PHOSPHONATES IN OLEFIN SYNTHESIS

A thesis presented by

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ABSTRACT.

The 'Wittig Reaction' in general, as well as the utility of phosphinoxy and phosphonate carbanions in olefin synthesis, is reviewed and the following original contributions are presented:-

(1) A method for the synthesis of mono-alkyl fulgenic esters.

(2) A general method for the synthesis of 1:3 dienes using phosphonate carbanions.

(3) Synthesis of diethyl 1-carboethoxy-but-2-enyl phosphonate.

(4) A novel method for the synthesis of cross-conjugated compounds.

(5) Some interesting reactions of unsaturated phosphonates.

ACKNOWLEDGEMENTS.

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INTRODUCTION AND REVIEW.

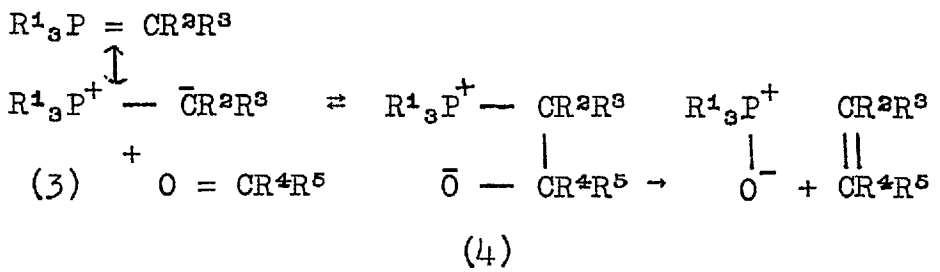
WITTIG REACTION.

The principle of carbonyl olefination by means of organophosphorous compounds was developed towards the end of the second decade of the twentieth century, when H. Staudinger and J. Meyer[1] first published on this topic. Since then the general attention was not focussed on this problem for the long period of thirty years until G. Wittig and his associates,[2-5] in the course of their studies on N-ylids and P-ylenes discovered a method for converting carbonyl compounds into the corresponding olefins by means of alkylidinetriphenylphosphoranes (1), known as 'Wittig reagents', which are prepared from alkyl phosphonium salts (2) by the action of a suitable base.

$$\underset{(2)}{R_3P^+ - CH_2R^1\ X^-} \xrightarrow{base} \underset{(1)}{R_3P = CHR^1}$$

The reaction[4], universally known as the 'Wittig Reaction', involves the addition of an alkylidinephosphorane to a carbonyl compound to give olefin with the elimination of phosphine oxide. The mechanism of the reaction is known. The first step of the reaction is a reversible process.

It involves the formation of a carbon-carbon bond between the electronegative carbon of the phosphorane and the electropositive carbon of the carbonyl group to form a dipolar intermediate 'betaine' (4) which then decomposes to give, generally, a mixture of isomeric olefins through a four-membered cyclic transition state.



(3) (4)

The discovery of 'Wittig Reaction' was a great boon in the chemical world, specially for those who were then engaged in polyene synthesis. Many people at once took the advantage of this important discovery and applied it with great success in different fields[6,7] e.g. carotenoids, polyenes and vitamins. But, though the reaction is of immense synthetic value in Organic Chemistry, it has a number of limitatiohs too.

The inability of some ylids to undergo this reaction can be due to their inherent instability or alternatively their lack of reactivity. The reactivity or nucleophilicity

of alkylidinephosphoranes (3) is determined by the distribution of negative charge in the molecule which in turn depends on the nature of the substituents R^2 and R^3 in the alkylidine portion as well as of the groups R^1 on phosphorous. If R^2 and R^3 are electronwithdrawing substituents, the lone pair of electrons on the α-carbon atom may be delocalised resulting in a decrease in the nucleophilicity of the molecule to such an extent as to make it difficult for it to participate in Wittig Reactions. Thus, some ylids, a list of which is given below, show peculiar behaviour with some carbonyl compounds.

(a) Cyclopentadienylidinetriphenylphosphorane[8,9] does not react with aldehydes and ketones.

(b) Fluorenylidinetriphenylphosphorane[10] reacts with aldehydes but not with ketones.

(c) Benzylmethylenetriphenylphosphorane[11] reacts with benzaldehyde but not with cyclohexanone.

(d) Carbethoxymethylenetriphenylphosphorane[12] reacts much faster with aldehydes than with ketones.

(e) Stable cyclic phosphoranes[13] do not react with carbonyl compounds.

The degree of nucleophilicity of the phosphorane molecules is responsible for the inability of the above compounds to undergo normal Wittig Reaction. This idea

led Bergelson and Shemyakin[14] to put forward an alternative mechanism for Wittig Reaction, suggesting that the nucleophilicity of some phosphoranes may be so much reduced that the reaction with the carbonyl group will proceed by the attack of the negative oxygen of the carbonyl on the positive phosphorous of the phosphorane which will ultimately be decomposed to give the olefin. This hypothesis, of course, did not have any experimental support.

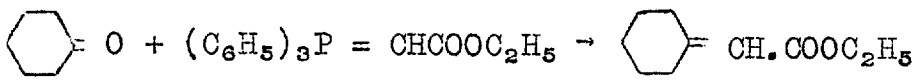
This reaction is not only limited for the preparation of alkyl or aryl substituted ethylene derivatives but is also applicable ~~for~~ to the synthesis of α-β unsaturated carbonyl compounds, carboxyllic esters as well as vinylhalides and vinylethers. Out of all these reactions, the interaction of carbalkoxymethylenetriphenylphosphoranes with carbonyl compounds was very interesting. Aldehydes reacted very readily whereas ketones did slowly or not at all.

Carbethoxymethylenetriphenylphosphorane (5) reacted with different aldehydes, e.g. benzaldehyde[5], nitrobenzaldehyde[15], furfural[16], pyridine aldehyde[12] and 8-xanthine carboxaldehyde[17] to give the corresponding α-β unsaturated esters in good yield; but with ketones, experimental conditions must be very rigorous to bring about the reaction.

For instance, the above phosphorane reacted with benzaldehyde under ordinary condition to give ethyl-cinnamate (6) in good yield

$$C_6H_5CHO + (C_6H_5)_3P = CH.COOC_2H_5 \rightarrow C_6H_5CH = CHCOOC_2H_5$$
(5) (6)

whereas, with cyclohexanone, a low yield of cyclohexylidine-acetate (7) was obtained when the two reactants were heated at 170°C for 10 hours.



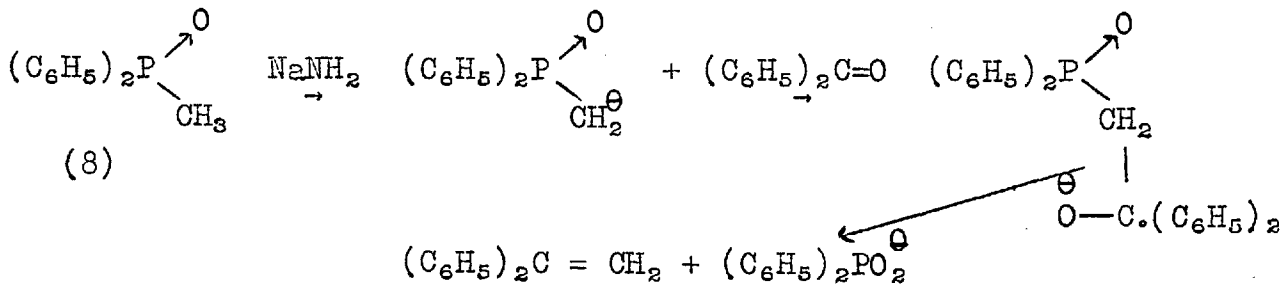
(7)

Recently Wadsworth and Emmons[18] have shown that the compound (7) can be very easily prepared in good yield when the anion of diethylcarbethoxymethylphosphonate was made to react with cyclohexanone at room temperature. The above phosphonate anion proved to be superior to the phosphorane in its reactivity towards other ketones[19,20] also.

PHOSPHINOXY CARBANIONS.

Horner and his co-workers[21,22] were the first to show that phosphine oxide and phosphonate anions react with carbonyl groups to give intermediates which eliminate

phosphinate or phosphate anions to form olefins. The anions were usually generated using bases like sodamide or potassium-t-butoxide. They treated diphenylmethyl phosphine oxide (8) with sodamide and then with benzophenone which ultimately gave them 70% yield of 1,1-diphenylethene (9) and a 95% yield of diphenyl phosphinic acid. They proposed that a phosphinoxy carbanion was first formed which attacked the carbon of the carbonyl group forming an intermediate which was thought to undergo oxyanion transfer to the phosphorous atom, resulting in the formation of an olefin.

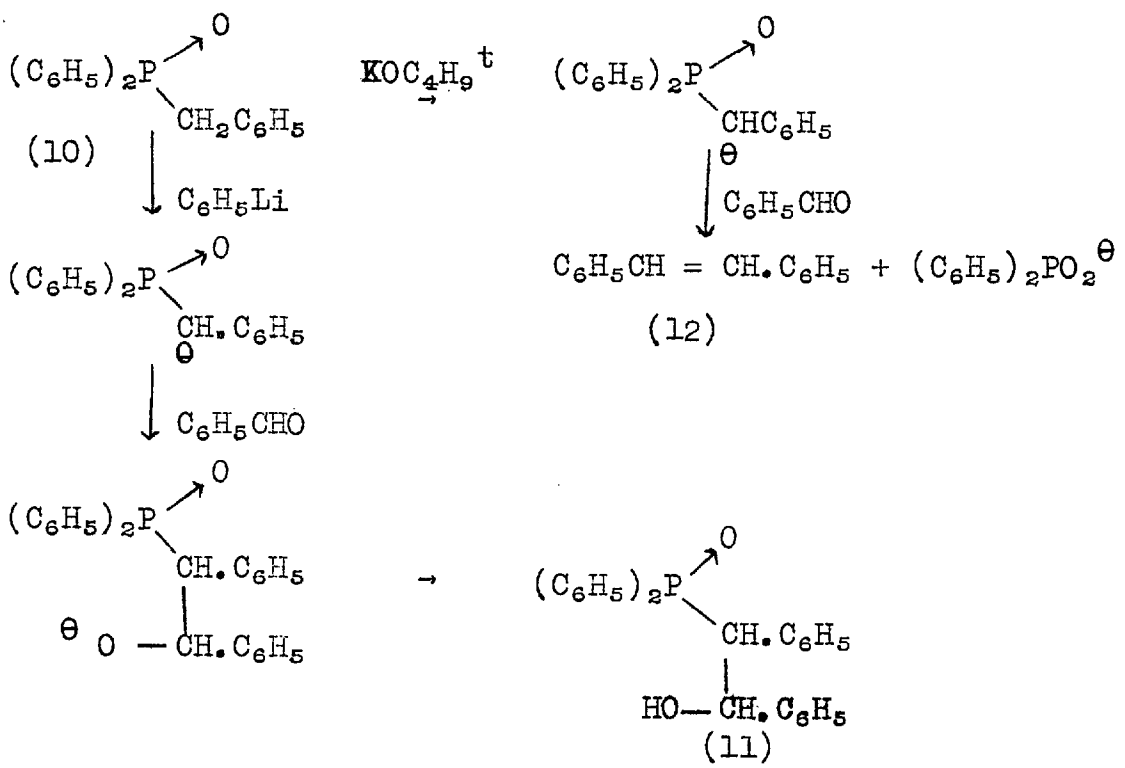


(8)

(9)

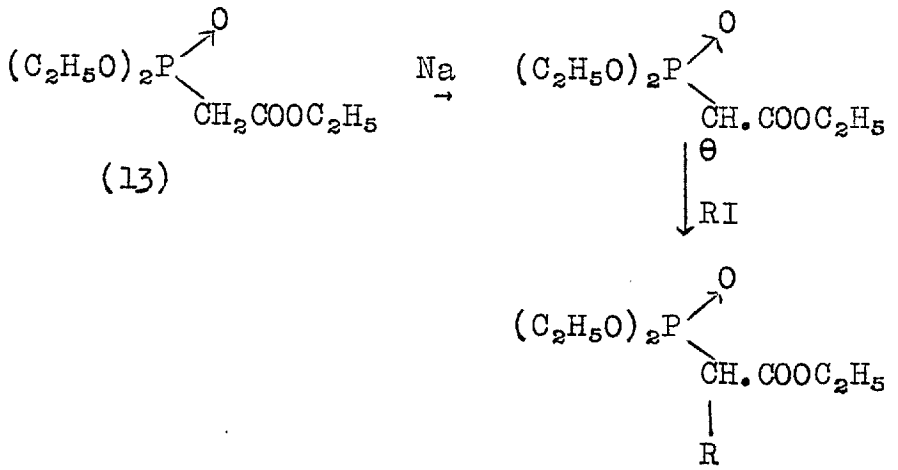
The formation of the carbanion and its subsequent reaction with carbonyl compounds to give olefins, is dependent on the nature of the base used in the reaction. Thus when diphenylethylphosphine oxide was treated with benzophenone in the presence of sodium or sodium alkoxides, no olefin was formed. On the other hand, the same mixture

in the presence of sodamide or potassium-t-butoxide, gave a good yield of the olefin. However, the most interesting observation on this line was made by Horner et al[22] in 1959 and Richards and Banks[23] in 1963. They found that the reaction of diphenylbenzylphosphine oxide (10) with benzaldehyde in the presence of phenyllithium gave no olefin but hydroxyphosphine oxide (11) was obtained in good yield. This finding gave convincing evidence showing that a betaine was an intermediate in the reaction and thus the mechanism of the reaction was explained to a great extent. However, the above reaction mixture in the presence of potassium-t-butoxide gave the olefin (12) in good yield.



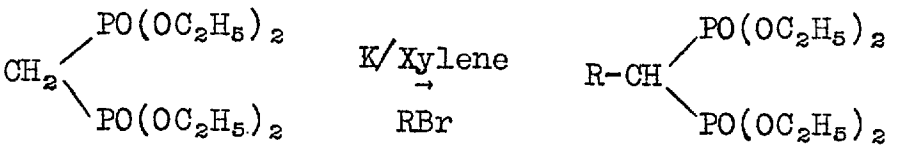
PHOSPHONATE CARBANIONS.

