, the tri-n-butyl substituted phosphoranes give nearly quantitative yields with all of the listed aldehydic carbonyls, even the deactivated species, and in addition give substantial yields with many of the ketones noted. The triphenyl

nucleophilicity and stability are dependent on the inductive nature

of both the alkylidene and phosphorus substituents. Although the

direction of the inductive effects, i.e., the +I and -I directions,

of both types of substituents affect nucleophilicity in the same

direction, the effects are exerted in different manners. The

phosphorus substituents influence nucleophilicity by increasing or

decreasing $\underline{d}$ orbital resonance while alkylidene substituents affect

reactivity through charge dispersal.

<u>History of Phosphonium Ylids and Development of the Wittig Reaction</u>

The history of ylids reaches back to 1894, when Micheails and

Gimborn unknowlingly prepared a ylid which they incorrectly described

as a "phosphonium betaine" XXI (43). In 1961, Asknes showed that

they had actually prepared carbethoxymethylenetriphenylphosphorane, XXII

(44). In 1899, Micheails and Kohler synthesized two more "phosphonium

$$(C_6H_5)_3\overset{|}{\underset{|}{P}}-\overset{|}{\underset{|}{CH_2}} \qquad\qquad (C_6H_5)_3P\overset{-}{=}CHCOOC_2H_5$$
$$O-C(R)OM$$
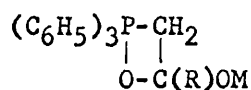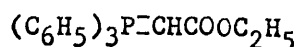
XXI   XXII

betaines" (45) which were shown by Rameriz and Dershowitz in 1957,

to be the ylids $(C_6H_5)_3P\overset{-}{=}CHCOCH_3$ and $(C_6H_5)_3P\overset{-}{=}CHCOC_6H_5$ (37).

Phosphonium ylid chemistry enjoyed a brief renaissance in

1919, when Staudinger and his co-workers studied the chemistry of

the ylid diphenylidenetriphenylphosphorane that they obtained by the

pyrolysis of the corresponding phosphinazine (46). Staudinger and

his group were the first to study the chemistry of phosphonium ylids

and found that diphenylidenetriphenylphosphorane would react with phenylisocyanate to give triphenylketenimine and triphenylphosphine oxide, Equation 5 (46).

$$(C_6H_5)_3P\!=\!C(C_6H_5)_2 + C_6H_5NCO \longrightarrow C_6H_5N\!=\!C\!=\!C(C_6H_5)_2 + (C_6H_5)_3PO \qquad 5$$
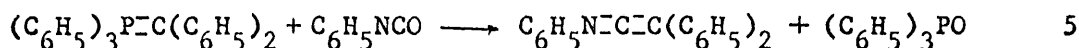
In 1922, Luscher, a member of the Straudinger group, found that the same ylid reacted with diphenylketene to yield tetraphenyl-allene and triphenylphosphine oxide, Equation 6 (47). This work, by

$$(C_6H_5)_2C\!=\!C\!=\!O + (C_6H_5)_3P\!=\!C(C_6H_5)_2 \longrightarrow (C_6H_5)_2C\!=\!C\!=\!C(C_6H_5)_2 + (C_6H_5)_3PO \qquad 6$$
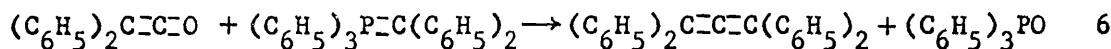
both Straudinger and Luscher, is said to be the foundation leading to the development of the Wittig reaction thirty five years later (1).

During the interim, however, only isolated flurries of activity occured in phosphorus ylid chemistry. Inspired by the work of Straudinger, C.S. Marvel, in search of pentavalent phosphorus compounds, made $(C_6H_5)_3P\!=\!CH_2$ and $(C_6H_5)_3P\!=\!C(CH_3)_2$, and noted their reaction with water (48). Worral in 1930 (49), and Schonberg and Ismail in 1940 (50), prepared ylids, but both compounds were incorrectly reported as "phosphonium betaines." Apparently Pinck and Hibert in 1947, were the first to deliberately synthesize an ylid of phosphorus, fluorenyl-idenetriphenylphosphorane (51).

In 1949, while attempting to form pentamethylphosphorane by treating tetramethylphosphonium iodide with methyllithium, Wittig and Reiber obtained instead, methylenetrimethylphosphorane, Equation 7,

$$(CH_3)_4PI + CH_3Li \longrightarrow (CH_3)_3P\!=\!CH_2 + LiI + CH_4 \qquad 7$$

$$(CH_3)_3P\bar{\ }CH_2 + (C_6H_5)_2CO \xrightarrow[\text{2) HO}^-\text{, KI}]{\text{1) (C}_2\text{H}_5)_2\text{O}} (C_6H_5)_2C(OH)CH_2\overset{+}{P}(C_6H_5)_3I^- \quad 8$$
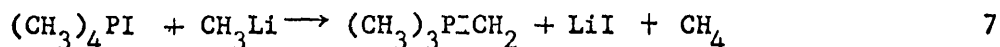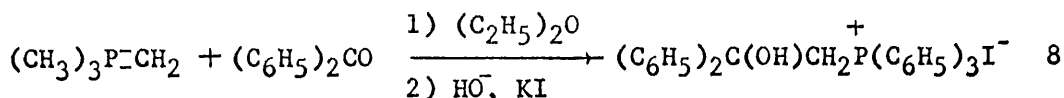
which reacted with benzophenone to yield a betaine obtained as a

salt, Equation 8 (28).

The Wittig reaction was discovered in 1954, when Wittig and

Geisler who found that methylenetriphenylphosphonium iodide when

treated with phenyllithium yielded methylenetriphenylphosphorane,

Equation 9 (52). The ylid was then condensed with benzophenone to

$$(C_6H_5)_3\overset{+}{P}CH_3I^- + C_6H_5Li \longrightarrow (C_6H_5)_3P\bar{\ }CH_2 + C_6H_6 + LiI \qquad 9$$

$$(C_6H_5)_3P\bar{\ }CH + (C_6H_5)_2CO \longrightarrow (C_6H_5)_2C\bar{\ }CH_2 + (C_6H_5)_3PO \qquad 10$$
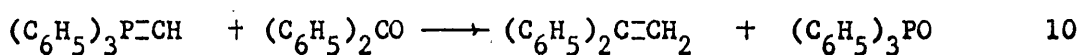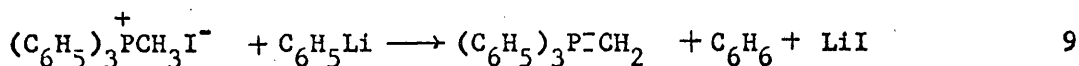
1,1-diphenylethylene in 84% yield, Equation 10 (53).

Although the condensation-elimination reaction known now as

the Wittig reaction was originally discovered by Staudinger, it was

Wittig and his group during the 1950's that actually established this

process as a useful synthetic approach to olefins (1). This approach

to olefin synthesis has three advantages: 1) it introduces a double

bond simultaneously with an enlargement of the carbon skeleton, 2) it

affords two routes in the synthesis of a given olefin, Equation 11,

and 3) it presents no possibility of double bond isomerization, a

problem that is common to most approaches to the formation of an

olefinic bond. This latter point arises from the fact that the Wittig

reaction is generally carried out under mild conditions and in a

neutral media. Only when unstable ylids are formed and the process

must be carried out _in situ_ with an excess of base is there any need

for the presence of extraneous ions, none of which attack a carbon-

carbon double bond.

$$R_1 \atop R_2 \!\!\!> \!C\!\!=\!\!P(R)_3 \;+\; O\!\!=\!\!C\!\!<\! {R_3 \atop R_4} \;\longrightarrow\; {R_1 \atop R_2}\!\!\!>\!C\!\!=\!\!C\!\!<\!{R_3 \atop R_4}$$

<div align="right">11</div>

$$R_3 \atop R_4 \!\!\!> \!C\!\!=\!\!P(R)_3 \;+\; O\!\!=\!\!C\!\!<\! {R_1 \atop R_2} \;\longrightarrow\; {R_3 \atop R_4}\!\!\!>\!C\!\!=\!\!C\!\!<\!{R_1 \atop R_2}$$
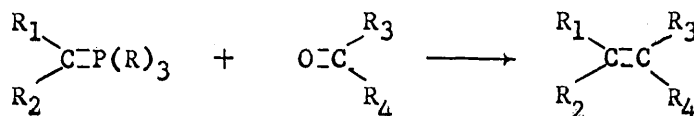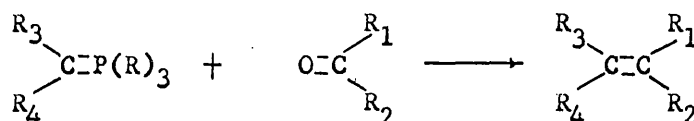
The Wittig reaction has the limitations described previously.

Substituents on both the alkylidene and phosphorus portions of the

molecule affect the nucleophilicity or the amount of ylide character

of the ylid. Also, steric factors seem to be important, as shown by

the difference in reactivity between aldehydes and ketones noted in

Table III.

Generalized Mechanism of the Wittig Reaction

The mechanism of the reaction as described by Wittig and

generally accepted by workers in the field (53,54) is a three step

process involving first a reversible formation of a betaine, then

formation of a four membered intermediate, and finally decomposition

of the cyclic intermediate to give an olefin and a phosphine oxide,

Equation 12 (55).

Actually, two different _specific_ mechanisms are accepted

(7, 55). If a stabilized phosphorus ylid is used, then the initial

step is defined as the slow step and the decomposition of the

$$(R)_3P \! \doteq \! C \! \overset{R_1}{\underset{R_2}{\diagdown}} \quad + \quad \overset{R_3}{\underset{R_4}{\diagup}} C \! \doteq \! O \longrightarrow (R)_3 \overset{+}{P} \! - \! \overset{\overset{R_1}{|}}{\underset{\underset{R_4}{|}}{\underset{|}{C}}} \! - \! R_2$$