Phosphonate carbanions can be extensively utilised in the synthesis of olefins. In 1927 Arbuzov et al[24,25] showed that carbethoxymethyldiethylphosphonate (13) on treatment with sodium or potassium, formed a carbanion which could be alkylated by a variety of alkyl halides.



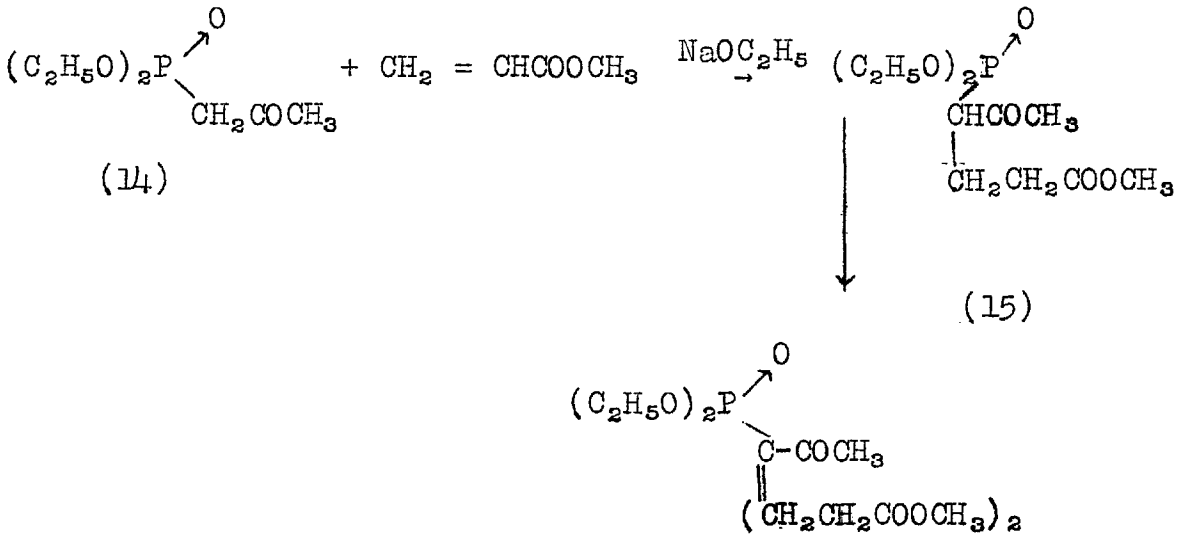
(13)

Kosolapoff[24] could also alkylate a bis-phosphonylcarbanion.



Phosphonate carbanions have also been found to undergo Michael-type additions to conjugated carbonyl systems. Thus the carbanion obtained from acetonyl diethylphosphonate (14) with sodium ethoxide-ethanol, when added to methyl acrylate, gave an adduct (15) which with excess base was

converted to its carbanion which then reacted with a second molecule of methylacrylate to give (16).



(14)

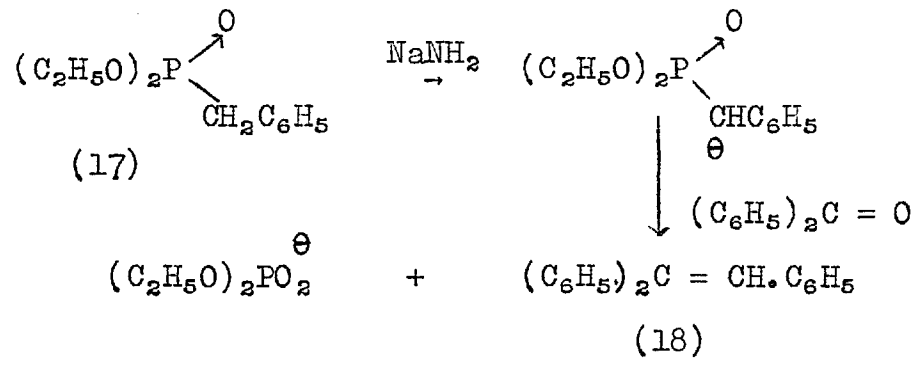
(15)

(16)

On the basis of the above examples, it is apparent that alkyldiethylphosphonates do form carbanions which give normal carbanionic reactions. Thus it is expected that these carbanions will react with carbonyl compounds to form betaines which will undergo oxyanion transfer to give olefins and diethylphosphate, analogous to that of phosphinoxy and phosphonium carbanions.

In 1958, Horner et al[21] were the first to observe this reaction. They treated diethylbenzylphosphonate (17) with benzophenone in the presence of sodamide to give

triphenylethylene (18) in good yield.



(17)

Later on, Wadsworth and Emmons[18] extended the use of phosphonate anions in olefin synthesis by using sodium hydride for their generation either at room temperature or at elevated temperature. High temperature is not generally encouraged as the self-condensation of the anions may take place. In the phosphonate condensation, the nature of the bases and solvents varies from sodium-hydride to sodamide and sodiumethoxide and from tetra-hydrofuran, dimethylformamide to benzene. If high temperature (generally 60°C) is necessary for the generation of anions, because of their thermal instability, they are generated in the presence of the compound with which they are to react. Sodium alkoxides in dimethylformamide, for example, was also used as a base for the more reactive phosphonates[19].

In many cases, the phosphonate anions have a number

of advantages over the Wittig reagents.

(a) They are much more nucleophilic than the corresponding phosphoranes and hence react with a wider variety of carbonyl compounds, usually under milder conditions. Thus, for example, Trippett and Walker[17] have shown that carbethoxymethyldiethylphosphonate reacts with most ketones, whereas carbethoxymethylenetriphenylphosphorane does not. Similarly, Wadsworth and Emmons[18] have reported that the carbanion from phenacyldiethylphosphonate was much more reactive than phenacylidinetriphenylphosphorane. But the convincing proof showing that phosphonate carbanions are more nucleophilic than the phosphorane was demonstrated by Horner and his co-workers[25] in their novel experiment. They treated a mixture of one equivalent of benzyldiethylphosphonate and one equivalent of benzyltriphenylphosphoniumbromide with one equivalent of benzophenone and 3.6 equivalent of potassium-t-butoxide to form 67% yield of triphenylethylene with a recovery of 70% of the phosphonium salt unchanged from the reaction mixture. This clearly proves that a minor amount of the olefin may probably be formed by the reaction of phosphonium carbanion with benzophenone, while the rest must have been formed due to the phosphonate carbanion.

(b) In the case of phosphonate condensations, the by-product is a water soluble phosphate which can be easily separated from the olefins.

(c) Alkylphosphonates are easily prepared by 'Arbuzov Reaction' and are cheaper than alkylphosphonium salts.

After an extensive study on phosphonate carbanions, Wadsworth and Emmons[18] have utilised them not only for the synthesis of olefins, but also for the synthesis of a variety of organic compounds which are summarised below.

1. The phosphonate anions reacted with a wider variety of aldehydes and ketones, usually under milder conditions.

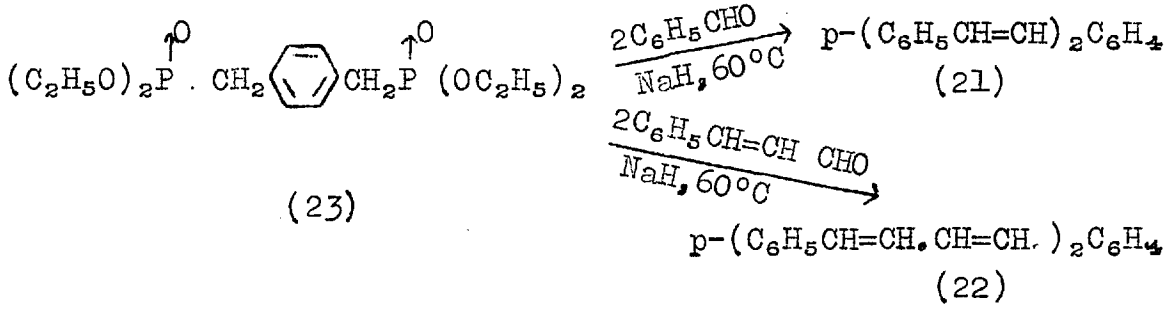
(a) Diethylphenacylphosphonate anion reacted with benzaldehyde to give α-β unsaturated ketone (19)

$$(C_2H_5O)_2P(O)\overset{\ominus}{C}HCOC_6H_5 + C_6H_5CHO \rightarrow C_6H_5CH = CH.COC_6H_5 \qquad (19)$$

(b) The mixture of diethylbenzylphosphonate and benzaldehyde, when heated with sodiumhydride at 60°C, gave stilbene (20) in good yield.

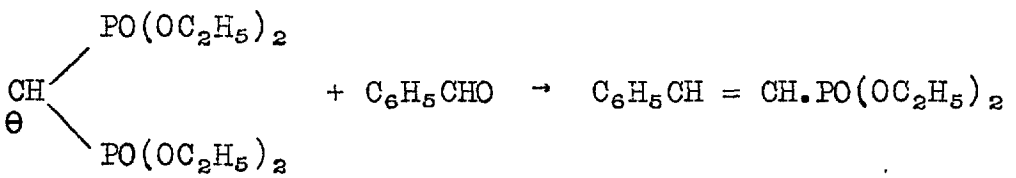
$$(C_2H_5O)_2P(O)CH_2C_6H_5 + C_6H_5CHO \xrightarrow[60°C]{NaH} C_6H_5CH = CH.C_6H_5 \qquad (20)$$

(c) Distyryl benzene (21) and p-bis-4-phenylbutadinyl-benzene (22) were obtained by heating (23) with benzaldehyde and cinamaldehyde respectively in the presence of sodium hydride.



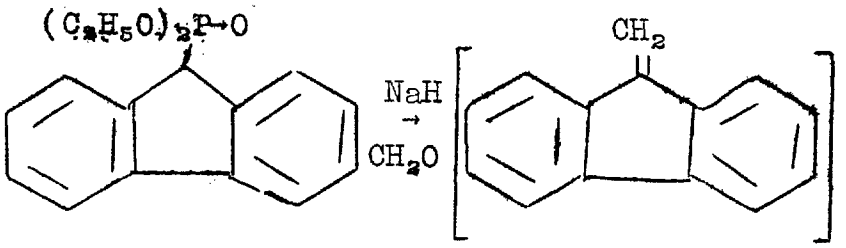
(23)

(d) Tetraethylmethylene bis-phosphonate (24), prepared from methyleneiodide and triethylphosphite, formed the anion with sodiumhydride, which reacted with benzaldehyde to give vinyl phosphonate (25)



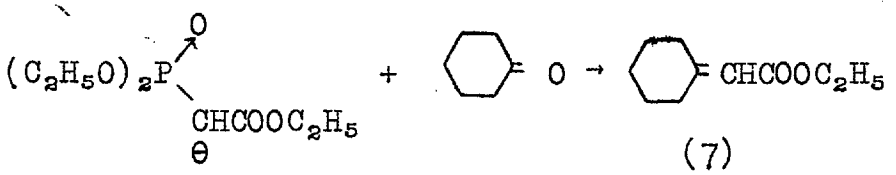
(24) (25)

(e) Diethyl fluorenylphosphonate (26) prepared from 9-bromofluorene and triethylphosphite formed an anion with sodium hydride which reacted with paraformaldehyde exothermically to give 9-methylene fluorene (27)



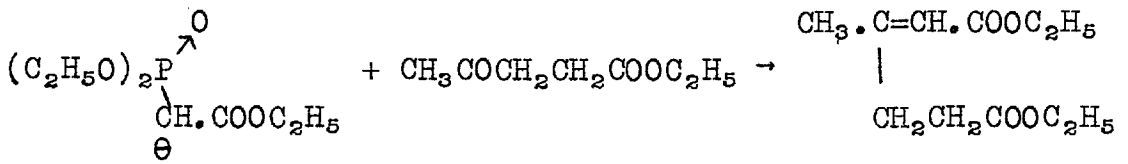
(26) (27)

(f) Diethylcarbethoxymethylphosphonate anion reacted with cyclohexanone to give cyclohexylidine acetate (7)



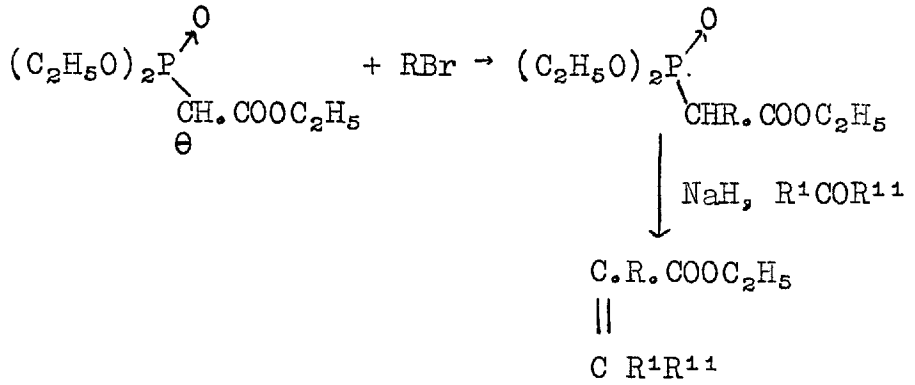
(7)

2. Diethylcarbethoxymethylphosphonate anion reacted with ketoester to form (28)

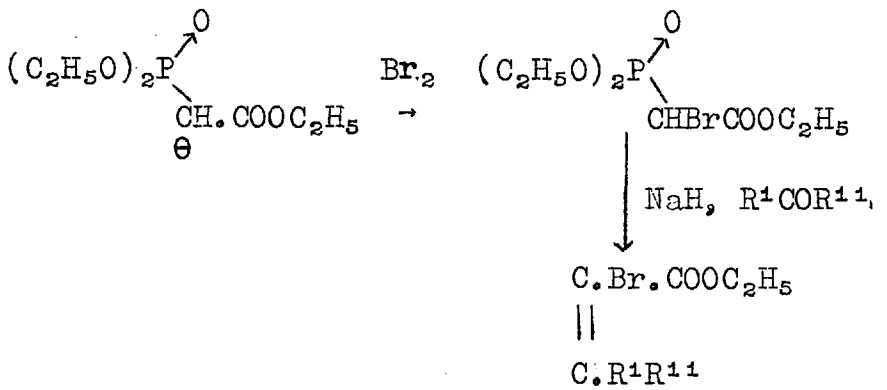


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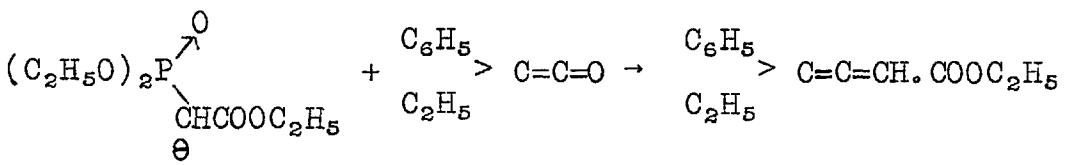
3. Phosphonate anions reacted with alkyl halides to give α-substituted phosphonates,[25] which in turn formed the anion with more sodiumhydride and the new anion could be treated with a carbonyl compound to give the olefin.



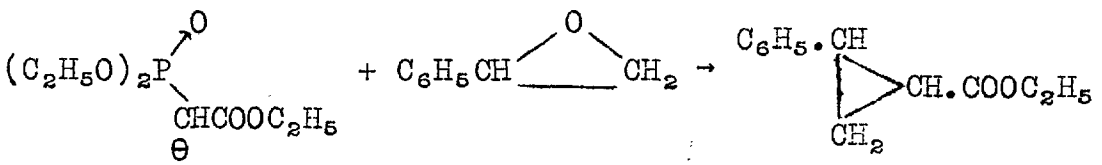
4. The phosphonate anion was halogenated and the anion of the product, on subsequent reaction with aldehydes or ketones, gave vinyl halides.



5. Phosphonate anions reacted with ketenes to give allenes.

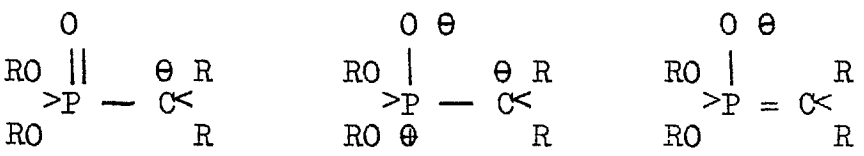


6. Some phosphonate anions reacted with epoxides to give cyclopropanes. This reaction was restricted to those phosphonates which contain on activating group e.g. carbethoxy or cyano group. For example, diethylbenzylphosphonate having no activating group did not react with styrene oxide, though the anion was formed in situ.



It was shown by Denney and Boskin[28] that triarylphosphoranes also reacted with epoxides, giving cyclopropanes in lower yield, even under vigorous conditions of reaction.

Like Wittig reagents, the phosphonate anion is a resonance hybrid having three contributing structures (29), (30) and (31).

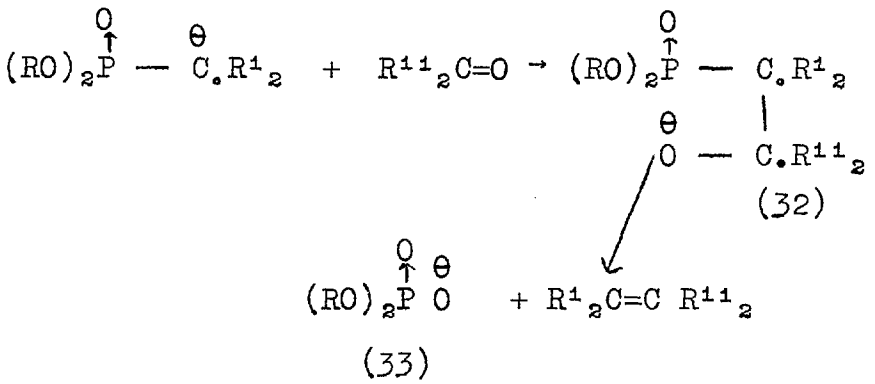


(29) (30) (31)

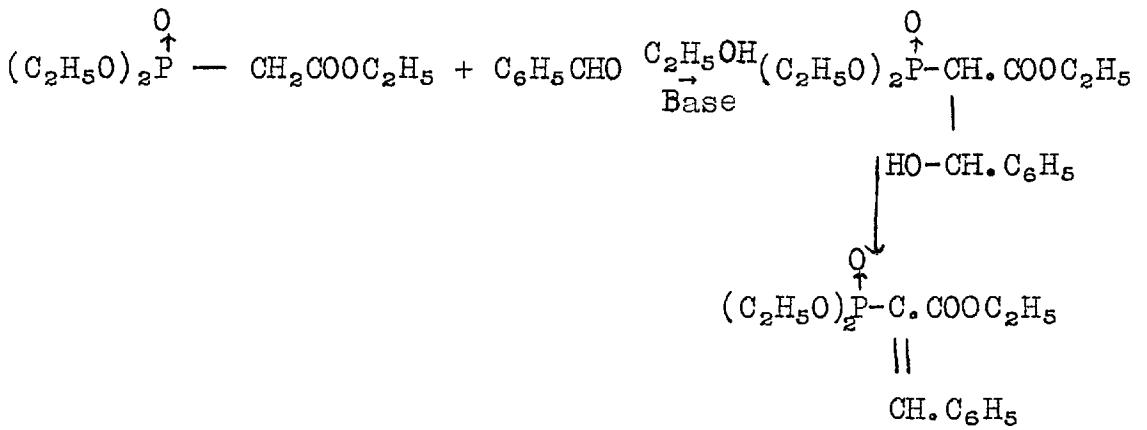
It is known that the P=O bond in phosphates and phosphonates has some single bond character which enables

structures (30) and (31) to contribute.

The mechanism of phosphonate carbanion condensations is very much like that of the Wittig Reaction. The initial step is the attack of the carbanion of the phosphonate to the carbonyl group forming an intermediate (32), which most probably does not undergo a reversible reaction but ultimately decomposes to give olefin via a cis elimination.



The driving force for the above reaction is provided by the formation of a stable phosphate anion (33) which is certainly a more thermodynamically stable species than the phosphonate anion. The above mechanism was confirmed by S. Patai and A. Schwartz[29], as they could obtain the dehydration product of the intermediate from the following reaction, when it was carried out in the presence of a proton donating solvent.



It has been mentioned earlier, that carbonyl olefination by Wittig Reaction is intrinsically a stereo-unselective reaction which generally provides a mixture of isomeric olefins. According to Shemyakin et al[30,31], the reaction can be made stereospecifically cis by the addition of certain halogen salts to the reaction. Although reactants and reaction conditions play an important role on the stereochemistry of the Wittig Reaction[30-34], phosphonate carbanions on the otherhand have been reported to invariably furnish a great preponderance of trans-olefin[22].

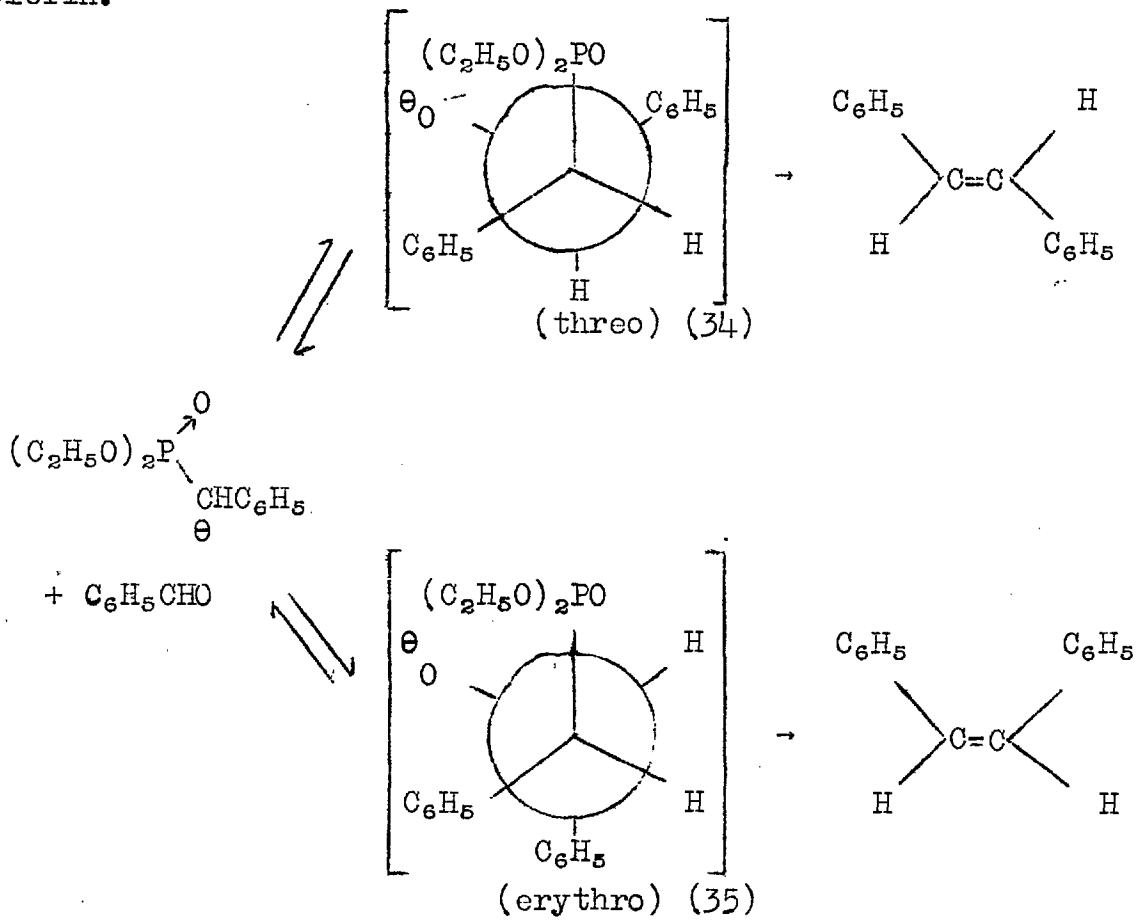
D.H. Wadsworth and his associates[35] attempted to establish reaction systems which would result in the formation of cis-olefins only, but without much success. A number of stilbene analogues, distyrylbenzene, ethyl-cinnamate and cinnamic acid were prepared by using

phosphonate modification of the Wittig Reaction, but in all cases trans-product was isolated though vapour-phase chromatography indicated the presence of trace amounts of cis-isomer.

A new scheme[34] with starting materials containing large groups, was put forward to increase the amount of cis isomer. Even then, only 7-9% of cis-1,2-(1,1'-dinaphthyl)-ethylene was obtained by reacting dimethyl-1-naphthylmethylphosphonate with 1-naphthaldehyde, although the trans-dinaphthylethylene was predominantly present in the reaction mixture. Environmental changes, such as solvent, temperature, Lewis acids or bases, were ineffective in changing the tendency of the aldehydephosphonate condensations to produce trans olefins.

The abnormal stereochemistry of phosphonate condensation with respect to Wittig Reaction, may be hypothetically explained by assuming that the rate of threo-betaine (34) formation should have to be faster than that of erythro-betaine (35) as in that case only the trans-isomer will predominate. In other words, this means that if betaine formation is irreversible and olefin isomerisation is absent, the threo-betaine must be formed the fastest. On the otherhand, if betaine formation is reversible, the results would mean that the combined rates of threo-betaine formation and decomposition are greater than the combined

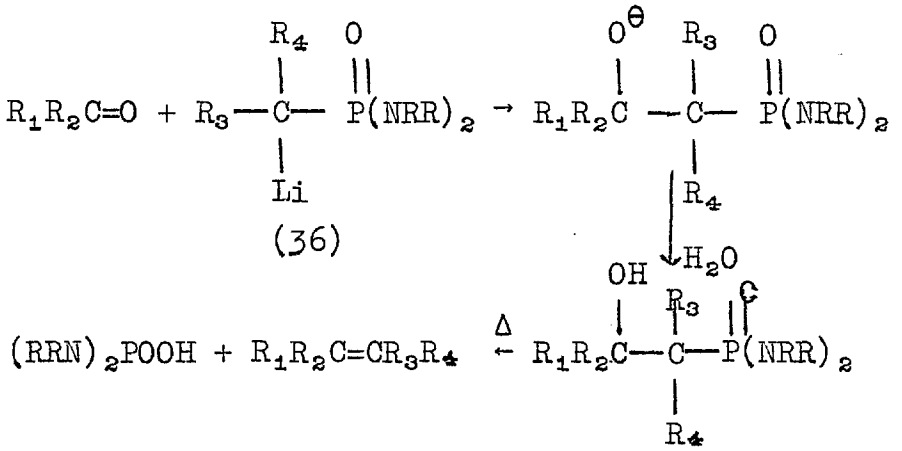
rates of threo-betaine dissociation, erythro-betaine formation and erythro-betaine decomposition to cis-olefin.



However, the stereochemistry of the phosphonate condensation is not yet clear and it requires experimental support.

Recently E.J. Corey and G.T. Kwiatkowski[36] have put forward a new and two-step synthesis of olefins from carbonyl compounds and α-lithiophosphonic acid bis-amide (36). Phosphonylamides are generally prepared from

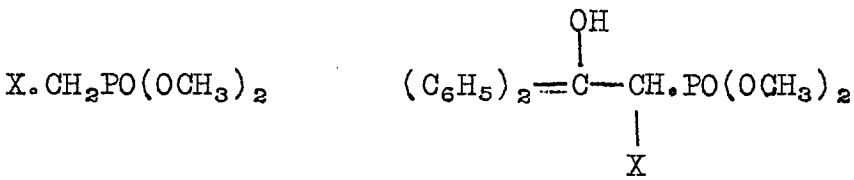
phosphonyldihalides[39] in the procedure described by A.M. Kinner and E.A. Perren[39]. The reaction of (36) with a carbonyl compound gave an intermediate which was pyrolysed to give the olefin.