$$(R)_3 \overset{+}{P} \! - \! \overset{\overset{R_1}{|}}{\underset{\underset{R_4}{|}}{\underset{|}{C}}} \! - \! R_2 \longrightarrow R_1 R_2 C \! \doteq \! C R_3 R_4 \quad + \quad (R)_3 P \! \doteq \! O \qquad (12)$$
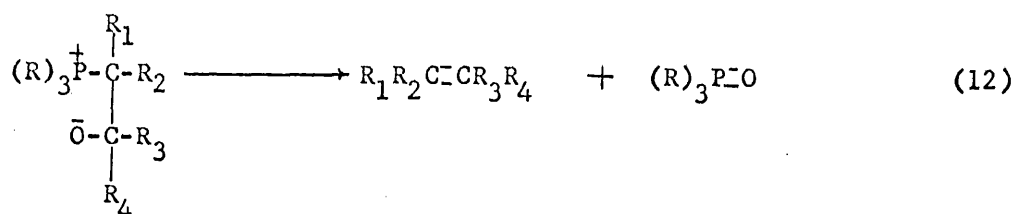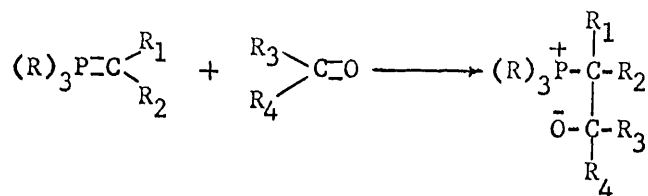
intermediate betaine as the fast step. The reverse has been shown to be true for nonstabilized ylids as described by the energy profile offered by Wittig (Fig. 1) (56). The difference between stabilized and non-stabilized ylids has not been rigorously defined. However, stabilized ylids are considered to be those that can be isolated and, due to a lowered basicity, are not sensitive to water or do not suffer from autoxidation (56).
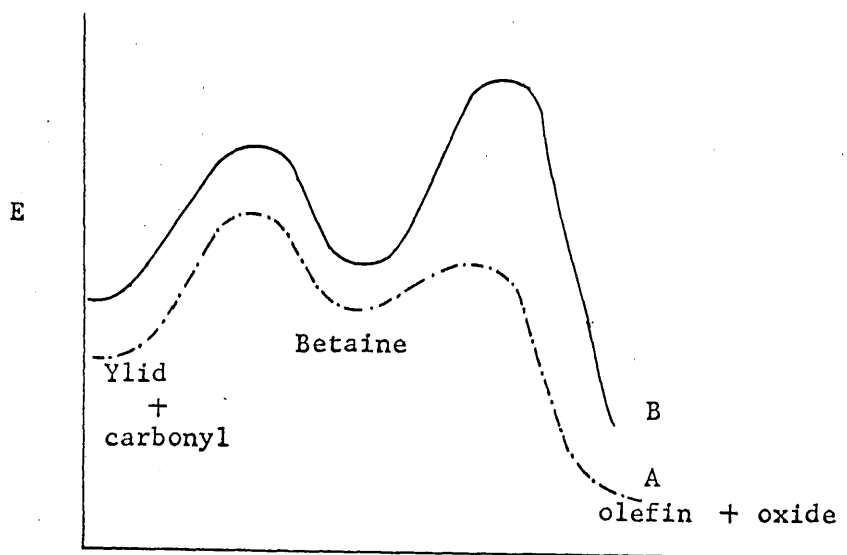
Fig. 1 Wittig reaction profile. A $\doteq$ stabilized ylid route; B $\doteq$ nonstabilized ylid route.

Modifications of the Wittig Reaction

Major modifications of the Wittig reaction have centered around the nature of either the phosphorus substituents or the carbonyl substrate employed. It is interesting to note that Wittig examined the possibility of utilizing trialkylphosphoranyl ylids and concluded that the second step of the process, the decomposition of the betaine intermediate, was either nonexistent or too slow to be of practical value (57). However, as pointed out on page 9, the use of alkyl groups leads to an increase in the reactivity of ylids (7).

Another process, that may be considered a modification of the Wittig reaction, is the use of dialkylphosphonates of the form $(RO)_2POCH(R_1)CO_2R_2$. Ylids with carbonyl functions tend to be stable but analogous phosphonates are considerably more reactive, leading to good yields of olefins with a wide variety of aldehydes and ketones. The reaction, developed by Wadsworth and Emmons, involves the formation of a salt of the phosphonate and subsequent condensation of the anion with a carbonyl function as shown in Equation 13 (58).

$$(C_2H_5O)_2\overset{O}{\overset{\|}{P}}\text{-}CH_2CO_2C_2H_5 + NaH \longrightarrow (C_2H_5O)_2\overset{O}{\overset{\|}{P}}\text{-}\overset{..}{\overset{-}{C}}HCO_2C_2H_5Na^+ + H_2$$

$$\underset{\xrightarrow{\hspace{1cm}}}{R_1R_2C\text{=}O} \qquad R_1R_2C\text{=}CHCO_2C_2H_5 + Na^+ + (C_2H_5O)_2\overset{O}{\overset{\|}{P}}O^-$$
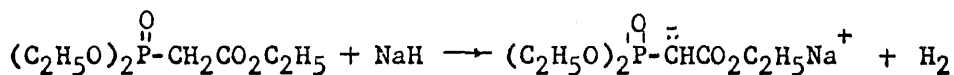
13
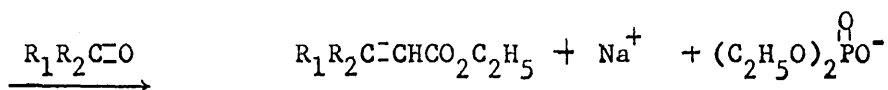
The reaction with the phosphonate requires milder conditions than does the "normal" Wittig reaction, for the reaction of phenacyl-idenetriphenylphosphorane with benzaldehyde required refluxing in tetrahydrofuran for three hours (37) while the comparable process

utilizing diethylphenacylphosphonate was exothermic at room tempera-
ture (58). Carbethoxymethylenetriphenylphosphorane and cyclohexanone
gave only an O-alkylated product (59), whereas the anion of ethyl-
diethylphosphonoacetate reacted exothermically with cyclohexanone to
give a 70% yield of the expected olefin (58).

The primary difficulty with the phosphonate reaction is that
the starting phosphonate is prepared by the stereochemically sensi-
tive Arbuzov reaction, Equation 14. In syntheses requiring R_1 to
be larger than a methyl group, the yields of the desired phosphonates

$$(RO)_3P \; + \; R_1-\overset{\overset{\displaystyle R_2}{|}}{\underset{\underset{\displaystyle Br}{|}}{C}}-H \; \longrightarrow \; (RO)_2\overset{\overset{\displaystyle O}{\|}}{P}-\overset{\overset{\displaystyle R_1}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}-R_2 \; + \; RBr \qquad 14$$
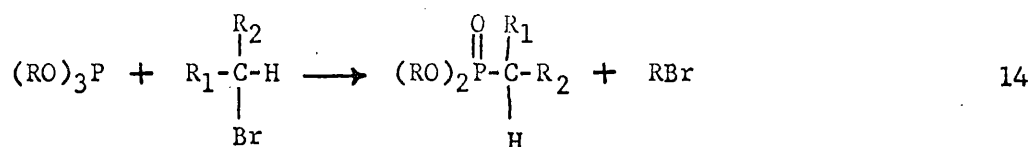
are low (60,61,62). Furthermore, the generation of an alkyl halide
supplies the attacking phosphite with another and possibly more
reactive substrate, for example, ethyldiethylphosphonoacetate was
formed in only 50% yield (61).

The major modification of the Wittig reaction, with respect to
carbonyl substrates, has been to include carboxylic acid derivatives
of the form RCOX, that is, an acyl halide (63), an ester (41,57,64),
or a thioester (30,65). When treated with a phosphorus ylid, the
acid derivatives lead to the formation of carbonyl substituted ylids,
Equation 15. The product of the first step is generally not isola-
ted.

$$R_1COX \; + \; R_2CH=P(R)_3 \; \longrightarrow \; (R)_3\overset{+}{P}-\overset{\overset{\displaystyle R_2}{|}}{\underset{\underset{\displaystyle //O}{|}}{C}}-H \;\; X^- \;\; \overset{B:}{\longrightarrow} \;\; (R)_3P=C\overset{\diagup R_2}{\diagdown \underset{\underset{\displaystyle O}{\|}}{C}-R_1} \; + \; BH \qquad 15$$
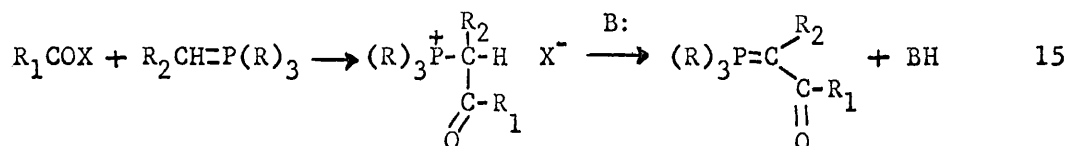
The introduction of the acyl function increases the acidity of the hydrogen _alpha_ to the phosphorus and the carbonyl group. This hydrogen can be removed either by the starting ylid or by the anion removed from the acylating agent.

The acylation of ylids has been developed by Bestmann into a synthetic approach to the formation of allenes. By condensing a phosphorus ylid of the form $(C_6H_5)_3P{=}CRCO_2C_2H_5$, where R is either a hydrogen or an alkyl group, with an acyl chloride, Bestmann synthesized a wide range of ethyl allenyl esters but only with yields no greater than 50%. The low yield is due to the fact that a second mole of the starting ylid is involved in the decomposition of the phosphonium intermediate, Equation 16 (64,66).

$$(C_6H_5)_3P{=}C\overset{R_1}{\underset{CO_2C_2H_5}{\diagup}} \; + \; R_2\overset{R_3}{\underset{}{CHCOCl}} \longrightarrow (C_6H_5)_3\overset{+}{P}{-}\overset{R_1}{\underset{\underset{R_3}{\overset{O{=}C-CHR_2}{|}}}{\underset{}{C}}}{-}CO_2C_2H_5 \; Cl^-$$

$$16$$

$$(C_6H_5)_3P{=}C\overset{R_1}{\underset{CO_2C_2H_5}{\diagup}}$$

$$\xrightarrow{\hspace{3cm}} (C_6H_5)_3\overset{+}{P}{-}\overset{\overset{O}{\parallel}}{\underset{\underset{\downarrow R_3}{\overset{O-C{=}CR_2}{|}}}{C}}{-}CO_2C_2H_5 \; + \; (C_6H_5)_3\overset{+R_1}{\underset{CO_2C_2H_5}{PCH}} \; Cl^-$$

$$(C_6H_5)_3PO \; + \; R_2R_3C{=}C{=}CR_1CO_2C_2H_5$$
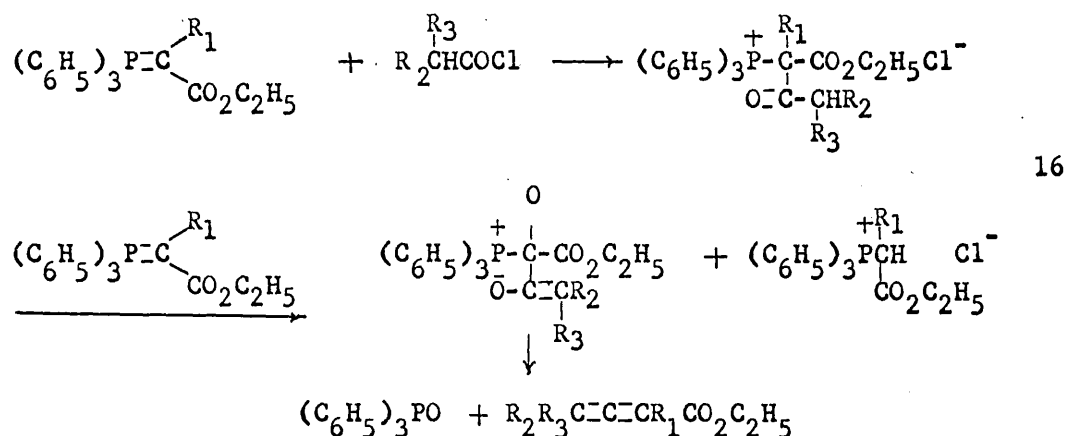
Objective:

The primary objective of this work was to ascertain whether the Wittig reaction, as modified by Bestmann, could be adapted to the synthesis of butatrienes. The problem is complicated by the fact that over 80% of the known butatrienes are tetraaryl substituted and the vast majority of the remaining recorded butatrienes have

electron-withdrawing substituents at all available positions.
Alkyl and hydrogen substituted structures, apparently, for the most
part, are unstable (67). In light of the noted structural require-
ment, it was decided to prepare $(C_6H_5)_2C=C=C=C(C_6H_5)CO_2C_2H_5$, which
satisfies the stability requirement of butatrienes while being of
the general form of the allenes prepared by Bestmann. The butatriene
is of such form, that it can only be prepared by one synthetic route,
Equation 17. The alkylidene portion of the required ylid has substi-

$$(C_6H_5)_2C=CHCOCl \ + \ (R)_3P=C \begin{smallmatrix} C_6H_5 \\ \\ CO_2C_2H_5 \end{smallmatrix} \xrightarrow{\ B: \ } (C_6H_5)_2C=C=C=C(C_6H_5)CO_2C_2H_5$$

17
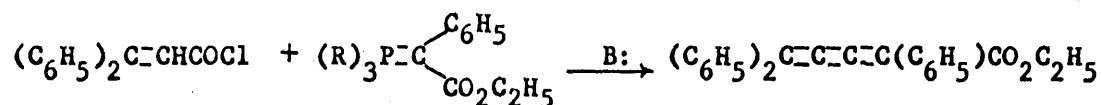
tuents which lead to a stabilized ylid and therefore one of low reac-
tivity. This factor dictates that trialkylphosphoranes as well as
triphenylphosphoranes be examined in this approach to cumulene synthe-
sis. In addition, the feasability of using phosphonates together with
acyl halides as an approach to cumulene production was to be studied.
It should be underlined that this is a novel application of the
Wittig reaction as well as an original approach to the preparation of
butatrienes.