The main advantage of phosphonylamides as reagents for olefin synthesis over other reagents, is that it can be applied to the formation of mono, di, tri and tetra-substituted ethylenic systems.

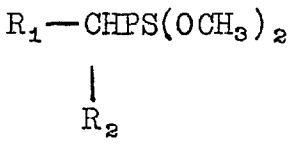
Later on, the same authors[39] extended the utility of carbanions derived from thiophosphonate ester in the synthesis of olefins. It has already been discussed earlier that anions derived from phosphonate esters (37) which possess a charge stabilizing electron withdrawing substituents, e.g. X = cyano, carbonyl or phenyl, can be used in the synthesis of olefins. Anions of the

type (37) where X=H or alkyl, have not been previously generated and therefore their use in olefin synthesis is not known. Corey and Kwiatkowski[37] have recently shown that such an anion can conveniently be formed as lithioderivatives by the action of n-butyllithium in tetrahydrofuran at -78°C for 5 minutes. The above finding was demonstrated in the reaction with benzophenone to form the adduct (38) in high yield

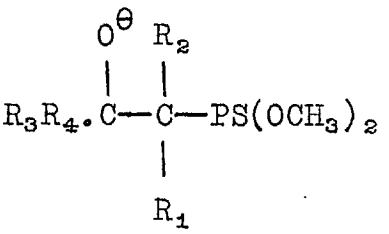


(37) (38)

These adducts (38) do not undergo decomposition to form olefins. In contrast, α-thioderivative of alkylphosphonothiates (39) prepared with n-butyl lithium, reacts rapidly with aldehydes and ketones to form adducts (40) which can be used as reagents for the synthesis of 1,1-disubstituted, trisubstituted and tetrasubstituted olefins. During the above reaction, low temperature, e.g. -78°C to 0°C, is generally maintained for the formation of the adduct. The adduct on standing at room temperature is decomposed to give the olefin.



(39)



(40)

The same authors[37] have also been able to alkylate 0,0'dilkyl α-lithioalkylphosphonothiates with alkyl halides.

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Attempted Synthesis of 2-(1-butenyl)-3-methylmaleic anhydride (1).

During the investigation of the biosynthesis of glauconic (2), glaucanic (3) and byssochlamic (4) acids,[1-9] it was shown[10] that 2-(1-butenyl)-3-methyl-maleic anhydride (1), when added to a growing culture of Penicillium purpurogenum,[11,12] was incorporated in 55% yield into glauconic and glaucanic acids. This led to the postulate that the above C_9 unit (1) might have undergone a biochemical dimerisation. (Fig. I.) Later on, attention was focussed on a study of the chemically induced dimerisation of the C_9-anhydride unit. It was with this idea that attempts were made to synthesise the above compound (1). Although the compound (1) had been synthesised by previous workers,[13,14] a more convenient and easier scheme was planned for its synthesis as shown in Fig. II.

The starting materials for the synthesis of the above compound were ethylpyruvate (5) and diethyl carboethoxyethylphosphonate (6): The condensation of ethylpyruvate with the anion of diethyl carboethoxy-ethylphosphonate in 1,2-dimethoxyethane by the method of Wadsworth and Emmons[15] gave a mixture of two products

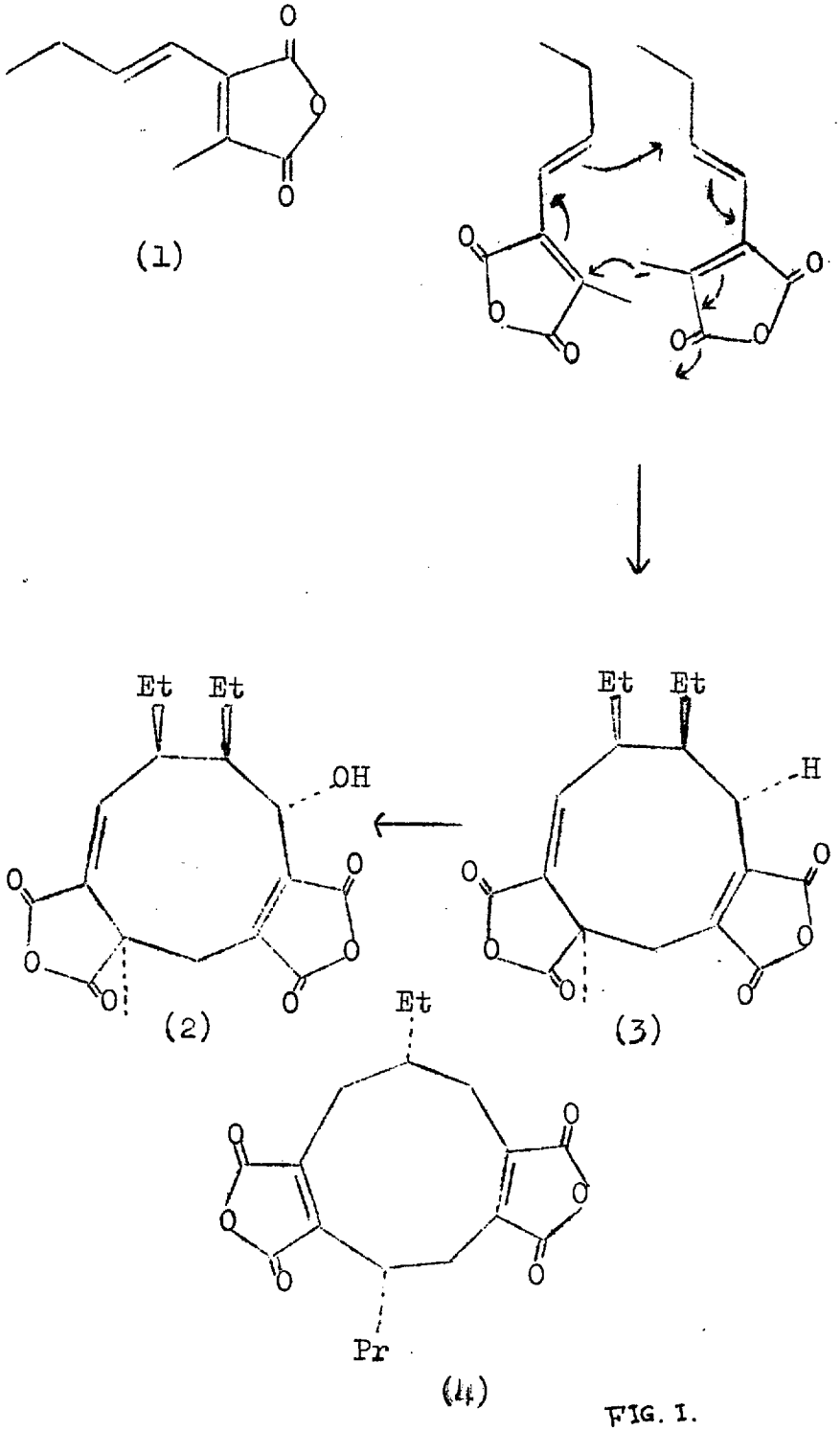


FIG. 1.

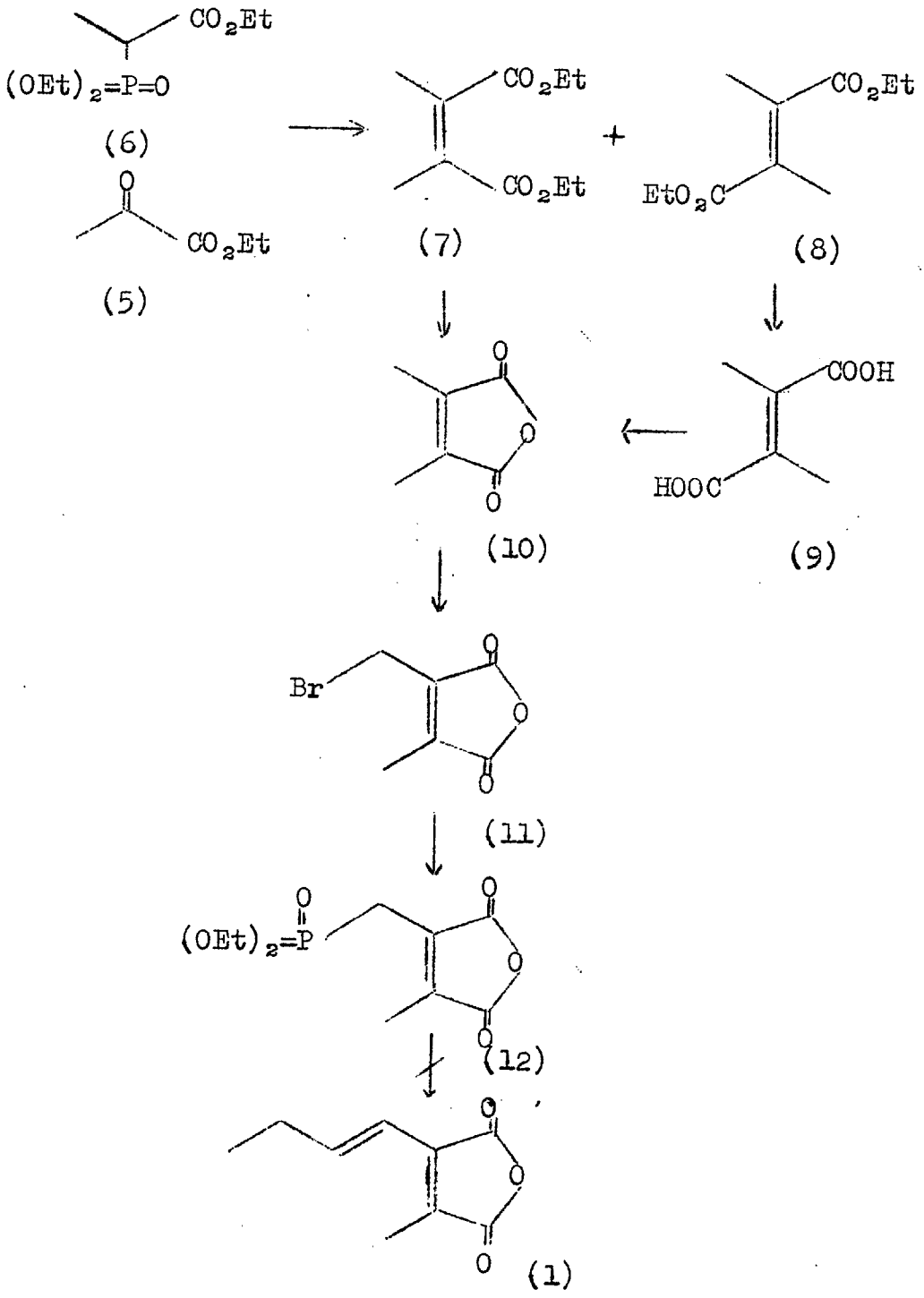

CO2Et
(OEt)2=P=O
(6)
CO2Et
(5)
CO2Et
CO2Et
(7)
+
CO2Et
EtO2C
(8)
COOH
HOOC
(9)
(10)
Br
(11)
(OEt)2=P
(12)
(1)

Fig. II.

which were separated by column-chromatography in silica-gel. The major product was proved to be diethylpyrocinchonate(7), ν_{max} (film) 1720, 1645cm^{-1}. The n.m.r. spectrum showed a quartet at τ5.86 (4 carboethoxymethylene protons) and a singlet at τ8.10 (6 protons, 2 methyl groups on double bond). The minor product was found to be dimethylfumarate (8), ν_{max} 1720, 1640cm^{-1}, the n.m.r. spectrum showing a quartet at τ5.86 (4 carboethoxymethylene protons) and a singlet at τ8.00 (6 protons, 2 methyl groups on double bond). The structure (8) was further confirmed by converting it into the corresponding acid (9) by saponifying with sodiumhydroxide. The acid thus obtained was a solid, m.p. 231°d, which was found to be identical with an authentic sample. The compound (9) on refluxing with acetic anhydride was isomerised to dimethylmaleic acid which finally gave dimethylmaleic anhydride (10).

The compound (7), on saponification, was directly converted into (10) which was a solid m.p. 95°C. The infra-red and n.m.r. spectra were in agreement with the formulation of the compound; ν_{max} (film) 1840, 1780cm^{-1} and the n.m.r. spectrum showed a singlet at τ7.90 (methyl on double bond). The dimethylmaleic

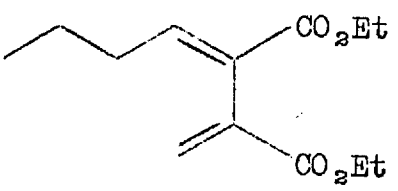
anhydride was then brominated by refluxing with N-bromosuccinimide in carbontetrachloride to form the bromo-anhydride (11) with signals at τ5.83 (singlet, 2 methylene protons on carbon bearing bromine atom) and τ7.80 (singlet, 3 protons, methyl on double bond) in the n.m.r. spectrum. The bromoanhydride (11) was then heated with triethylphosphite at 140°C for two hours in an atmosphere of nitrogen, when the phosphonate anhydride (12) was formed (ν_{max} (film) 1760, 1645, 1250, 1050cm^{-1}). The n.m.r. spectrum showed a quartet at τ5.94 (4 ethoxymethylene protons), a doublet at τ6.95 (2 methylene protons coupled with phosphorous, J = 22 CPS) and a doublet at τ7.88 (3 protons, methyl on double bond, with a long range coupling with phosphorous J = 6 CPS).

The condensation of the anion form (12) with propionaldehyde in an attempt to form the compound (1) gave a mixture of compounds and the scheme was abandoned at this stage.

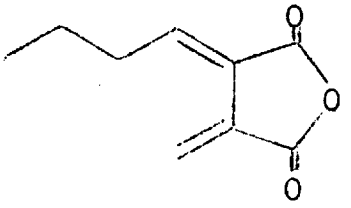
Synthesis of propyl fulgenic ester.

Following the failure of the above scheme, attention was diverted to the preparation of fulgenic ester (13), Fig. III, which could be converted into the corresponding anhydride (14), the postulated precursor of byssochlamic acid (4). Again the fulgenic anhydride (14) might be isomerised to 2-(1-butenyl)-3-methylmaleic anhydride (1) which is a precursor[13] of glauconic and glaucanic acids.

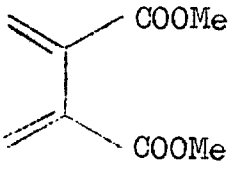
Even today, very little is known about the chemistry of fulgenic acids, esters, and anhydrides. The parent compound dimethylfulgenate (15) was prepared[16] by the pyrolysis of cyclobutene diester (16), though no mention of the corresponding acid or anhydride was made. Many aryl substituted fulgenic esters, acids and anhydrides have been prepared and their properties have been investigated[17,18] but the only monoalkyl fulgenate ester known to us was the compound (17) which was reported by Sharkey and his co-workers[19]. Thus we were interested in a general synthesis of fulgenic esters, and it was thought that unsaturated phosphonate ester, diethylcarboethoxypent-1-ene phosphonate (18) might be a suitable precursor for the synthesis of (I.). Attempts were therefore first directed towards the synthesis of (18).



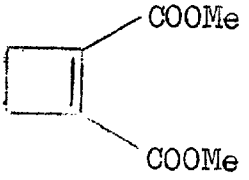
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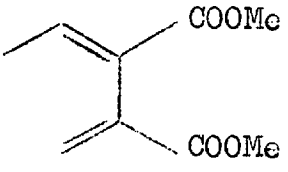
(14)



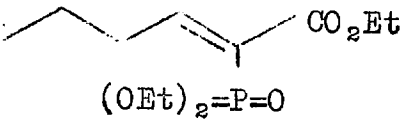
(15)



(16)



(17)



(18

Fig. III.

Attempted Synthesis of diethyl 1-carboethoxypent-1-ene phosphonate (18).

The starting material for the synthesis of the above compound was n-hexanoic acid (19), Fig. IV, which was brominated to give 2-bromo-hexanoic acid (20) and then esterified in the usual way to form ethyl 2-bromo-hexanoate (21). The compound (21), on heating with triethylphosphite at 140°C for three hours gave diethyl 1-carboethoxypentylphosphonate (22), ν_{max} (film) 1730, 1259, 1059, 1036, 976cm^{-1}. Attempts to dehydrogenate the compound (22) to give (18) by refluxing with (a) selenium dioxide/acetic acid, and (b) 2:3 dichloro 5:6 dicyano-p-benzoquinone failed.

The anion of the compound (22) was then made to react with benzoylperoxide to give (23), having the infra-red spectrum ν_{max} (film) 1725, 1595, 1275, 1036, 976cm^{-1}. The n.m.r. spectrum showed signals at τ2.00 and 2.50 (complex, 5 phenyl protons), τ5.80 (multiplet, 6 methylene protons of carboethoxy and ethoxy groups). An attempt to pyrolyse the compound (23) to give (18) proved unsuccessful.

Another attempt to prepare the compound (18) from (22) was made by converting it into the corresponding

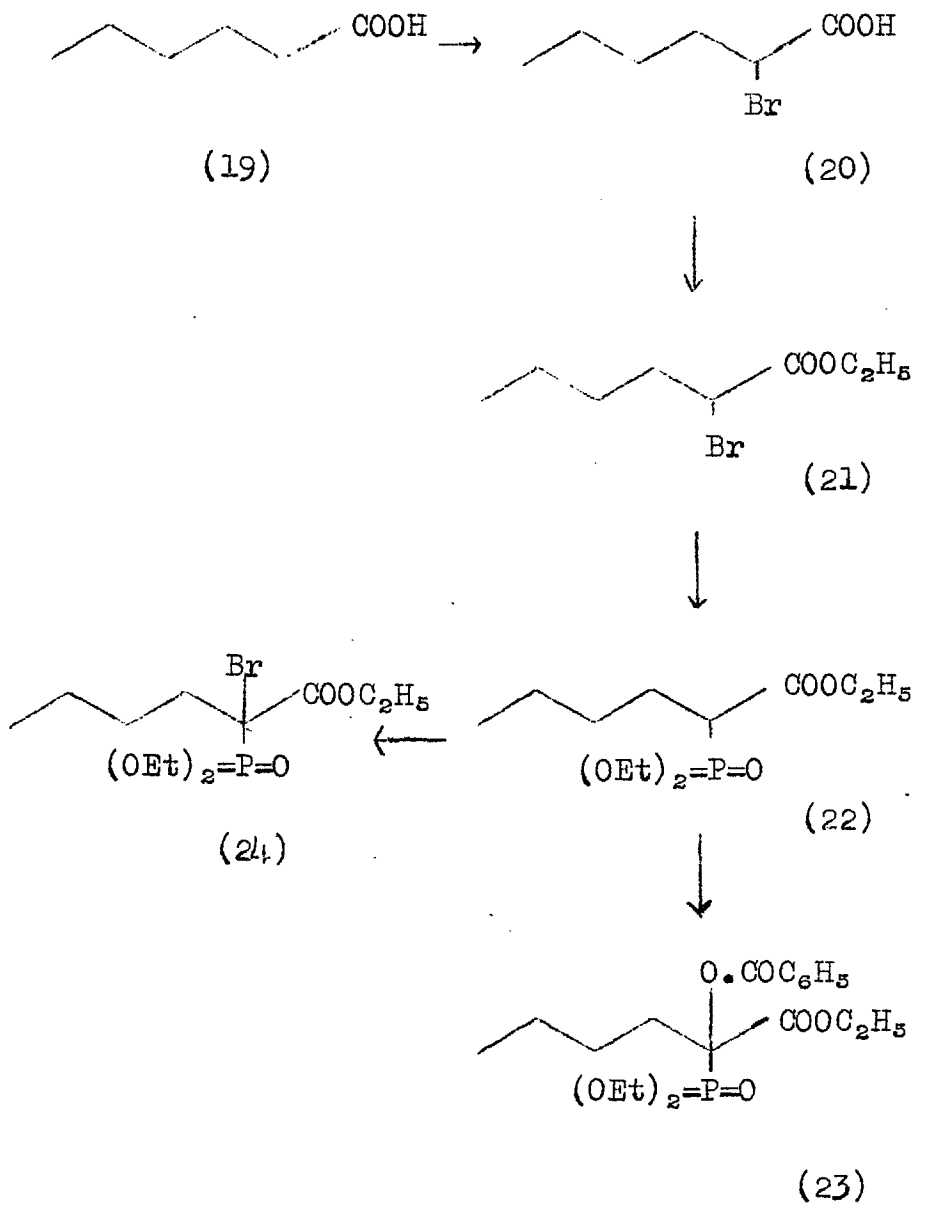

COOH
COOH
Br
(19)
(20)
$COOC_2H_5$
Br
(21)
$COOC_2H_5$
$(OEt)_2=P=O$
(22)
Br
$COOC_2H_5$
$(OEt)_2=P=O$
(24)
$O.COC_6H_5$
$COOC_2H_5$
$(OEt)_2=P=O$
(23)

Fig. IV.

bromo-derivative (24), followed by unsuccessful dehydrobromination with (a) pot-t-butoxide/butanol, and (b) lithium chloride/dimethylformamide.

A new approach to prepare the compound (18) was made from diethyl 1-carboethoxy-1-hydroxypentyl-phosphonate (28), Fig. V. The starting material for the preparation of (28) was 2-hydroxyhexanoic acid (25) which was obtained from 2-bromo-hexanoic acid (20) by refluxing with sodiumcarbonate. The compound (25), on esterification in the usual way gave ethyl 2-hydroxy-hexanoate (26) which after oxidation with Jones' reagent[20] formed ethyl 2-keto-hexanoate (27), ν_{max} (film) 1740 shoulder, 1723cm^{-1}. The n.m.r. spectrum of this ester confirmed its structure as it showed a quartet at τ5.78 (2 carboethoxymethylene protons) and a triplet at τ7.29 (2 methylene protons α to keto group). The condensation of ethyl 2-keto-hexanoate with diethylphosphite in the presence of 0·1 mole sodium-ethoxide/ethanol gave the compound (28), ν_{max} (film) 3475, 1740 shoulder, 1260, 1059, 1036, 980cm^{-1}. The compound (28), unfortunately, on treatment with the following reagents did not dehydrate to give (18).

(i) Phosphorous oxychloride/pyridine.

(ii) Thionyl chloride/pyridine.

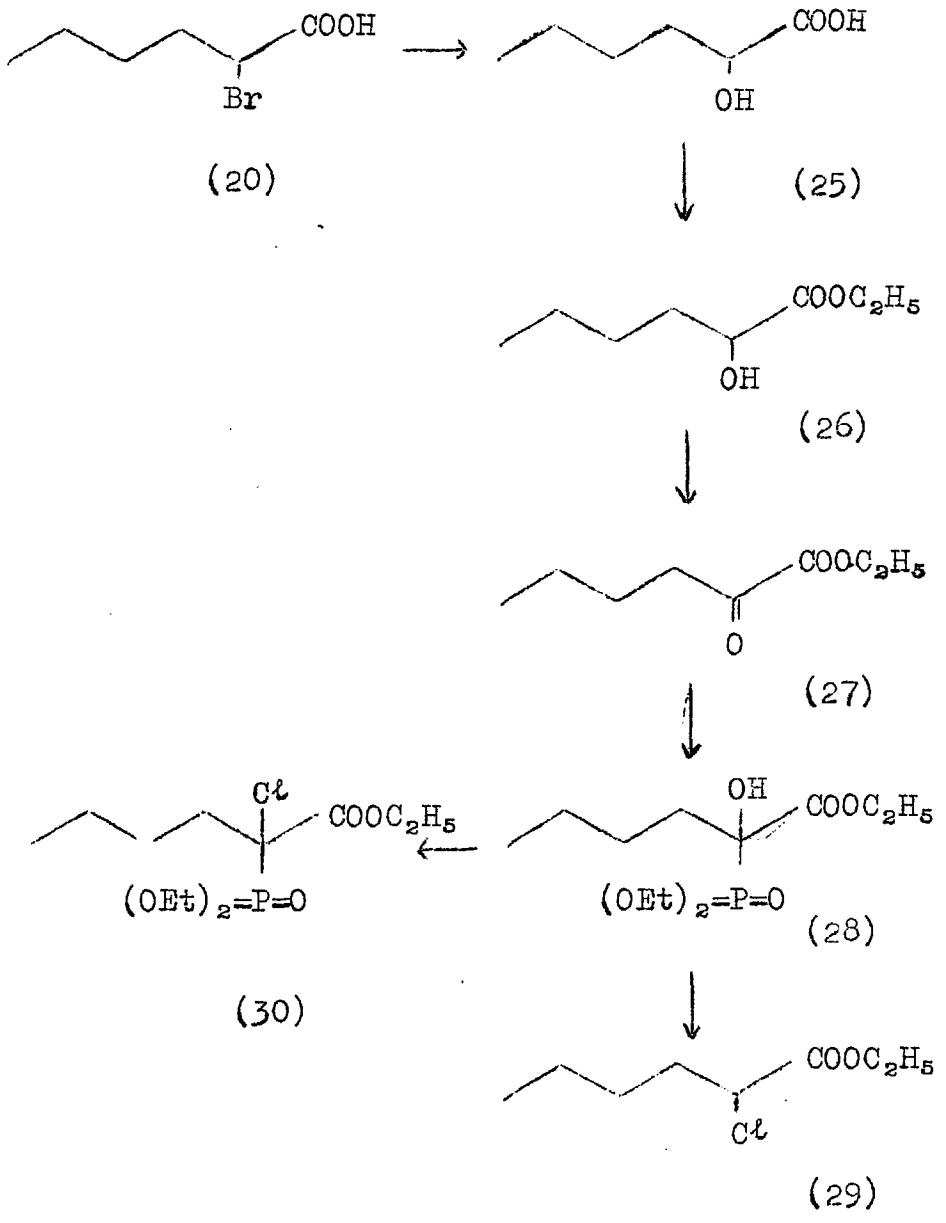

COOH
Br
(20)
COOH
OH
(25)
$COOC_2H_5$
OH
(26)
$COOC_2H_5$
O
(27)
OH
$COOC_2H_5$
$(OEt)_2=P=O$
(28)
Cl
$COOC_2H_5$
$(OEt)_2=P=O$
(30)
$COOC_2H_5$
Cl
(29)

Fig. V.

(iii) Phosphorous pentoxide/benzene.

(iv) Distillation with boric acid.

(v) Distillation from p-toluene sulphonic acid.

(vi) Distillation with polyphosphoric acid.

(vii) Distillation with iodine crystals.

(viii) Formic acid at 100°C.

(ix) Concentrated sulphuric acid.

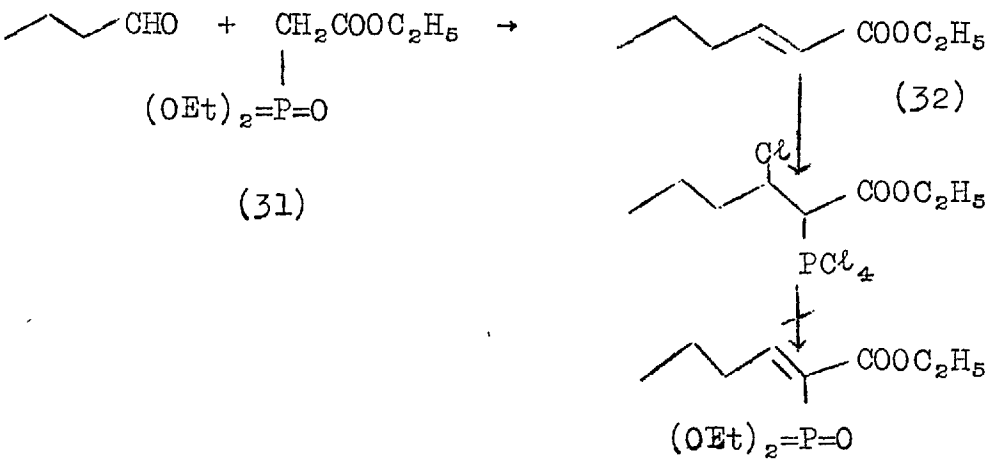
(x) Borontrifluoride in ether.