II. DISCUSSION

Preparation of Phosphonium ylids

The application of the Wittig reaction was modified by
Bestmann and as outlined on page 20, required ylids of the form
$(R_1)_3P=C(C_6H_5)CO_2R_2$. The salts of the ylids were to be prepared
by causing a trialkyl or triaryl phosphine to react with either the
ethyl or methyl ester of α-bromophenylacetic acid. The ylids them-
selves were to be formed by treating the corresponding phosphonium
salt with a base, Equation 18.

$$(R_1)_3P \ + \ C_6H_5CH(Br)CO_2R_2 \longrightarrow (R_1)_3\overset{+}{P}CH(C_6H_5)CO_2R_2Br^-$$
$$(R_1)_3\overset{+}{P}CH(C_6H_5)CO_2R_2Br^- \ + \ B:^- \longrightarrow (R_1)_3P\bar{=}C(C_6H_5)CO_2R_2 \ + \ Br^- \ + \ BH \qquad 18$$
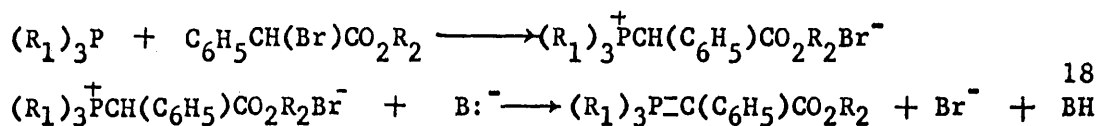
The α-halo esters were prepared by two different methods:
1) the esterification of α-bromophenylacetic acid, and 2) the
esterification and bromination of mandelic acid. The second approach
became the method of choice due to the comparatively high expense of
the first method and due to the observation that the yield of ester
products through the two-step process (84.5%) was not substantially
lower than the first method (89%).

The triphenyl ylids were prepared by two methods: 1) the
general method of Bestmann and Hartung (64) and Bestmann and Schulz
(40), and 2) the "melt method" as mentioned by Johnson (68).

The first method was employed by Bestmann and Schulz to
prepare the carbomethoxyphenylmethylenetriphenylphosphorane.
Although the yields of other ylids were reported by the authors,

they failed to mention the yield for the methyl ester of the ylid, presumably due to an unsatisfactory yield.

The approach described by the authors consisted of refluxing a benzene solution of triphenylphosphine and the α-haloester to form a phosphonium salt, which when isolated and treated with sodium hydroxide afforded the desired ylid.

It was found, however, that the yield of the reaction could be improved by as much as 13% when the salt was removed by filtration at thirty minute intervals, and the reaction mixture allowed to continue to reflux after the removal of the salt. The precipitates when dissolved in water and treated with sodium hydroxide formed the methyl ester of the ylid in a yield of 23% while the ethyl ester of the ylid was formed in only 15% of the theoretical. It is not apparent why removal of the salt from the reaction mixture enhanced the production of additional phosphonium salt.

Literature sources suggested that ylids of this type are best purified by recrystallization from a fifty-fifty mixture of ether and ethyl acetate (69). Experimentally, however, it was found that recrystallization carried out in boiling cyclohexane afforded the greatest purification.

The melt method suggested by Johnson consisted of refluxing the α-haloester with melted triphenylphosphine at 100°C. The melt formed a precipitate which when treated with sodium hydroxide gave carbethoxyphenylmethylenetriphenylphosphorane in a yield of 64% and carbomethoxyphenylmethylenetriphenylphosphorane in a yield of 63%. Both yields were much higher than those afforded by the method of

Bestmann and Hartung.

Carboethoxyphenylmethylenetriphenylphosphorane has not been synthesized before and was characterized by infra-red, NMR, and elemental analysis data. The infra-red spectrum demonstrated adsorptions for a carbonyl function at 6.27 μ, for a P-C stretching frequency at 7.68 μ, and for asymmetric and symmetric ester stretching frequencies at 8.17 μ and 9.14 μ, respectively. Aromatic and alkane C-H stretching in the region from 3.30 μ, to 3.42 μ as well as the out of plane bending modes of aromatic hydrogen atoms at 13.29 μ, 14.07 μ, and 14.42 μ were also noted. NMR data demonstrated a triplet with a chemical shift (δ.94) characteristic of a methyl group adjacent to a methylene function. A quartet of peaks was observed with a chemical shift (δ.93) expected for methylene group bound to oxygen in an ester function and adjacent to a methyl group. In addition, two different sets of peaks for phenyl protons were observed with one set three times larger and further downfield than the other (δ6.92, δ7.50). The aromatic hydrogens with the greatest downfield shift were assigned to the phenyl groups on the phosphorus atom. Finally, the elemental analysis agreed with the calculated composition for carbon, hydrogen, and phosphorous within +.24%.

The preparation of carbethoxyphenylmethylenetri-n-butylphosphorane was attempted using the procedure suggested by Johnson and LaCount (7). The authors had prepared the phosphonium salt of 9-fluorenylidenetri-n-butylphosphorane under nitrogen by adding tri-n-butylphosphorane to an acetone solution of 9-bromofluorene at room temperature. The same approach utilizing ethyl α-bromophenyl-

acetate and tri-n-butylphosphine afforded no precipitate even when the reaction mixture was refluxed at 70°C for four hours.

Since the reaction is essentially a bimolecular nucleophilic substitution process, it was felt that the steric interactions of the n-butyl groups of the phosphine and the phenyl and ester functions of the ester were too great for the reaction to proceed as outlined. A minor adjustment often employed in reactions of this type is to use the iodo compound, as the iodide ion serves as a more efficient leaving group than the bromide ion. Utilization of ethyl α-iodophenyl-acetate did not apparently enhance the process since the formation of the desired phosphonium salt was not noted.

The synthesis of (carbethoxyphenylmethylene)trimethylphosphonium bromide as suggested by Trippet and Walker (41), was carried out by adding phosphorous tribromide to an etheral solution of methylmagne-sium bromide and distilling the formed trimethylphosphine into an etheral solution of ethyl α-bromophenylacetate. The reaction yielded a salt in only two of a dozen attempts. Variations included distilling the reaction mixture at higher temperatures and using an excess of materials forming the phosphine. It is not evident as to the reasons why the process was not reproducible.

The process did afford, however, enough salt to permit superficial analysis. No attempt was made to purify the salt except for washing with anhydrous ether and for extensive drying. Extraction of an aqueous solution of the salt to remove organic impurities was not attempted since the stability of trialkylphosphonium ylids is low. Usually, salts of this type are not isolated but are converted to the

ylid and caused to react with a carbonyl substrate _in situ_. The salt

had an infra-red spectrum with adsorptions as noted for C-H stretching

at 3.42 μ and 3.51 μ, for C=O stretching at 5.82 μ, C-P stretching at

7.78 μ with a shoulder at 7.91 μ, asymmetric and symmetric C-O-C

stretching at 8.71 μ and 9.78 μ respectively, an unidentified broad,

strong band at 10.32 μ, and aromatic hydrogen out of plane bending

modes at 12.79 μ, 13.48 μ, and 14.10 μ. NMR data demonstrated

characteristics expected of a structure of the desired salt, XXIII.

$$(CH_3)_3\overset{+}{P}\text{-}\underset{\underset{CO_2C_2H_5}{|}}{\overset{\overset{C_6H_5}{|}}{C}H} \qquad Br^-$$
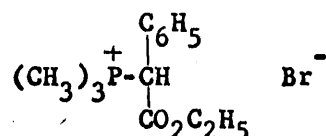
XXIII

A group of peaks from δ 1.02 ppm to δ 1.94 ppm showed a triplet centered

at δ 1.15 ppm with spacing of 7 cps and 2 pairs of doublets with the

stronger pair centered at δ 1.83 ppm with spacing of 14 cps while the

weaker pair is centered at δ 1.50 ppm and also has a splitting of 14 cps.

These peaks are probably due to two of the methyl groups whose reso-

nance is split by ^{31}P; the weaker pair may be due to either restricted

rotation of the methyl groups about the C-P bond or the ^{29}P isotopic

molecule, or the resonance of the methine hydrogen or a combination of

all of these factors. A pair of peaks centered at δ 4.29 ppm are in

reality the center two lines of the methylene quartet, and have the

same splitting as the methyl triplet at δ 1.83 ppm. A single sharp

line at δ 4.54 ppm represents the third non-equivalent methyl group

on the phosphorus atom. A group of peaks at δ 7.49 ppm indicative

of aromatic hydrogens, was also noted.

Of the attempts to prepare ylids of the form $(R)_3PC(C_6H_5)CO_2C_2H_5$ where R=phenyl, n-butyl, or methyl, only the preparation of the phenyl derivative succeeded. The attempts to prepare the n-butyl derivative failed, apparently due to steric hindrance involved in the initial nucleophilic attack of tri-n-butylphosphine on both the α-iodo and α-bromoesters. No attempt was made to prepare the methyl ylid from its phosphonium salt as ylids of this type are not stable and are generally not isolated but prepared and used in situ.

Synthesis of Acyl Halides

The preparation of β-phenylcinnamoyl chloride was attempted utilizing the general process afforded by Bergmann et. al., (71), which involved the addition of oxalyl chloride to 1,1-diphenyl-ethylene, Equation 19. The process was carried out by refluxing

$$2(C_6H_5)_2C=CH_2 \ + \ (COCl)_2 \longrightarrow 2(C_6H_5)_2C=CHCOCl \ + \ 2HCl \qquad 18$$
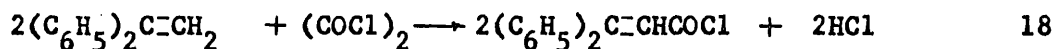
the reactants for five hours with the exclusion of water.