However, when the compound (28) was refluxed with phosphorous oxychloride/pyridine, ethyl 2-chloro-hexanoate (29) was formed. The n.m.r. spectrum of this compound showed a quartet at τ5.78 (2 carboethoxy methylene protons and one proton attached to carbon bearing chlorine atom) and a triplet at τ8.10 (2 methylene protons α to chlorine atom).

The hydroxy-phosphonate ester (28) when heated with phosphorous pentachloride was converted to the corresponding chloro-phosphonate ester (30) which did not eliminate hydrogenchloride to give (18), even after refluxing with (a) zinc/acetic acid, and (b) lithium carbonate/dimethylformamide.

Another attempted preparation of diethyl 1-carbo-ethoxypent-1-enephosphonate (18) was made through

the scheme given below:

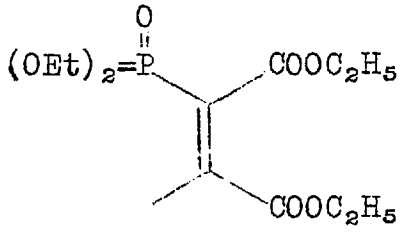


The anion from diethyl carboethoxymethylphosphonate (31) was condensed with butyraldehyde in 1,2 dimethoxyethane by the method of Wadsworth and Emmons, to form ethyl hex-2-en-oate (32) in good yield, ν_{max} (film) 1715, 1645, 1265, 1180, 985cm^{-1}. The n.m.r. spectrum of this compound was very informative as it showed a pair of triplets at τ3.02, and 3.28 (one vinyl proton), a doublet at τ4.7 (one vinyl proton, J = 16 CPS, showing the trans double bond), a quartet at τ5.9 (2 carboethoxymethylene protons) and a multiplet at τ 7.88 (2 methylene protons adjacent to double bond). The compound (32) was then heated with phosphorous pentachloride and the adduct[21]

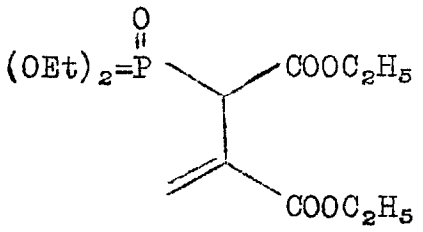
thus obtained was refluxed with ethylalcohol but the desired compound (18) was not obtained.

At this point, the problem of the synthesis of fulgenic ester (13) was attacked from a different angle. This time compound (34), Fig. VI, was selected as a suitable precursor. It was hoped that the compound (34) could be easily obtained from the compound (35) which was itself prepared by reacting diethyloxalopropionate with p-toluenesulphonylchloride in pyridine at room temperature. Analytical results as well as infra-red and n.m.r. data were in full agreement with structure (35). It had ν_{max} (film) 1720, 1645, 1590, 1290, 1190cm^{-1} and showed a pair of doublets at τ2.15 and 2.73 (2+2 = 4 aromatic protons), a multiplet at τ5.84 (4 carboethoxymethylene protons), a singlet at τ7.5 (3 protons, methyl attached to benzene ring) and a singlet at τ8.15 (3 protons, methyl on double bond). The compound (35) was then treated with sodium salt of diethylphosphite to form (34) but the reaction failed.

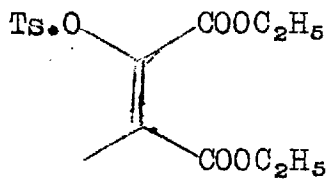
In another approach, a bromo-derivative (36) of the diethyloxalopropionate was made by refluxing it with bromine on a steam-bath, the product showing ν_{max} (film) 1745, 1725, 1240, 1030cm^{-1}. The n.m.r. spectrum of (36) revealed a pair of quartets at τ5.73 and 5.64



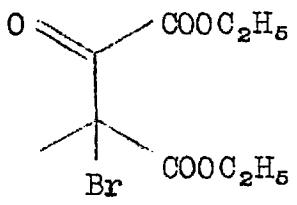
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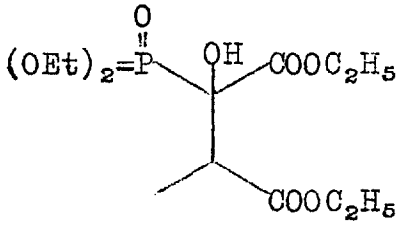
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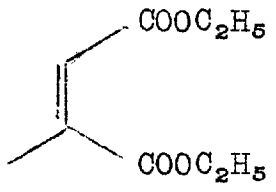
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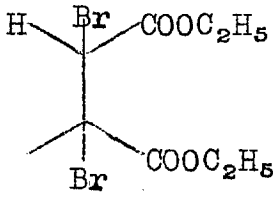
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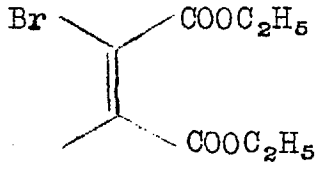
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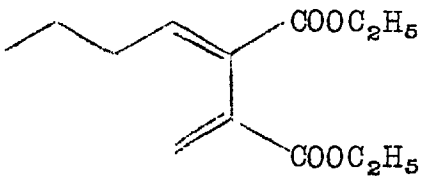
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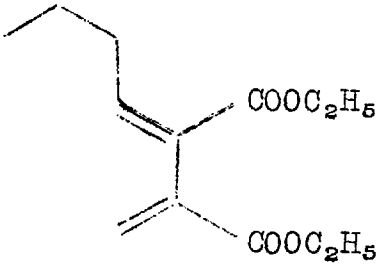
(39)



(40)



(13.c)



(13.t)

Fig. VI.

(4 carboethoxymethylene protons) and a singlet at τ7.95 (3 protons, methyl attached to carbon bearing bromine atom). Attempted condensation of (36) with diethylphosphite in the presence of sodiumethoxide in ethanol to give (34) failed.

At last a successful synthesis of the compound (34) was achieved from 1,4-diethyl-2-hydroxy-2-diethylphosphono-3 methyl-succinate (37). The compound (37) was prepared by the condensation of diethyloxalopropionate with diethylphosphite in the presence of sodiumethoxide in ethanol. Its infra-red spectrum, ν_{max} (film) 3460, 1740, 1640, 1270, 1040cm^{-1}, showed the presence of a hydroxyl group and the n.m.r. spectrum was consistent with this structure and showed it was probably a stereoisomeric mixture. Elemental analysis was consistent with $C_{13}H_{25}PO_8$, the molecular formula of (37). The compound (37), on treatment with phosphorous oxychloride in pyridine gave the expected vinyl phosphonate (34). In addition, however, there was obtained 50% of an unidentified compound, ν_{max} (film) 1725, 1625, 1265, 1040cm^{-1}. The n.m.r. spectrum showed a multiplet at τ3.30 and a signal at τ7.00, apart from its usual features. On the otherhand the vinyl phosphonate (34) had ν_{max} (film)

1725, 1625, 1265, 1040cm^{-1} and the n.m.r. spectrum exhibited a doublet at τ7.77 (3 protons, methyl on double bond). The splitting of the methyl signal was undoubtedly due to allylic coupling with the phosphorous atom (J = 1.6 CPS).

However, a mixture of the vinyl phosphonate (34) and the allyl phosphonate (33) was obtained more satisfactorily by the reaction of diethylbromocitraconate with triethylphosphite. Diethylbromocitraconate was prepared from ethylcitraconate (38), as the starting compound. This ester was brominated with bromine to give a dibromo-compound (39), ν_{max} (film) 1740cm^{-1}. The n.m.r. spectrum showed a singlet at τ4.95 (1 proton on carbon bearing bromine atom and a carboethoxy group) and a singlet at τ7.82 (3 methyl group protons) apart from usual features. The dibromoester (39) was then dehydrobrominated by refluxing it in pyridine to give diethyl 2-bromocitraconate (40), ν_{max} (film) 1725, 1625cm^{-1}, showing a singlet at τ7.90 (3 protons; methyl on double bond) in the n.m.r. spectrum.

Diethyl 2-bromocitraconate (40) was then heated with triethylphosphite at 150°C in an atmosphere of nitrogen to yield a mixture of vinyl phosphonate (34) and allyl phosphonate (33). The vinyl phosphonate (34)

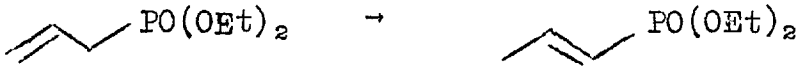
had ν_{max} (film) 1725, 1625, 1265, 1040cm^{-1}, and the n.m.r. spectrum showed a doublet at τ7.77 (3 protons; methyl on double bond). The splitting of the methyl signal was undoubtedly due to allylic coupling with the phosphorous atom (J = 1.6 CPS). The allyl phosphonate (33) had an infra-red spectrum with ν_{max} (film) 1725, 1625, 1265, 1040cm^{-1}, and its n.m.r. spectrum had a pair of doublets (J = 4.5 CPS) at τ3.67 and τ3.53 (2 terminal methylene protons). Each signal of the doublets was of equal area and was broadened by allylic coupling with a proton.

The final stage of the synthesis of the fulgenate ester (13), was carried out by R.K. Huff and involved the condensation of the mixture of allyl (33) and vinyl (34) phosphonate with butyraldehyde. This condensation was carried out in the presence of sodiumhydride and tetrahydrofuran when a mixture of two isomeric fulgenate esters (13c) and (13t) was obtained. The ratio of (13c) to (13t) varied between 70:30 and 50:50 during several condensations carried out. The infra-red spectrum of the esters had ν_{max} (film) 1723, 1643, 1625cm^{-1}. The n.m.r. spectrum of the cis-ester (13c) showed a triplet at τ3.15 (one vinyl proton), a pair of singlets at τ3.64 and 4.54 (2 terminal methylene protons) and a double triplet at τ7.84 (2 methylene

protons adjacent to double bond). The n.m.r. spectrum of the trans-ester (13t) showed a triplet τ3.88 (one vinyl proton), a pair of singlets at τ3.94 and 4.42 (2 terminal methylene protons) and a double triplet at τ7.48 (2 methylene proton adjacent to double bond).

Synthesis of 1:3 dienes.

Following from our interest in the reactions of unsaturated ester phosphonates we began a systematic study of the reaction between simple unsaturated phosphonates and carbonyl compounds. The results of these investigations lead to a general method for the preparation of 1:3 dienes. Generally, a low yield of olefins was obtained in these condensation reactions. The low yield of the olefins, in case of allyl phosphonate (41) condensations, was due to the isomerisation[22] of the allyl phosphonate on treatment with bases to the vinyl phosphonate (42) which did not condense with carbonyl compounds to yield olefins. Thus allyl phosphonate, when treated with sodium hydride was isomerised to the vinyl one, having an infra-red spectrum



(41) (42)

ν_{max} (film) 1635, 1240, 1040, 980cm^{-1}. The n.m.r. spectrum of this compound showed one vinyl proton as a broad signal between τ3.0 and τ4.0, and another as an apparent broadened triplet, τ4.48 (J = 18 c.p.s.)

a multiplet at τ6.02 (4 ethoxymethylene protons) and a doublet at τ8.09 (J = 7 c.p.s.), each signal being further split into triplets, (J = 2 c.p.s.) (3 protons, methyl on double bond). It was therefore decided to carry out the condensation reactions by forming the anion in the presence of the carbonyl compound, so that the anion of allyl phosphonate would immediately react with the carbonyl compound and the chance of isomerisation could be avoided to a great extent.

Thus a mixture of allyl phosphonate and cyclohexanone dissolved in dry 1,2-dimethoxyethane, when treated with sodium hydride at room temperature, yielded the diene[28] (43), Fig. VII, having an infrared spectrum with ν_{max} (film) 1645, 1605, 1450, 995, 905cm^{-1}. The ultravoilet spectrum[24] showed absorption at λ_{max} 237mμ (ε29,170) and the n.m.r. spectrum showed a pair of triplets at τ3.37 and 3.64 (one vinyl proton), a doublet at τ4.22 (one vinyl proton), a multiplet at τ5.04 (2 terminal methylene protons) and a broad complex at τ7.80 (4 methylene protons adjacent to double bond). The above data, as well as the analytical results were in full agreement with the structure (43). In an attempt to purify the compound (43) from the oil present in sodium hydride, by distillation, it was observed