The reaction was stopped after the evolution of hydrogen chloride ceased. Attempted distillation at 1.5 mm gave a small quantity of material that solidified in the distillation head and a thick brown-black tar in the distillation pot. The material that formed in the distillation head gave adsorptions in the infra-red consistent with a conjugated acyl halide, except for the C=O band at 5.66 μ that was lower than expected.

The tar-like residue was treated with sodium hydroxide, and the

alkaline solution was acidified with glacial acetic acid. A precipitate formed which had an infra-red spectrum inconsistent with the known spectra for β-phenylcinnamic acid.

The process was repeated with the exception that isolation of the acyl halide was attempted by means of column chromatography and distillation on a spinning band column. The tar-like residue, formed upon the removal of excess oxalyl chloride, was eluted on a neutral alumina column with 30°C-60°C petroleum ether. A red-brown tar that was eluted from the column had adsorptions in the infra-red consistent with the desired acyl halide except that the C⁼O stretching band was at 5.9 μ rather than in the expected range of 5.7 μ to 5.85 μ.

Distillation of the tar-like residue at 25 mm in a spinning band column afforded a solid that formed in the delivery arm of the apparatus. The solid gave a spectrum that could not be identified and had adsorptions only for an olefinic C-H stretching vibrations at 3.29 μ and a C⁼C stretching frequency at 6.21 μ.

A benzene solution of the tar-like resudue formed a precipitate when treated with low boiling petroleum ether. The solid gave an infra-red spectrum similar to that for benzoic acid. This indicated that there was enough moisture present in the reaction system to cause hydrolysis of the acid halide formed.

Since the above process did not seem to be productive while simultaneously being expensive, a new approach was used involving the general method of Shriner for the Reformatsky condensation (71) as outlined in Equations 20-23. The process gave a good yield of β -phenylcinnamic acid, but the formation of the acyl halide by the

$$(C_6H_5)_2C=O \ + \ BrCH_2CO_2C_2H_5 \xrightarrow[\text{2) H}^+]{\text{1) Zn}} (C_6H_5)_2C(OH)CH_2CO_2C_2H_5 \qquad 20$$

$$(C_6H_5)_2C(OH)\text{-}CH_2CO_2C_2H_5 \xrightarrow{C_6H_5SO_3H} (C_6H_5)_2C=CHCO_2C_2H_5 + H_2O \quad 21$$

$$(C_6H_5)_2C=CHCO_2C_2H_5 \xrightarrow[\text{2) H}^+]{\text{1) OH}^-} (C_6H_5)_2C=CHCO_2H + C_2H_5OH \qquad 22$$

$$(C_6H_5)_2C=CHCO_2H \xrightarrow{SOCl_2} (C_6H_5)_2C=CHCOCl + HCl + SO_2 \qquad 23$$
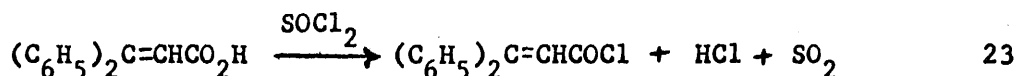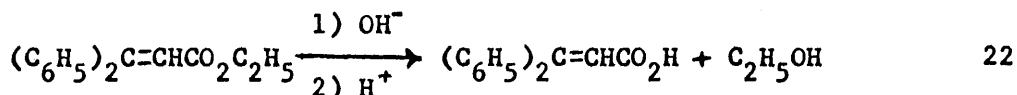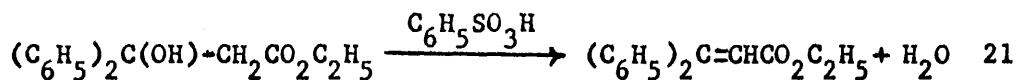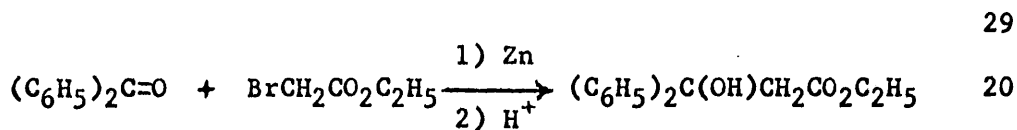
addition of thionyl chloride, Equation 23, was not productive and was

similar in result to that afforded by the process involving the

addition of oxalyl chloride, Equation 18.

Thionyl chloride was added to a solution of β-phenylcinnamic

acid in benzene with careful exclusion of moisture. The product, a

green liquid was distilled at 140°C-160°C at 2.8 mm. The distillate

gradually turned to a brown tar and gave an infra-red spectrum with

C=O bands at 5.68 µ, 5.85 µ, and 5.92 µ.

The formation of tar, the multiplicity of C=O adsorptions in the

infra-red, the generation of hydrogen chloride in both processes, and

the susceptability of the olefinic band to acid catalyzed polymeriza-

tion, indicated that polymerization was hampering the synthesis of

β-phenylcinnamoyl chloride.

The condensation process utilized to prepare β-phenylcinnamic

acid was applied to the synthesis of fluorenylacetic acid which was

formed in a yield of 83%. Conversion of the acid to an acid chloride

was not attempted due to the discovery that the reaction of the

triphenylphosphonium ylids with the acyl halides was not productive.

Reaction of Triphenylphosphonium Ylids with Carbonyl Compounds

$$(C_6H_5)_3P=C(C_6H_5)CO_2C_2H_5 \qquad\qquad (C_6H_5)_3P=C(C_6H_5)CO_2CH_3$$
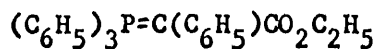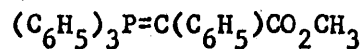
A   B

The reaction of ylid A and B with benzaldehyde was carried out by the general method offered of Maescher (69). The reactants, along with a catalytic quantity of benzoic acid, were refluxed on a steam bath for 15 hours. The process offered 98.5% recovery of the starting ylid.

The same procedure was used in the attempted condensations of both ylids, A and B, with p-nitrobenzaldehyde. The p-nitrobenzaldehyde was employed due to the fact that the carbonyl carbon was more electrophilic than the analogous carbon atom in the unsubstituted benzaldehyde. The reactions apparently failed as both ylids did not offer condensation products.

The failure of the ylids to offer the expected olefinic products indicated that the nucleophilicity of the ylids was not great enough to induce a condensation with neither benzaldehyde nor p-nitrobenzaldehyde. There is no record in the literature regarding a previous condensation using ylids of the type employed here.

The reaction of ylids A and B with acid chlorides, primarily propanoyl chloride, was carried out in the manner suggested by Bestmann and Hartung (64). The ylid and the acyl halide were refluxed in benzene, and a precipitate formed. The precipitate was an easily decomposed complex of the ylid, for treatment with alkali regenerated the starting ylid in a recovery of 62% to 72%.

The organic solution, upon distillation, offered only low boiling materials, indicating only the acid chloride and solvent were present.

The process was repeated with the modification that the acid chloride was added to a rapidly stirred mixture of the ylid in benzene containing silver nitrate. It was thought that the reaction may be enhanced by the addition of silver nitrate by forcing the formation of a more electrophilic carbon as shown in Equation 24. However, the

$$R-\overset{\overset{}{\underset{O}{\|}}}{C}-Cl \ + \ AgNO_3 \longrightarrow R-\overset{\overset{+}{}}{\underset{\overset{\|}{O}}{C}} --- \overset{-}{Cl} --- AgNO_3 \qquad\qquad 24$$
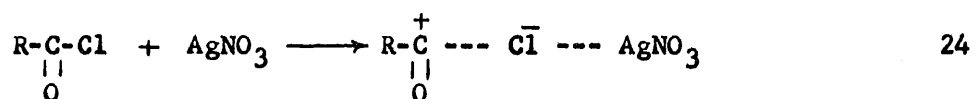
alteration did not favorably change the results and only the salts of the reacting ylids were isolated.

The reasons for the formation of the salts of the ylids were not apparent, and only one plausable explanation is offered. The evidence for the enolate structure for ylids of the type employed as discussed on pages 10 and 11 led to the proposal that the enolate structure formed an O-alkylated salt as shown in Equation 25 and that the

$$R-\overset{\overset{}{\underset{O}{\|}}}{C}-Cl \ + \ \overset{\overset{+P(C_6H_5)_3}{|}}{\underset{\overset{|}{OC_2H_5}}{\bar{O}-C \equiv C-C_6H_5}} \longrightarrow R-\overset{\overset{}{\underset{O}{\|}}}{C}-O-\overset{\overset{+P(C_6H_5)_3}{|}}{\underset{\overset{|}{OC_2H_5}}{C \equiv C-C_6H_5}} \ Cl^- \qquad 25$$
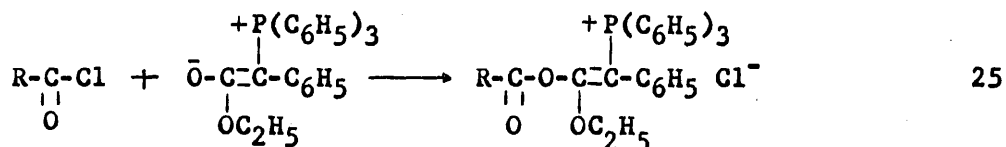
O-alkylated product decomposes in water as shown in Equation 26. The

$$R-\overset{\overset{}{\underset{O}{\|}}}{C}-O-\overset{\overset{+P(C_6H_5)_3}{|}}{\underset{\overset{|}{OC_2H_5}}{C \equiv C-C_6H_5}} \ Cl^- \ + \ H_2O \longrightarrow R-\overset{\overset{}{\underset{O}{\|}}}{C}-OH \ + \ \overset{\overset{+P(C_6H_5)_3}{|}}{\underset{\overset{|}{OC_2H_5}}{HO-C \equiv C-C_6H_5}} \quad Cl^- \qquad 26$$
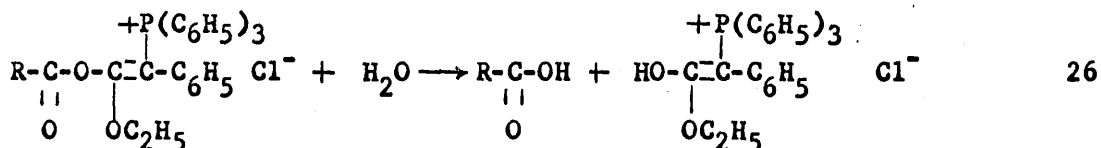
ylid is formed again when the solution is treated with sodium

hydroxide, Equation 27.

$$\underset{\underset{OC_2H_5}{\overset{\overset{+P(C_6H_5)_3}{|}}{HO-C^-_{}C-C_6H_5}}}{} \xrightarrow{\quad OH^- \quad} (C_6H_5)_3P^-C(C_6H_5)CO_2C_2H_5 + H_2O \qquad 27$$
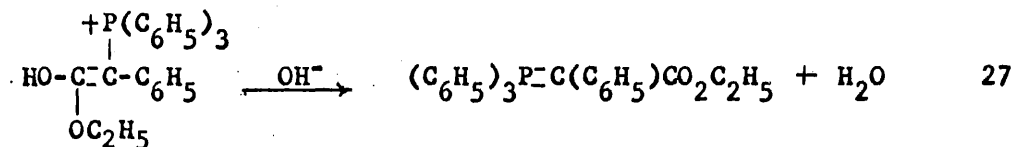
It should be noted that not all of the reacting ylids were re-
covered. This indicates that conversion of the salt to ylid might not
have been complete.

Synthesis of Diethyl Phosphonates

Since the approach to cumulene synthesis utilizing stabilized
ylids failed, it was thought that the use of phosphonates as suggested
by Wadsworth and Emmons (58) would be more productive.

The preparation of the phosphonates followed the general procedure
suggested by Arbuzov (60,61), which entailed refluxing triethyl phos-
phite with the pertinent alpha-bromo ester. The preparation of ethyl
diethylphosphonophenylacetate failed presumably due to the aforemen-
tioned steric factors (page 19).

Ethyldiethylphosphonoacetate was formed in a yield of 53%
compared to that reported by Arbuzov of 50%. The yield of phospho-
nate was held low presumably due to a competing reaction of the formed
ethyl bromide as shown in Equation 14.

Reaction of Ethyl Diethylphosphonoacetate with Benzoyl Chloride

Even though the original objective of butatriene synthesis was
abandoned due to the failure to prepare ethyl diethylphosphono-

phenylacetate, it was decided to attempt to cause the reaction of an

acid chloride with ethyl diethylphosphonoacetate, since the process

had not been attempted previously on acid halides. The general method

offered by Wadsworth and Emmons for the reaction of ketones and

aldehydes with phosphonoacetates was utilized with the minor modifi-

cation of adding a second mole of sodium hydride. Additional sodium

hydride was necessary to decompose the proposed intermediate as shown

in Equation 30.

$$(C_2H_5O)_2\overset{\overset{O}{\|}}{P}CH_2CO_2C_2H_5 + NaH \longrightarrow (C_2H_5O)_2\overset{\overset{O}{\|}}{P}\overset{..}{\overset{-}{C}}HCO_2C_2H_5 + Na^+ + H_2 \qquad 28$$

$$(C_2H_5O)_2\overset{\overset{O}{\|}}{P}\overset{-}{C}HCO_2C_2H_5 + RCH_2COCl \longrightarrow (C_2H_5O)_2\overset{\overset{O}{\|}}{P}-\underset{O \cdots CCH_2R}{\overset{|}{C}}HCO_2C_2H_5 + Cl^- \qquad 29$$

$$(C_2H_5O)_2\overset{\overset{O}{\|}}{P}-\underset{O \cdots CCH_2R}{\overset{|}{C}}HCO_2C_2H_5 + NaH \longrightarrow RCH \cdots C \cdots CHCO_2C_2H_5 + (C_2H_5O)_2\overset{\overset{O}{\|}}{P}O^- \qquad 30$$

or

$$RCH_2C \cdots CCO_2C_2H_5$$
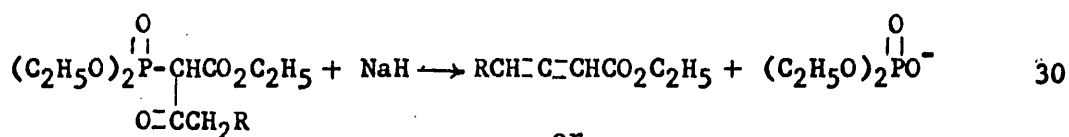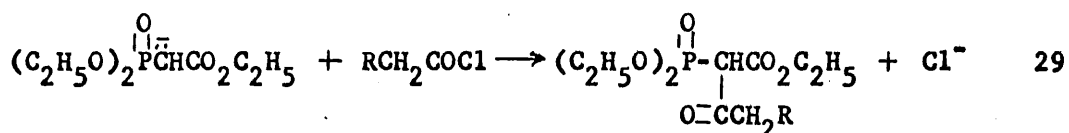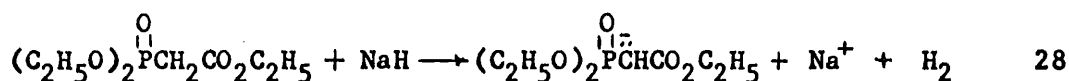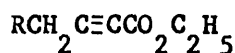
In addition, it was decided to utilize benzoyl chloride, for an

acid chloride with an alpha hydrogen could afford a mixture of products

as shown in Equation 30. Benzoyl chloride in contrast, would afford

only an acetylenic compound as shown in Equations 31 and 32.

$$(C_2H_5O)_2\overset{\overset{O}{\|}}{P}-\overset{-}{C}HCO_2C_2H_5 + C_6H_5COCl \longrightarrow (C_2H_5O)_2\overset{\overset{O}{\|}}{P}-\underset{O \cdots C-C_6H_5}{\overset{|}{C}}HCO_2C_2H_5 + Cl^- \qquad 31$$
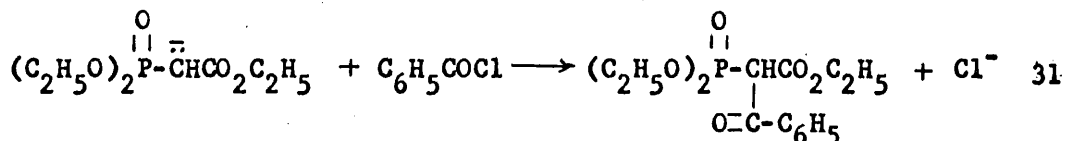
The process was carried out by adding the phosphonate to a

slurry of sodium hydride in 1,2-dimethoxyethane, followed by the

addition of benzoyl chloride. Benzoic acid corresponding to 62% of

the benzoyl chloride, was obtained from the aqueous fractions. The

$$(C_2H_5O)_2\overset{\overset{O}{\|}}{P}\text{-}\underset{\underset{O=C\text{-}C_6H_5}{|}}{CHCO_2C_2H_5} + NaH \longrightarrow (C_2H_5O)_2\overset{\overset{O}{\|}}{P}\text{-}\underset{\underset{O=C\text{-}C_6H_5}{|}}{\overset{\overset{CO_2C_2H_5}{|}}{C:}} + H_2 \longrightarrow$$

32

$$(C_2H_5O)_2\overset{\overset{O}{\|}}{P}\text{-}\underset{\underset{O\text{-}C\text{-}C_6H_5}{\|}}{\overset{\overset{CO_2C_2H_5}{|}}{C}} \longrightarrow C_6H_5C\equiv CCO_2C_2H_5 + (C_2H_5O)_2\overset{O}{\underset{}{\|}}PO^-$$
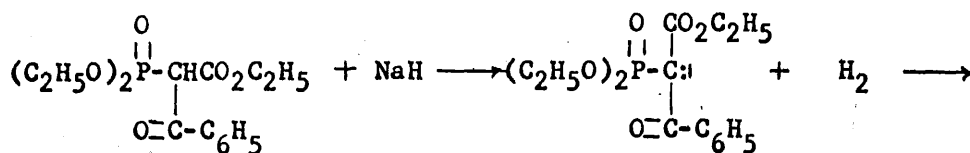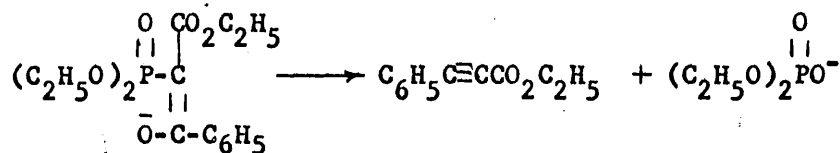
water insoluable material, upon standing, gave a solid and a liquid phase. The solid phase was unidentifiable and decomposed on an attempted distillation at reduced pressure. The liquid phase had an infra-red spectrum consistent with the desired ethyl phenyl-propynoate. The liquid was distilled at 260°C-270°C with decomposition, exactly as described in the literature (72).

The formation of benzoic acid and the low yield of the propynoate was thought to arise from two possible sources - 1) water in 1,2-dimethoxyethane and 2) water in ethyl diethylphosphonoacetate. The dimethoxyethane was dried over phosphorus pentoxide; however, the ether was not completely dry for when it was mixed with sodium hydride, there was an evolution of gas presumably hydrogen. The phosphonate appears to be hydrosocopic. The material gave an infra-red spectrum identical to that offered in Sadtler Spectrum No. 15583, which demonstrated an O-H stretching band which was identified as water. Drying the phosphonate over anhydrous magnesium sulfate did not alter the infra-red spectrum. In addition, NMR data demonstrated a mole of water associated with a mole of the phosphonate.

The presence of water in the reaction meant that in all

probability sodium hydroxide was formed from sodium hydride. The sodium hydroxide probably reacted with benzoyl chloride to form benzoic acid and effectively remove substrate for the condensation with phosphonate. The formation of sodium hydroxide would effectively decrease the amount of sodium hydride in the reaction mixture with a concommitant loss of formed phosphonate anion.

III. SUMMARY

1) The preparation of carboalkoxyphenylmethylenetriphenyl-phosphoranes was substantially enhanced by refluxing the α -bromoester with triphenylphosphine in a melt of the phosphine rather than in solution as suggested in the literature (64) .

2) A new compound, carbethoxyphenylmethylenetriphenylphosphorane, was prepared and characterized.

3) The formation of carbethoxyphenylmethylenetri-n-butylphosphorane failed, apparently due to steric factors.

4) The preparation of a new compound, carbethoxyphenylmethylene-trimethylphosphorane, was not reproducible, but the compound was characterized.

5) The Reformatsky reaction was shown to be a good approach to the synthesis of β -hydroxy esters of the form $(C_6H_5)_2C(OH)CH_2CO_2C_2H_5$.

6) The reactions of triphenyl ylids of the form $(C_6H_5)_3P\!=\!C(C_6H_5)$ $CO_2R(R\!=\!CH_3, C_2H_5)$ with benzaldehyde and p-nitrobenzaldehyde failed, indicating the ylids are weak nucleophites.

7) The reaction of the triphenylphosphonium ylids with acid chlorides led to the formation of a salt of the reacting ylids, indicating a possible O-alkylated product.

8) The reaction of the triphenylphosphonium ylids with acid chlorides was not favorably altered by the presence of silver nitrate. Only a salt of the starting ylids was isolated.

9) The preparation of ethyl diethylphosphonophenylacetate failed, apparently due to steric factors.

10) The synthesis of ethyl diethylphosphonacetate was carried out with a slight improvement of yield compared to the identical process in the literature (72).

11) The reaction of ethyl diethylphosphonoacetate and benzoyl chloride led to the formation of ethyl phenylpropynoate as was proposed.

IV. EXPERIMENTAL

<u>Ethyl α-bromophenylacetate:</u> $C_6H_5CH(Br)CO_2C_2H_5$

Method A - esterification of α-bromoacetic acid.

In a 250 ml., round-bottom flask, equipped with a Dean and Stark tube and a reflux condenser was placed 12.6 g (0.58 mole) of α-bromophenylacetic acid, 60 ml. of absolute ethyl alcohol, 275 ml. of dry benzene, and .5 ml. of concentrated sulfuric acid. The solution was refluxed continuously for six hours with 20 ml. portions of distillate removed from the Dean and Stark tube every 30 minutes, (the water-alcohol azeotrope layer was not distinguishable from the alcohol-benzene aseotrope). At the end of the third hour, 25 ml. absolute alcohol and 75 ml. dry benzene were added. The temperature of the vapor in the reflux condenser remained at 65°C, at which point the reaction mixture was allowed to cool. The solution was washed with 100 ml. water, 100 ml. 1% sodium carbonate, and 100 ml. water. The organic layer was dried over anhydrous magnesium sulfate, filtered, and fractionally distilled. The product was collected at 142°C at 16 mm. (Lit. 164°C at 20 mm.) (73). The infra-red spectrum of the liquid was identical to that given in Sadtler spectrum No. 20467 for ethyl α-bromophenylacetate. Yield 12.97 g., or 89% of the theoretical.