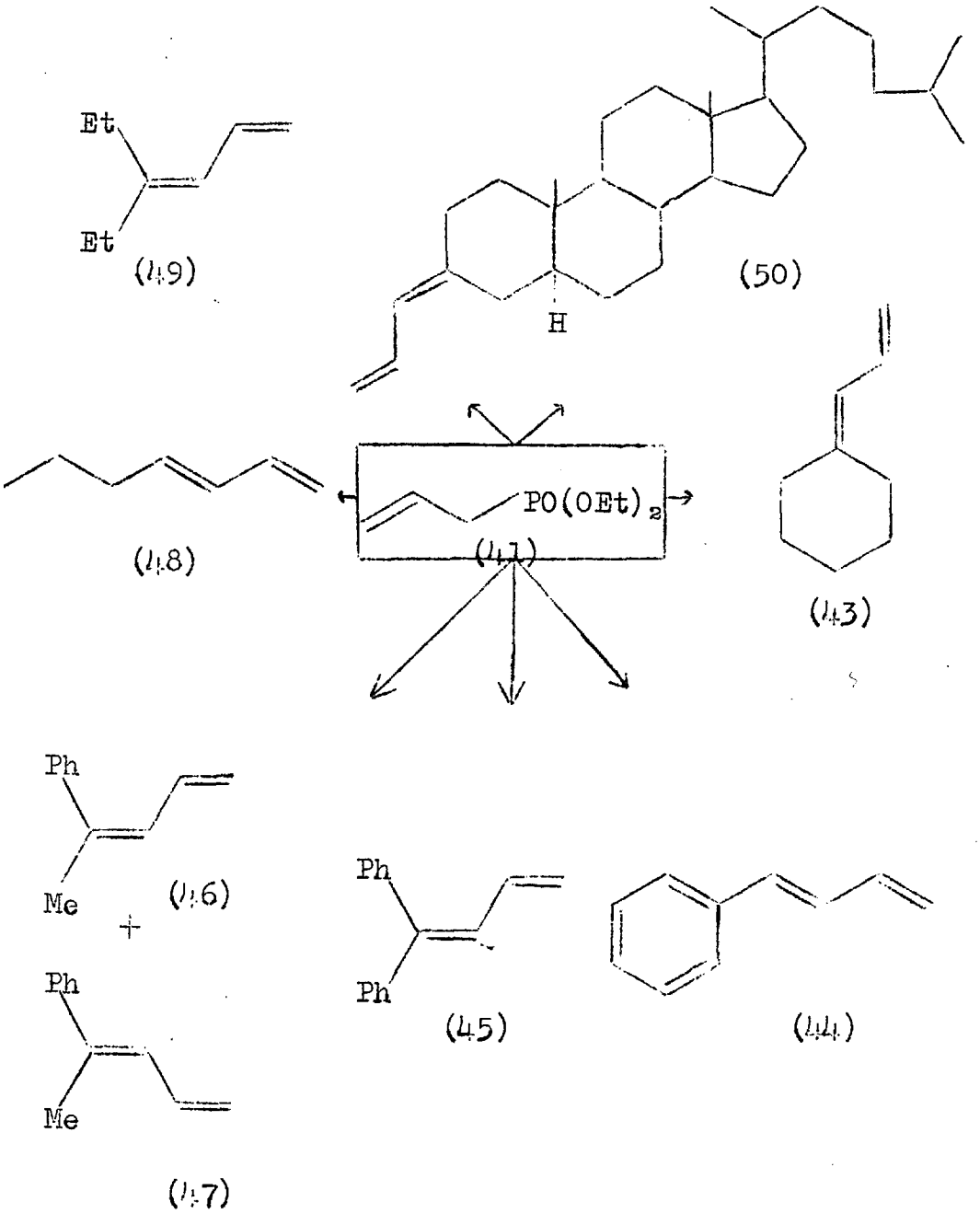


Fig. VII.

that the compound was partly polymerised resulting in a lower yield of the pure product. The purification of the compound was also effected by a column-chromatography through silica-gel, eluting with benzene but a quantitative recovery was not obtained. An attempt to purify the material through an alumina-column, eluting with benzene, yielded an unidentified product, most probably a polymer, as well as the pure compound (43). The new product was a solid, m.p. 85-87°C, crystallised from a mixture of ethanol-petrol and sublimed at 55°C/0.35 mm.Hg. The solid compound had infra-red absorptions at ν_{max} (nujol) 3340, 1645, 1465, 1380, 980, 855cm^{-1} and ultraviolet spectrum, λ_{max} 237, 244, 251mμ (ε22400). The n.m.r. spectrum showed signals at τ3.67 and 4.35 (vinyl protons), a complex multiplet at τ7.79 (methylene protons adjacent to double bond) and a broad singlet at τ8.45 (methylene protons), in the ratio 1:2:8. The mass spectrum showed the molecular ion peak at 202. On analysis, the compound was found to contain C = 81.5% and H = 10.9%. These data do not allow us to postulate a structure for the above compound.

The above condensation reaction of allyl phosphonate anion with cyclohexanone was repeated in

different basic media in an attempt to increase the yield of the olefin. The condensation did not take place at all in the presence of the bases, sodium ethoxide in ethanol; 1,5-diazobicyclo [4.3.0] non-5-ene (DBN), and 1,5-diazobicyclo [5.4.0] undec-5-ene (DBU); whereas bases like potassium t-butoxide in dimethylformamide and methyllithium in ether, effected the condensation but with lower yield. However, a better yield of the compound was finally obtained when the condensation was carried out in the presence of oil-free sodium hydride at -10°C.

The results obtained from the condensation of allyl phosphonate with cyclohexanone in different basic media indicated sodium hydride in 1,2-dimethoxyethane to be the most suitable base for the reaction and henceforth subsequent condensation of allyl phosphonate with other carbonyl compounds were carried out with this reagent.

The condensation of allyl phosphonate with benzaldehyde in the presence of sodium hydride in 1,2-dimethoxyethane gave the expected olefin 1-phenyl 1-3-butadiene[25,26] (44), having the infra-red absorptions at ν_{max} (film) 1630, 1603, 1015, 915, 760, 705cm^{-1}. The ultra-violet spectrum[26] of the

compound was characteristic showing λ_{max} 205, 208, 219, 226, 233, 280, 306mμ (ε29,800). The n.m.r. spectrum showed a complex at τ2.80 (5 aromatic protons), a complex multiplet between τ3.20 and 3.90 (3 vinyl protons) and a multiplet at τ4.90 (2 terminal methylene protons). The analytical data conformed to the molecular formula $C_{10}H_{10}$ of the compound (44), which was susceptible to polymerisation[27].

The olefin 1,1-diphenyl 1:3-butadiene (45) was prepared in the same manner by the condensation of allyl phosphonate with benzophenone. The compound, a solid of m.p.34-35°C, was confirmed by infra-red, ultra-violet, n.m.r. spectra and analytical results. The infra-red spectrum showed ν_{max} 1645, 1610, 1590, 915, 760cm^{-1} and the ultraviolet spectrum had λ_{max} 285mμ (ε9,500). The n.m.r. spectrum of the compound exhibited the following signals: a complex at τ2.85 (10 aromatic protons), multiplet between τ3.20 and 3.86 (2 vinyl protons) and a multiplet at τ4.90 (2 terminal methylene protons). The above compound (45) showed signs of polymerisation[28].

The condensation of allyl phosphonate with acetophenone under identical reaction conditions gave a mixture of almost equal amounts of isomeric 1-phenyl-1-methyl-1:3-butadiene (46) and (47). This mixture was

also very susceptible to polymerisation and decomposition. The mixture, after immediate work-up, showed the infra-red spectrum with ν_{max} 1640, 1608, 1590, 915cm^{-1}, and the ultra-violet spectrum with λ_{max} 285mμ. The n.m.r. spectrum showed a complex at τ2.83 (5 aromatic protons), a complex at τ3.65 (2 vinyl protons) and a complex at τ4.90 (2 terminal methylene protons) and two singlets at τ7.90 and 7.86 (3 protons accounting for both signals, methyl on double bond). These two singlets could be assigned to the two methyl groups arising from the two isomers (46) and (47), as expected due to their different environments.

Butyraldehyde on condensation with allyl phosphonate under identical conditions yielded the expected 1-3 heptadiene[29] (48), ν_{max} 1640, 1600, 1010, 900cm^{-1} and λ_{max} 228mμ (ε21,600). The n.m.r. spectrum of the compound exhibited a multiplet between τ3.40 and 4.67 (3 vinyl protons), a pair of triplets at τ5.01 (2 terminal methylene protons) and a multiplet at τ7.95 (2 methylene protons adjacent to double bond). Elemental analysis was found to be consistent with C_7H_{12}, the molecular formula for 1-3-heptadiene (48).

Diethylketone was condensed with allyl phosphonate to yield 1,1-diethyl 1-3-butadiene (49), as established by

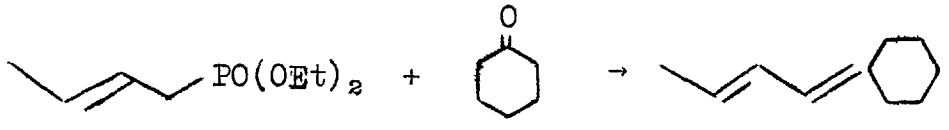
spectral data. It had the correct analysis for C_8H_{14}, the molecular formula for (49). The infra-red spectrum showed absorption at ν_{max} 1640, 1595, 1010, 900cm^{-1} and the n.m.r. spectrum was very informative, showing the following signals: a pair of triplets at τ3.36 and 3.64 (1 vinyl proton), a doublet at τ4.30 (1 vinyl proton), an apparent triplet at τ5.00 (2 terminal methylene protons) and a quartet at τ7.89 (4 methylene protons adjacent to double bond). The same compound (49) was also prepared by the condensation of allyl phosphonate with diethyl ketone in the presence of pot-t-butoxide in dimethyl-formamide but the yield obtained was poorer than in the previous case.

Finally, the condensation for the synthesis of 1-3-dienes, was tried on a bulky molecule of the steroid series, e.g. cholestanone. Thus allyl phosphonate on condensation with cholestanone in the presence of sodium hydride in dimethylformamide at 80°C, gave allylidine cholestane (50). The compound (50) was a solid m.p. 52-53°C, crystallised from petrol-methanol. The infra-red spectrum of the compound (50) had ν_{max} 1640, 1590, 1010, 900cm^{-1} and the ultraviolet spectrum had λ_{max} 234, 241, 244mμ. The n.m.r. spectrum was informative, as it showed a pair of triplets at τ3.39

and 3.68 (1 vinyl proton), a doublet at τ4.35, (1 vinyl proton), a triplet at τ5.05, (2 terminal methylene protons).

In all these condensation reactions mentioned earlier, it had been observed that ketones reacted with allyl phosphonates much more slowly than aldehydes to yield olefins. Our studies show that the method can be regarded as a general method for the preparation of 1:3 dienes. To confirm the generality of the above reaction, the condensation reactions were then extended to some higher allyl phosphonates.

Obviously, the next higher member which caught our attention was crotyl phosphonate (51) and this was successfully subjected to a condense with a typical carbonyl compound yielding 1:3 dienes. Thus crotyl phosphonate on condensation with cyclohexanone in the presence of sodium hydride in 1,2-dimethoxyethane yielded the diene[30] (52)

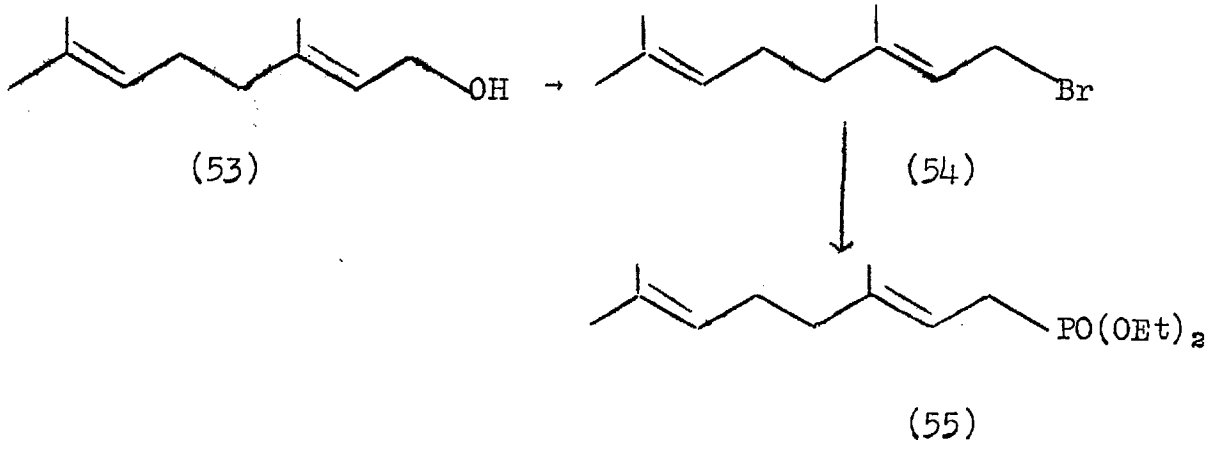


(51) (52)

The compound (52) was also prepared using methyl lithium as a base. It was observed that, unlike allyl phosphonate,

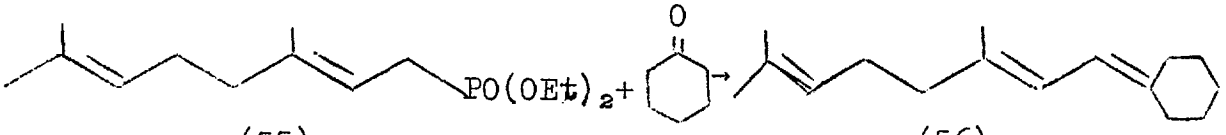
crotyl phosphonate did not isomerise to the corresponding vinyl one. The condensation was therefore carried out by first forming the anion of the crotyl phosphonate with a base and then reacting the anion with the carbonyl compound to form the olefin. The structure (52) was established by its analytical results and spectral data. It showed ν_{max} 1648, 1610, 970cm^{-1} and λ_{max} 235, 241, 244mμ (ϵ21,170). The n.m.r. spectrum showed multiplet between τ3.60 and 4.84 (3 vinyl protons), complex at τ7.83 (4 methylene protons adjacent to double bond) and a doublet at τ8.28 (3 protons, methyl on double bond, J = 7 c.p.s.).