Method B - esterification and bromination of mandelic acid.

Esterification of mandelic acid was carried out by a procedure

identical to that described in method A, except that the following quantities and materials were used: 12.81 g (.094 mole) mandelic acid, 80 ml. absolute ethanol, 350 ml. dry benzene, and 1 ml. concentrated sulfuric acid. Washing and drying procedures were identical to that described previously. After the mixture was dried, the solvents were removed under aspiration. The crude liquid product gave an infra-red spectrum, which is identical to Sadtler Spectrum No. 2346 for ethyl mandelate. Yield 14.71 g, 95% of the theoretical.

The bromination of ethyl mandelate was carried out in a 250 ml., three-necked flask equipped with dropping funnel, magnetic stirrer, thermometer, reflux condenser, and calcium chloride drying tube. Ethyl mandelate (20.9 g, .13 mole) was dissolved in 100 ml. dry benzene, and phosphorous tribromide (11.65 g, .043 mole) was added dropwise to the solution with stirring. Replacement of hydroxy functions with phosphorous tribromide is described in the literature as being exothermic; however, this process required heating to approximately 70°C before any formation of a phosphorous acid layer was observed.

The solution was cooled, the acid layer drawn off, and the organic layer was washed with 100 ml. water, 100 ml. 1% sodium carbonate, and 100 ml. water. The organic layer was dried over anhydrous magnesium sulfate, filtered, and fractionally distilled. The fraction boiling at 142°C at 16 mm. was collected and gave adsorptions in the infra-red identical to that in Sadtler Spectrum No. 20467. Yield 27.51 g, 89% of the theoretical.

<u>Methyl α-bromophenylacetate</u>: $C_6H_5CH(Br)CO_2CH_3$

The preparation of methyl α-bromophenylacetate was carried out as described in method B for the preparation of the ethyl ester. In the esterification step, methyl mandelate was prepared in the same manner as the ethyl ester, except that 20 g (.13 mole) mandelic acid, 50 ml. methyl alcohol, 375 ml. dry benzene, and 1 ml. concentrated sulfuric acid were employed. Washing and drying procedures were also carried out as described previously, and after the organic solution was filtered free of magnesium sulfate, the solvents were removed under aspiration. The crude liquid product slowly solidified and gave an infra-red spectrum that agreed with the predicted spectrum of methyl mandelate when compared to ethyl mandelate spectrum found in Sadtler No. 2346. Yield $=$ 19.75 g, 83% of the theoretical.

Bromination of methyl mandelate was carried out as in the previous bromination, except that the following quantities were used: 19.75 g (.119 mole) of methyl mandelate, 10.11 g (.039 mole) of phosphorous tribromide, and 100 ml. of dry benzene. After washing, drying, and removal of solvent, the crude product was weighed and immediately used in the synthesis of its corresponding triphenyl phosphorane. Yield $=$ 19.31 g or 71% of the theoretical.

<u>β-Phenylcinnamyl Chloride</u>: $(C_6H_5)_2C=CHCOCl$

<u>Method A</u> - the addition of oxalyl chloride to 1,1-diphenylethylene.

The reaction was carried out as described by Bergman, et.al. (71). Diphenylethylene 5.4 g (.03 mole) and 12.6 g (.1 mole) of oxalyl chloride were refluxed in a 100 ml. round-bottom flask, equipped with a reflux condenser and an acid trap. The literature source claims the reaction should be complete in two hours and can be determined when the production of hydrogen chloride ceases. However, the process required five hours of refluxing, during which time the solution became first orange, then green, and finally black. Removal of excess oxalyl chloride under aspiration left a solid tarrish residue that resisted distillation at 1.5 mm. A small amount of material solidified in the distillation head and gave an infra-red spectrum which had adsorptions at the following wave lengths; 3.3 μ, 5.66 μ, 6.32 μ, 6.41 μ, 6.80 μ, 6.99 μ, 7.41 μ, 9.72 μ, 9.85 μ, 10.62 μ, 12.85 μ, 13.05 μ, 13.59 μ, 13.93 μ, and 14.38 μ. The tarrish residue was treated with 200 ml. 5 $\underline{N}$ sodium hydroxide at $100^{\circ}C$ for two hours. After filtration (a considerable amount of tarrish material was removed), acidification of the aqueous solution with 12 $\underline{N}$ hydrochloric acid did not yield the expected precipitate of β-phenylcinnamic acid. The tarrish material removed by filtration from the basic solution was dissolved in 25 ml. concentrated acetic acid with warming. The acidic solution upon cooling formed a red-gray precipitate. The precipitate was removed by filtration and dried in a dessicator under vacuum. The material gave an infra-red spectrum which did not compare in a favorable way with Sadtler Spectrum No. 4022 for

β -phenylcinnamic acid.

The experiment was repeated, and after the excess oxalyl chloride was removed, the solid tarrish residue was distilled at 25 mm. in a spinning band column. A solid condensed in the delivery arm of the distillation apparatus. The material gave an infra-red spectrum that displayed adsorptions for carbon-hydrogen stretching (3.29 μ) and carbon-carbon double bond stretching (6.21 u) frequencies only. No other attempt was made to identify the solid due to extensive decomposition occuring during the distillation.

An attempt to separate the acyl chloride by column chromatography produced confusing results. A 20 inch column was packed with activated, neutral alumina and a solution of 2 g. of tar in 20 ml. of benzene was placed in the column. The column was eluted with low boiling (30°C - 60°C) petroleum ether. One hundred milliliter samples of eluted solution were taken. Bands on the column appeared from top to bottom as dark green, green, light brown, crimson, and brown. Continuous elution with low boiling petroleum ether gave 100 ml. samples five through twelve, which upon evaporation of the solvent yielded a red brown tar that gave an infra-red spectrum that could have been that of the expected acyl chloride. However, the adsorption for the carbonyl stretching frequency appeared at 5.9 μ rather than in the expected range of 5.7 μ - 5.85 μ.

A benzene solution of the tar residue upon treatment with low boiling petroleum ether formed a precipitate that gave an infra-red spectrum which is quite similar to that for β -phenylcinnamic acid, as demonstrated in Sadtler Spectrum No. 4022.

Method B - Condensation of ethyl α-bromoacetate and benzophenone.

Synthesis of ethyl β-hydroxy-β,β-diphenylpropionate was carried out by the general method outlined by R. L. Shiner in Organic Reactions (71). In a three-necked, 500 ml. flask fitted with a thermometer, magnetic stirrer, reflux condenser equipped with a calcium chloride drying tube, and a dropping funnel, was placed 4.35 g. (.025 mole) benzophenone, 150 ml. dry benzene, and 1.56 g cleaned 20-mesh zinc. Ethyl bromoacetate, 4 grams (.024 mole), was placed in dropping funnel and added dropwise to the rapidly stirred solution. A few crystals of iodine were added to initiate the reaction. After a few moments the solution started to froth and a copious white precipitate formed. After all of the ethyl bromoacetate had been added, the solution was refluxed for two hours and allowed to cool. The reaction mixture consisting of a liquid and a precipitate was washed twice with 100 ml. of 5 $\underline{N}$ sulfuric acid, once with 100 ml. 1% sodium carbonate, and finally with two 100 ml. portions of water. The organic layers were combined and dried over anhydrous magnesium sulfate. The solution was filtered free of the drying agent, and the solvents were re- moved under aspiration leaving a white residue. The white solid demonstrated adsorptions in the infra-red, as would be expected for the desired hydroxyester and as follows; 2.92 μ, 3.03 μ, 3.42 μ, 5.88 μ, 6.02 μ, 6.95 μ, 7.35 μ, 7.89 μ, 8.37 μ, 8.59 μ, 9.85 μ, 12.99 μ, 13.34 μ, and 14.37 μ. Yield ⁻ 5.32 g, or 82% of the theoretical.

The dehydration of ethyl β-hydroxy-β,β-diphenylpropionate was attempted by refluxing 5.32 g of the β-hydroxy ester in 50 ml.

benzene while hydrogen chloride was continuously bubbled through the solution. Upon removal of the benzene, a white residue was obtained which gave an infra-red spectrum identical to that of the starting material.

The refluxing of 5.32 g of the hydroxy ester in 50 ml. benzene with 4 ml. benzenesulfonic acid yielded a liquid which had an infra-red spectrum identical to Sadtler Spectrum No. 4023 for ethyl β-phenylcinnamate. Yield ⁻ 3.73 g or 78% of the theoretical.

Saponification of ethyl β-phenylcinnamate was carried out by refluxing 3.73 g of the ester with 600 ml. 2 N sodium hydroxide for six hours. After being cooled, the solution was acidified with concentrated hydrochloric acid. A precipitate formed which was dried in a dessicator over calcium chloride under vacuum. The material gave an infra-red spectrum which was identical to Sadtler spectrum No. 4022 for β-phenylcinnamic acid. M.P. 156°C (Lit. 161°C) (70). Yield ⁻ 1.27 g or 42% of the theoretical.

Synthesis of β-phenylcinnamoyl chloride was carried out in a three-necked 500 ml. flask, fitted with a dropping funnel, thermometer, spin bar, reflux condenser, calcium chloride drying tube, and an acid trap. In the flask was placed 10.85 g (.048 mole) of β-phenylcinnamic acid and 200 ml. dry benzene. Thionyl chloride (10 g, .084 mole) was added dropwise from the dropping funnel while the solution was stirred and heated at 80°C. After all of the thionyl chloride had been added, the mixture was stirred and heated for an additional four hours. The reaction mixture was cooled and solvent and excess thionyl chloride were removed by aspiration. The remaining material

was distilled at 140°C - 160°C at 2.8 mm. leaving a brown tar behind.
The green liquid that was distilled gradually turned to a brown tar
and had a strong odor of hydrogen chloride. The material gave a
variety of infra-red adsorptions in the carbonyl stretching frequency
region, (5.68 μ, 5.85 μ, 5.92 μ). The formation of the tar and smell
of hydrogen chloride indicates the possibility of acid catalyzed
polymerization of the β-phenylcinnamoyl chloride or β-phenylcinnamic
acid.

<u>Fluorenylacetic acid</u>: $C_{12}H_8C=CHCO_2H$

Ethyl (9-hydroxy)-fluorenylacetate was prepared by the procedure
used for ethyl β,β-diphenyl-β-hydroxypropionate except that the
following quantities and materials were employed: 18.0 g (.1 mole)
fluorenone, 6.5 g (.1 mole) 20 mesh zinc, 16.7 g (.1 mole) ethyl
bromoacetate, and 300 ml. of dry benzene. On workup, a liquid was
obtained that gave an infra-red spectrum which was consistent with
the desired hydroxy ester and noted as follows: 2.92 μ, 3.30 μ,
3.42 μ, 5.81 μ, 5.85 μ, 6.21 μ, 6.91 μ, 6.94 μ, 8.31 μ, 8.71 μ, 9.70 μ,
9.84 μ, 13.04 μ, 13.62 μ, and 14.79 μ.

The hydroxy ester was immediately dehydrated as described in
the preparation of ethyl β-phenylcinnamate. Upon removal of solvent,
under aspiration, a yellow solid was formed which gave adsorptions in
the infra-red as follows: 3.30 μ, 3.42 μ, 5.87 μ, 6.11 μ, 6.26 μ,
6.94 μ, 6.99 μ, 8.36 μ, 8.66 μ, 9.71 μ, 12.82 μ, and 13.71 μ, which
were consistent with the expected olefenic ester.

Saponification of the dehydration product was carried out by

refluxing the material with 600 ml. 2 $\underline{N}$ sodium hydroxide for six hours.
Acidification of the basic solution yielded a precipitate that when
dried gave absorptions in the infra-red that are consistent with the
proposed structure. M.P. $\simeq$ 147.8°C. Yield $\simeq$ 18.65 g or 83% of the
theoretical.

Carbethoxyphenylmethylenetriphenylphosphorane: $(C_6H_5)_3P\bar{\simeq}C(C_6H_5)CO_2C_2H_5$

Method A - as described by the general method of Bestmann and
Hartung (64) and Bestmann and Schulz (40).

In a 500 ml., three-necked flask, equipped with a thermometer,
spin bar, and a reflux condenser, 12.79 g (.041 mole) triphenyl
phosphine was dissolved in 200 ml. of dry benzene. Ethyl α-bromo-
phenylacetate (10.00 g, .041 mole) was added and with stirring the
solution was brought to 50°C. After approximately thirty minutes a
precipitate formed, and the solution was maintained at 50°C for an
additional thirty minutes. After being cooled, the precipitate was
removed by filtration from the solution and the filtrate was returned
to the reaction flask. Another precipitate formed, the precipitate
was collected and procedure was repeated four more times with a pre-
cipitate collected each time.

The precipitates were dissolved in water. A few drops of the
aqueous solution were added to 15% silver nitrate and a precipitate
formed immediately indicating the presence of the bromide anion.

The aqueous solution was then treated with 2 $\underline{N}$ sodium hydro-
xide until basic, whereupon a yellow precipitate formed. The pre-
cipitate was filtered from the solution, washed with 100 ml. water,

and dried in a vacuum dessicator over calcium chloride. The dried crystalline material weighed 2.67 g or 15% of the theoretical yield. The material was recrystallized from a 50:50 solution of anhydrous ethyl ether and anhydrous ethyl acetate. Recrystallization was repeated from a ether-acetate solution. However, the best recrystallization was carried out in boiling cyclohexane. The recrystallized material had a melting point of 139.5°C - 140°C. Infra-red spectrum shows that the material gives adsorptions consistent with carbethoxyphenylmethylenetriphenylphosphorane and noted as follows: 3.30 μ, 3.42 μ, 6.27 μ, 6.41 μ, 6.81 μ, 7.03 μ, 7.40 μ, 7.68 μ, 8.17 μ, 9.14 μ, 9.30 μ, 10.37 μ, 13.29 μ, 13.42 μ, 14.07 μ, and 14.42 μ. Nuclear magnetic resonance data indicate protons with the following chemical shifts; a triplet at (δ) .94 ppm, a quartet at (δ) 3.93 ppm, and a group of peaks at (δ) 6.92 ppm, and at (δ) 7.50 ppm. The respective proportions were as follows; 3:2:5:15; all data being consistent with the proposed structure. <u>Anal</u>. Calculated for $C_{28}H_{30}O_2P_1$: C, 79.23; H, 5.94; P, 7.29. Found: C, 78.60; H, 6.01; P, 7.05.

Method B - in absence of solvent and in melt. In a 250 ml., round-bottom flask was placed 10 g (.042 mole) of triphenylphosphine. The mixture was refluxed at approximately 100°C for four hours. The undissolved triphenylphosphine melted at about 80°C and after an hour of heating at 100°C the reaction mixture formed a precipitate. After being cooled, the reaction mixture was washed with 50 ml. benzene. The residue was then dissolved in 200 ml. of hot water. The aqueous solution, when treated with 2 <u>N</u> sodium hydroxide until basic, formed a copious yellow precipitate which was freed from the solution by

suction filtration and washed with 100 ml. water. The precipitate

was stored in a vacuum dessicator over calcium chloride. Yield of

crude product $\approx$ 11.26 g, 64% of the theoretical. The infra-red

spectrum was found to be identical to that of established carbethoxy-

phenylmethylenetriphenylphosphorane. M.P. $\approx$ 136.5°C - 140°C.

Carbomethoxyphenylmethylenetriphenylphosphorane: $(C_6H_5)_3P\approx C(C_6H_5)CO_2CH_3$

The preparation of carbomethoxyphenylmethylenetriphenylphospho-

rane was carried out as a melt as described in method B for carbethoxy-

methylenetriphenylphosphorane except that the following materials and

quantities were employed: 2.28 g (.0087 mole) triphenylphosphine and

2 g (.0087 mole) methyl α-bromophenylacetate. The solid residue was

removed from the reaction flask with acetone. After the acetone evapo-

rated from the residue, the residue was dissolved in water and isola-

tion of the ylid was continued as described in method B above.

The crude ylid gave an infra-red spectrum which was identical

to Sadtler Spectrum No. 21156 for carbomethoxyphenylmethylenetriphen-

ylphosphorane. M.P. $\approx$ 151°C (Lit. M.P. $\approx$ 155°C) (66). Yield $\approx$ 2.24 g,

or 63% of the theoretical.

A preparation of the ylid was carried out as described in method

A for the ethyl ester of the ylid except that the following materials

and quantities were used: 5.76 g (.022 mole) triphenylphosphine,

5 g (.022 mole) methyl α-bromophenylacetate, and 100 ml. dry benzene.

Yield $\approx$ 2.1 g, or 23% of the theoretical.

<u>Carbethoxyphenylmethylenetri-n-butylphosphorane:</u>

$$(\underline{n}-C_4N_9)_3P=(C_6H_5)CO_2C_2H_5$$
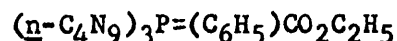
Method A - as described in the general method of Johnson and La Count (7).

In a 250 ml., three-necked flask equipped with a dropping funnel, reflux condenser, a calcium chloride drying tube, spin bar, thermometer, and an inlet for dry nitrogen, was placed 13.67 g (.039 mole) ethyl α-bromophenylacetate in 100 ml. dry benzene. Tri-$\underline{n}$-butylphosphine (8.08 g, .04 mole) was placed in the dropping funnel. After the flask was flushed with dry nitrogen for one hour, the phosphine was added dropwise to the reaction vessel. A nitrogen atmosphere was maintained throughout the process. Since no precipitate had formed after the addition of tri-$\underline{n}$-butylphosphine, the solution was brought to $70^\circ C$ for two hours, and the solution turned dark green. Fractional distillation yielded a liquid fraction, b.p. $110^\circ C$ - $171^\circ C$, that gave adsorptions in the infra-red identical to those noted for ethyl α-bromophenylacetate.

The reaction was repeated using an excess of the phosphine. The reaction system was flushed with nitrogen for two hours prior to addition of the phosphine. No precipitate formed after the addition, and the system was refluxed at $70^\circ C$ for four hours. The process apparently failed as no phosphonium salt precipitated.

Method B - the addition of tri-$\underline{n}$-butylphosphine to ethyl α-iodophenylacetate.

Ethyl α-bromophenylacetate (12.51 g, .055 mole) was shaken with

8.25 g (.055 mole) sodium iodide in 125 ml. dried acetone, and the pale yellow precipitate of sodium bromide was removed by filtration leaving a reddish brown solution of ethyl α-iodophenylacetate. The solution was then placed in a 250 ml., three-necked flask equipped as in previous attempts. Tri-n-butylphosphine, (10.5 g, .052 mole), was added as before, and after the solution was heated at 70°C for six hours, the only change noted was that the solution had turned light green. The reaction mixture was abandoned.

(Carbethoxyphenylmethylene) trimethylphosphonium bromide:

$$(CH_3)_3\overset{+}{P}CH(C_6H_5)CO_2C_2H_5Br^-$$
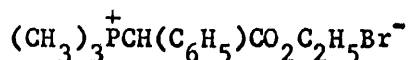
Synthesis of the phosphonium salt was carried out by the general method offered by Trippet and Walker (41).

In a 250 ml., three-necked flask equipped with a reflux conden-ser, a calcium chloride drying tube, a thermometer, a dropping funnel, and a spin bar, was placed 14 ml. of 3 $\underline{M}$ methylmagnesium bromide in ethyl ether (.042 mole). Phosphorous tribromide (11.92 g, .042 mole), in 100 ml. anhydrous ethyl ether was placed in the dropping funnel and was added dropwise to the Grignard reagent over a two hour period. A vigorous reaction with formation of a copious precipitate was noted. After all of the phosphorous tribromide had been added, stirring was continued for an additional thirty minutes.

The mixture was distilled directly into 5 g (.21 mole) ethyl α-bromophenylacetate dissolved in 100 ml. anhydrous ethyl ether immersed in an ice bath. The distillation appeared to be complete after approximately two hours, and the solution was stirred for ten

hours at room temperature and then at 70°C for five hours. A white precipitate formed, was collected by filtration, and washed with two 50 ml. portions of anhydrous ethyl ether. The crystalline material was allowed to dry over calcium chloride and under vacuum.

The dried material gave adsorptions in the infra-red consistent with the desired phosphonium salt, and were noted as follows: 3.42 μ, 3.51 μ, 5.82 μ, 7.78 μ, 8.29 μ, 8.71 μ, 9.85 μ, 10.32 μ, 12.79 μ, 13.48 μ, and 14.20 μ. Nuclear magnetic resonance data were consistent with the structure of the desired salt and were noted as follows: a triplet centered at δ1.15 ppm with spacing of 7 cps; 2 pairs of doublets with the stronger pair centered at δ1.83 ppm and spacing of 14 cps; and the weaker pair centered at δ1.50 ppm with a splitting of 14 cps; a pair of peaks centered at δ4.29 ppm with a splitting of 14 cps; a single sharp peak at δ4.54 ppm; and a group of peaks at δ7.49 ppm. The respective ratios from integration were consistent with proposed salt. Yield ⁻ 1.74 g, or 25% of the theoretical. The salt had a melting point greater than 280°C and demonstrated some decomposition.

Ethyl diethylphosphonophenylacetate: $(C_2H_5O)_2P(O)CH(C_6H_5)CO_2C_2H_5$

The preparation of ethyl diethylphosphonophenylacetate was attempted by the method offered by Arbuzow (61) and Kosolapoff (62).

In a 250 ml., three-necked flask equipped with a reflux condenser, a calcium chloride drying tube, a thermometer, and a spin bar, were placed 5 g (.021 mole) ethyl α-bromophenylacetate, 3.48 g (.021 mole)triethylphosphite, and 100 ml. cyclohexane. The solution was heated at 70°C for 15 hours. Fractional distillation at

1.8 mm. yielded a fraction with a boiling point range of 105°C to 151°C. The liquid collected gave an infra-red spectrum identical to that of ethyl α-bromophenylacetate, the starting material.

Repeating the process at temperatures up to 115°C yielded only starting materials.

Ethyl diethylphosphonoacetate: $(C_2H_5O)_2POCH_2CO_2C_2H_5$

The synthesis of ethyl diethylphosphonoacetate was carried out as described in the previous attempt to prepare a phosphonate except that the following quantities and materials were employed: 5 g (.029 mole) ethylbromoacetate, 4.96 g (.0229 mole) triethylphosphite, and 100 ml. cyclohexane.

Fractional distillation at 4.8 mm. yielded a liquid fraction at 121°C which gave adsorptions identical to Sadtler Standard spectrum No. 15583 for ethyl diethylphosphonoacetate. Yield ‾ 3.72 g, or 55% of the theoretical.

Repeating the experiment at 100°C, using the same quantities as in the previous process, reduced the yield to 2.85 g, or 41% of the theoretical.

Reaction of Carbethoxyphenylmethylenetriphenylphosphorane and Benzaldehyde

The reaction was carried out as in the general method offered by Shriner (71). In a 250 ml. flask equipped with a reflux condenser and spin bar, was placed .498 g (.0047 mole) benzaldehyde, 2 g (.0047 mole) benzene and a few crystals of benzoic acid. The reaction was

carried out on a steam bath for 15 hours. After being cooled, the solution was washed with 50 ml. water, 50 ml. 5 N hydrochloric acid, 50 ml. 10% sodium carbonate, 50 ml. water, and 50 ml. water. The aqueous washes were combined and were washed once with 100 ml. ether. The organic layers were combined and dried over anhydrous magnesium sulfate. The aqueous solution was treated with 2 N sodium hydroxide until basic. A yellow precipitate formed, and was collected, washed with water, and allowed to dry in vacuum over calcium chloride.

The organic solution was freed of magnesium sulfate by filtration, and the solvents were removed by distillation under aspiration. The liquid remaining in the distillation flask had a definite odor of benzaldehyde and except for the presence of an adsorption band at 3 μ due to contaminating water, gave an infra-red spectrum identical to Sadtler Standard spectra No. 4312, for benzaldehyde.

The material precipitated from the aqueous wash gave an adsorption spectrum in the infra-red identical to that for carbethoxyphenylmethylenetriphenylphosphorane listed previously. The ylid weighed 1.79 g which indicates a 98.5% recovery of the starting material.

Reaction of Carbethoxyphenylmethylenetriphenylphosphorane and p-Nitrobenzaldehyde

The procedure for this reaction was identical to that given in the reaction between the ylid and benzaldehyde with the exception that the following quantities and materials were employed: 6.0 g (.0013 mole) carbethoxyphenylmethylenetriphenylphosphorane, 2.11 g (.0014 mole)

p-nitrobenzaldehyde, 150 ml. benzene, and a few crystals of benzoic acid.

After the work-up described in the previous section, it was found that 71% of the starting ylid was recovered. A solid residue collected from the organic solution after the solvents were removed by evaporation gave adsorptions in the infra-red, identical to Sadtler Standard Spectrum No. 3517 for p-nitrobenzaldehyde.

The reaction was repeated with the only change being that the solution was refluxed at approximately 115°C for 24 hours. Only starting materials were isolated with only a 48% recovery of ylid.

Reaction of Carbomethoxyphenylmethylenetriphenylphosphorane and p-Nitrobenzaldehyde

Reaction was carried out as described in the process involving the ethyl ester ylid and benzaldehyde with the following exceptions in quantities and materials: 3 g (.007 mole) carbomethoxyphenyl-methylenetriphenylphosphorane, 1.057 g (.007 mole) p-nitrobenzaldehyde, 150 ml. benzene, and a few crystals of benzoic acid.

The process appeared to fail as .991 g of p-nitrobenzaldehyde and 2.83 g of carbomethoxylphenylmethylenetriphenylphosphorane were recovered.

Reaction of Carbethoxyphenylmethylenetriphenylphosphorane and Acetyl Chloride

The reaction was carried out as described in the general method offered by Bestmann and Hartung (64). In a 250 ml., three-necked flask

equipped with a reflux condenser, calcium chloride drying tube, ther-
mometer, and spin bar, was placed 2 g (.0047 mole) carbethoxyphenyl-
methylenetriphenylphosphorane, 3.93 g (.005 mole) acetyl chloride, and
100 ml. dry benzene. After the reaction mixture refluxed a few
minutes at 70°C, a precipitate formed. Reflux was continued for two
hours. Solvent and excess acetyl chloride were removed by distilla-
tion under aspiration. A solid residue was left which dissolved
readily in water and when the solution was made basic with 2 N sodium
hydroxide, a yellow precipitate formed. After being dried in a vacuum
over calcium chloride, the yellow solid gave adsorptions in the infra-
red identical to that for starting ylid. Recovered material 1.36 g,
or 68% of original quantity.

Reaction of Carbethoxyphenylmethylenetriphenylphosphorane and
Propanoyl Chloride

The reaction was carried out as in the procedure for the reaction
between the ylid and acetyl chloride with the following exceptions in
materials and quantities: 4 g (.0094 mole) carbethoxyphenylmethylene-
triphenylphosphorane, .977 g (.010 mole) propanoyl chloride, and 100 ml.
benzene.

A precipitate formed within a few moments of the addition of the
acyl chloride. The mixture was refluxed at 70°C for 12 hours. The
solvent and excess propanoyl chloride were removed by distillation,
and the solid residue was dissolved in water. The aqueous solution,
when treated with 2 N sodium hydroxide, yielded a yellow precipitate
which gave adsorptions in the infra-red identical to those of the

starting ylid. Yield of recovered ylid   2.89 g or 72% recovery.

The basic solution was distilled and only fractions indicative of

benzene and water were observed.

Reaction of Carbethoxyphenylmethylenetriphenylphosphorane and Propanoyl Chloride in the Presence of Silver Nitrate

In a 500 ml., three-necked flask equipped with a dropping funnel,

reflux condenser, thermometer, calcium chloride drying tube, and spin

bar, were placed 4 g (.0094 mole) carbethoxyphenylmethylenetriphenyl-

phosphorane, 1.7 g (.010 mole) silver nitrate, and 200 ml. dry benzene.

Propanoyl chloride (.997 g, .010 mole) was placed in the dropping

funnel and was added dropwise to the reaction flask when the

stirred mixture of ylid, benzene, and silver nitrate had reached

70°C. A pale yellow precipitate started to form with the addition

of propanoyl chloride. Refluxing conditions were maintained for six

hours.

Benzene and excess propanoyl chloride were removed by aspiration.

The solid residue was partially dissolved in water, and the insoluble

material was removed by filtration. The insoluble solid was discarded

after being washed with 100 ml. benzene and with 100 ml. ether. The

organic washes were combined and the solvents were allowed to evaporate

under a stream of air. Only a small, thin, yellow film remained.

The aqueous solution was treated with 2 $\underline{N}$ sodium hydroxide until

it was basic. A yellow precipitate formed, which was collected,

washed with water, and allowed to dry under a vacuum over calcium

chloride. The solid material gave adsorptions in the infra-red that

were identical to those of the starting ylid.

The remaining basic solution was washed once with 100 ml. benzene and once with 100 ml. ether and then discarded. The organic washes were combined and the solvents were allowed to evaporate. No residue was noted.

Reaction of Carbomethoxyphenylmethylenetriphenylphosphorane and Propanoyl Chloride

The reaction was carried out as described in the procedure for the reaction of carbethoxyphenylmethylenetriphenylphosphorane and acetyl chloride with the exception of the following quantities and materials: 2 g (.0048 mole) carbomethoxyphenylmethylenetriphenyl-phosphorane, .462 g (.005 mole) propanoyl chloride, and 100 ml. dry benzene. As in previous reactions of this type, a precipitate formed at the onset of refluxing. Reflux was maintained at 70°C for 12 hours.

Benzene and any residual propanoyl chloride were removed under aspiration. The solid residue that remained was completely dissolved in water. Upon being made basic with 2 $\underline{N}$ sodium hydroxide the aqueous solution yielded a precipitate of the starting ylid which was identified by infra-red spectrophotometery. Recovered ylid weighed 1.34 g or 67% of the amount originally added.

Reaction of Carbomethoxyphenylmethylenetriphenylphosphorane and Propanoyl Chloride in the Presence of Silver Nitrate

The reaction was carried out as described in the process involving carbethoxyphenylmethylenetriphenylphosphorane, propanoyl chloride, and

silver nitrate except that the following quantities and materials were
employed: 2 g (0048 mole) carbomethoxyphenylmethylenetriphenylphos-
phorane, .85 g (.005 mole) silver nitrate, and 200 ml. dry benzene.
Propanoyl chloride (.462 g, .005 mole), placed in the dropping funnel,
was added dropwise to the reaction flask, upon addition of the acyl
halide, a light colored precipitate formed. The mixture was refluxed
at 70°C for 12 hours.

Benzene and residual low boiling materials were removed under
aspiration. The remaining solid residue was partially dissolved in
water, and the insoluble material was removed by filtration. The
insoluble solid was washed once with 100 ml. benzene and once with
100 ml. ether. The organic layers were combined and allowed to
evaporate. No residue was noted.

The aqueous solution was treated with 2 N sodium hydroxide until
basic, and the starting ylid precipitated as was shown by infra-res
spectroscopy.

Reaction of Ethyl Diethylphosphonoacetate and Benzoyl Chloride

The reaction was carried out by the general method of Wadsworth
and Emmons (58). In a three-necked, 250 ml., round-bottom flask,
equipped with reflux condenser, calcium chloride drying tube, dropping
funnel, spin bar, and thermometer, was placed sodium hydride (50% in
mineral oil, 6.3 g, 1.35 mole) as a slurry in 175 ml. 1,2-dimethoxy-
ethane. Ethyl diethylphosphonoacetate (10 g, .058 mole) was added
dropwise from the dropping funnel. After the addition was completed,
the solution was heated to 80°C and maintained at this temperature

until the evolution of hydrogen ceased. During the refluxing, the
solution turned from white to yellow. After the solution was cooled,
9.84 g (.07 mole) benzoyl chloride was added dropwise from the dropping
funnel. After the addition of benzoyl chloride was complete, the
reaction mixture was refluxed at 83°C for two hours. The solution was
cooled and then was poured into 200 ml. water with a vigorous evolu-
tion of gas ensuing. The aqueous mixture was washed twice with 200 ml.
ether. The aqueous wash was acidified with 12 $\underline{N}$ hydrochloric acid. A
yellow oil formed which slowly crystallized. The solid material gave
an infra-red spectrum identical to Sadtler Spectrum No. 779 for benzoic
acid. Yield ≃ 5.85 g or 68% conversion of benzoyl chloride to benzoic
acid.

The organic wash was set aside, and the solvents were allowed to
evaporate, leaving a tan residue and a clear liquid. The liquid was
decanted and gave adsorptions in the infra-red at 3.42 μ, 3.51 μ,
5.80 μ, 6.82 μ, 7.30 μ, 7.90 μ, 9.05 μ, 9.71 μ, and 14.10 μ, which were
consistent with the proposed structure. The liquid was distilled at
260°C - 270°C with decomposition, characteristic for ethyl phenyl-
propynoate, (72). Yield ≃ 1.83 g, or 16% conversion from benzoyl
chloride.

The solid residue isolated from the organic wash (yield ≃ 1.34 g)
gave an infra-red spectrum that had adsorptions at the following wave
lengths: 3.30 μ, 3.42 μ, 5.60 μ, 5.81 μ, 6.27 μ, 6.92 μ, 8.28 μ,
8.55 μ, 9.67 μ, 9.88 μ, 10.05 μ, 12.87 μ, and 14.29 μ. The solid
decomposed when distillation was attempted at 2.5 mm.

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