The next unsaturated phosphonate of the allylic series, used in our present investigation, was geranyl phosphonate (55), which was prepared from geraniol (53) by the scheme given below:



(53) (54) (55)

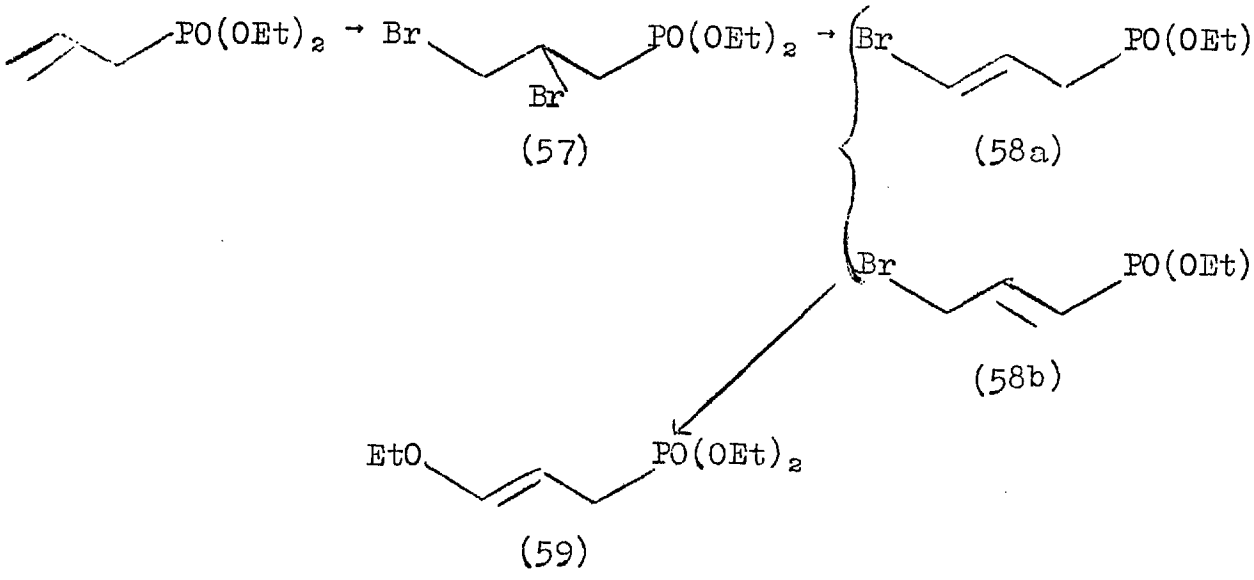
Geraniol (53) was brominated with phosphorous-tribromide to form geranyl bromide[31] (54), ν_{max} 1645, 1440, 1195cm^{-1}. The n.m.r. spectrum showed a triplet at τ4.53 (1 vinyl proton adjacent to carbon bearing bromine atom). The geranyl bromide (54) was then heated with triethylphosphite in the usual manner to form geranyl phosphonate (55), ν_{max} 1650, 1630, 1250, 1035, 965cm^{-1}. The n.m.r. spectrum was characteristic of allyl phosphonates, having a complex multiplet at τ4.96 (2 vinyl protons), a multiplet at τ6.02 (4 ethoxy methylene protons), a pair of doublets at τ7.44 and 7.80 (2 methylene protons on a carbon atom attached to phosphonate group, J = 22 cps), a complex at τ7.97 (4 methylene protons adjacent to double bonds) and a doublet at τ8.37 (9 protons, methyl on double bonds). Geranyl phosphonate was then condensed with cyclohexanone in the presence of oil-free sodium hydride in dimethylformamide at 100°C to yield the expected olefin, geranylidine cyclohexane (56).



(55) (56)

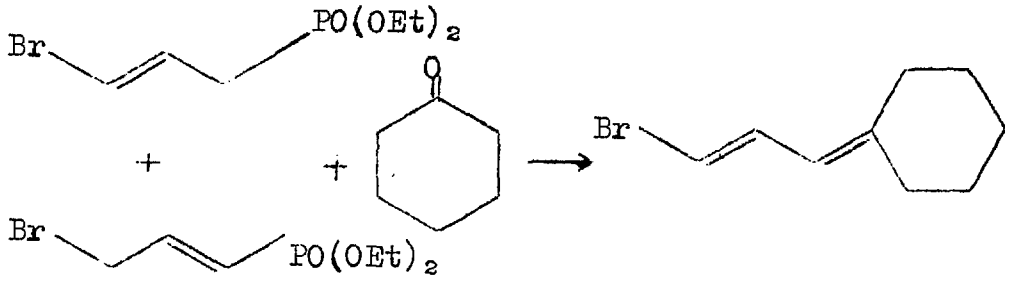
The formation of the compound (56) was proved by infra-red, ultraviolet, n.m.r. spectra and analytical results. It had ν_{max} 1605, 1440, 980, 850cm^{-1} and λ_{max} 243, 251, 259mμ (ϵ38,000). Its n.m.r. spectrum showed a doublet at τ4.16 (2 vinyl protons having conjugation), multiplet at τ5.00 (1 vinyl proton), complex at τ7.97 (8 methylene protons adjacent to double bonds) and a doublet at τ8.37, (9 methyl protons on double bond and 6 methylene protons).

The above condensation reaction of unsaturated phosphonates with carbonyl compounds to yield 1:3 dienes, was also applied to some derivatives of unsaturated phosphonates, e.g. 1-bromo-allyl phosphonate (58) and 1-ethoxy-alkyl phosphonate (59). The compounds (58) and (59) were prepared by the following sequence of reactions.



Allyl phosphonate was brominated in the usual way to form a dibromo-derivative (57), ν_{max} (film) 1245, 1030, 975cm^{-1}. The n.m.r. spectrum of the compound showed a complex multiplet between τ5.33 and 6.25 (7 protons; 4 ethoxy methylene protons and 3 others on carbon bearing bromine atoms), a pair of doublets at τ7.35 and 7.67 (2 methylene protons on carbon attached to phosphorous, J = 22 cps). The dibromo-compound (57) on treatment with sodium ethoxide in ethanol at room temperature yielded a mixture of 50% allyl mono-bromo-phosphonate (58a) and 50% vinyl mono-bromo-phosphonate (58b). The infra-red spectrum of the mixture had ν_{max} (film) 1632, 1240, 1040, 980cm^{-1} and the n.m.r. spectrum exhibited the following resonance signals: a complex multiplet between τ3.00 to 4.40, showing vinyl protons; a multiplet at τ5.04, showing ethoxy methylene protons and methylene protons on carbon attached to bromine atom; and a multiplet at τ7.38, showing protons on carbon attached to phosphorous. The ratio of protons from integration showed to be Ca 50:50 mixture of allyl and vinyl bromo phosphonates. The mixture of the bromo phosphonates (58a) and (58b) was then condensed with cyclohexanone in the presence of sodium hydride in 1,2-dimethoxy ethane to form 1-bromo-allylidine

cyclohexane (60).

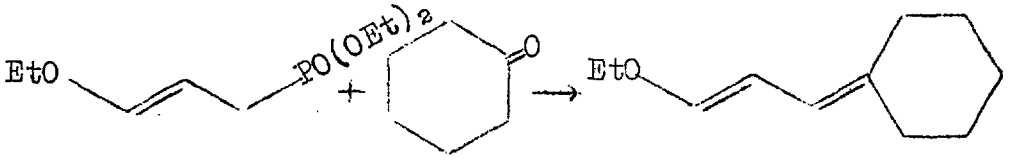


(58.a,b) (60)

The ultraviolet spectrum of the compound (60) had λ_{max} 248, 253, 262mμ and the n.m.r. spectrum showed a complex at τ3.20 (one vinyl proton on carbon bearing bromine atom) a triplet at τ3.95 (one vinyl proton), a complex at τ4.80 (1 vinyl proton) and a complex multiplet at τ7.80 (4 methylene protons adjacent to double bond).

The mixture of allyl and vinyl bromo-phosphonates was refluxed with sodium ethoxide in ethanol to give 1-ethoxy allyl phosphonate (59), ν_{max} (film) 1658, 1380, 1250, 1040, 980cm^{-1}. The n.m.r. spectrum showed a complex at τ4.00 (1 vinyl proton), a complex multiplet between τ5.42 to 6.42 (6 ethoxy methylene proton and one vinyl proton) and a pair of doublets at τ7.72 and 7.35 (2 methylene protons on carbon attached to phosphorous, J = 22 cps). The analytical data was consistent with its molecular formula $C_9H_{19}PO_4$. The ethoxy

phosphonate (59) was then condensed with cyclohexanone in the presence of sodium hydride in 1,2-dimethoxyethane at 70°C to yield the expected diene (61)



(59 (61)

The ultra-violet spectrum of the compound (61) had λ_{max} 228, 248, 254, 264mμ. The n.m.r. spectrum was not informative as the compound seemed to decompose rapidly.

All our results, hitherto discussed, conclusively prove that allyl phosphonates do condense with carbonyl compounds yielding 1:3 dienes. Since vinyl phosphonates are expected to form the same anion as the corresponding allyl phosphonates, it was hoped that these would also condense with carbonyl compounds yielding identical 1:3 dienes. We therefore turned our attention to investigate into the reactions of vinyl phosphonates with carbonyl compounds.

It may be recalled here that during our work on allyl phosphonate condensations, it was observed that allyl phosphonate on treatment with sodium hydride was isomerised to the vinyl phosphonate (42). The compound (42)

was treated with cyclohexanone under identical conditions, but the reaction did not take place. Again, the same vinyl phosphonate[32] (42) was prepared by a scheme given in Fig. VIII,(a). Propionaldehyde on condensation with diethylphosphite in the presence of sodium ethoxide in ethanol yielded diethyl 1-hydroxy-propyl phosphonate (62), ν_{max} (film) 3300, 1210, 1030, 970cm^{-1}. The n.m.r. spectrum showed a doublet at τ4.84 (proton of the hydroxyl, exchanged with D_2O), a multiplet at τ5.89 (4 ethoxymethylene protons) and a complex at τ6.42 (one proton on carbon bearing hydroxyl group). The hydroxy-phosphonate (62) on refluxing with acetic anhydride gave the corresponding acetoxy-phosphonate (63), ν_{max} 1740, 1225, 1040, 980cm^{-1}. The n.m.r. spectrum showed a pair of triplets at τ4.95 and 5.06 (one proton on carbon bearing acetoxy group; coupled with phosphorous, J = 6 cps), a multiplet at τ5.98 (4 ethoxy methylene protons) and a singlet at τ7.98 (3 protons of acetoxy group). The compound (63) on pyrolysis gave the vinyl phosphonate which was found to be identical with the previous one. Attempts to condense this vinyl phosphonate with cyclohexanone also failed.

Another vinyl phosphonate of interest was diethyl

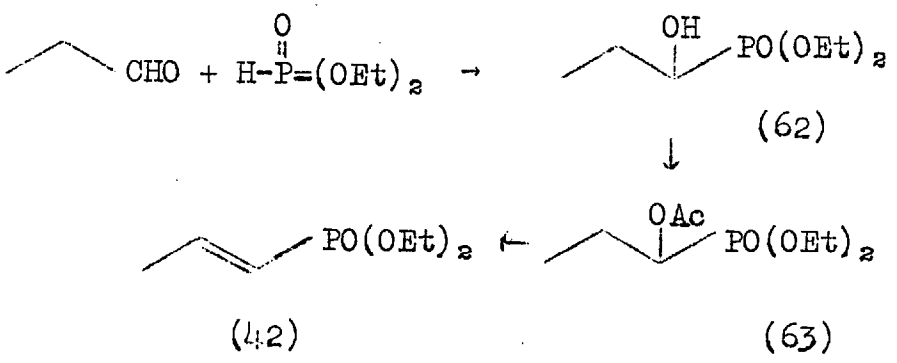


Fig. VIII.a.

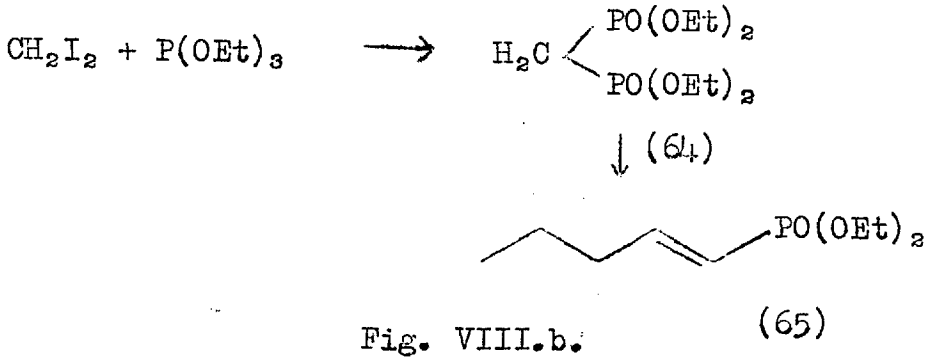


Fig. VIII.b.

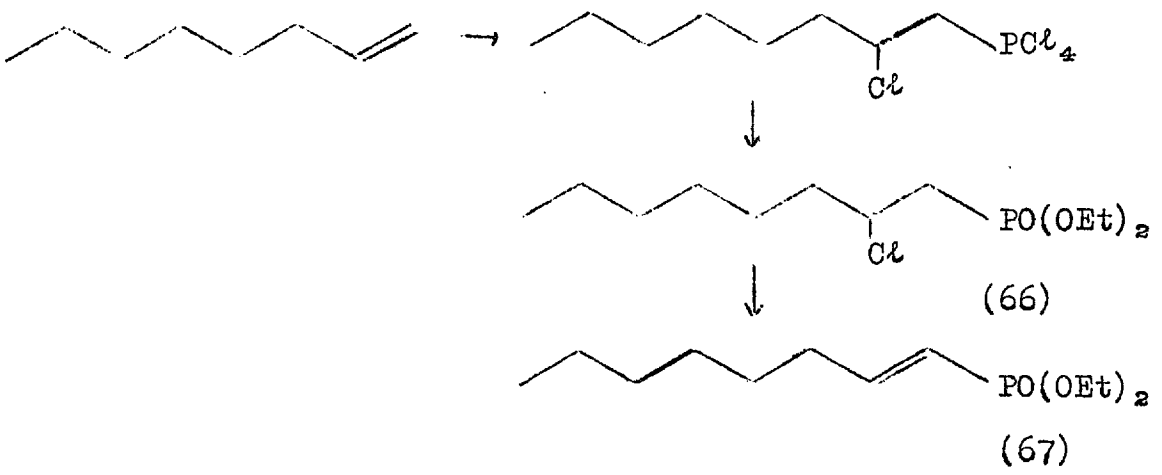


Fig. VIII.c.

pent-1-ene phosphonate (65) which was prepared from tetraethyl methane diphosphonate[32] (64), Fig. VIII,(b). The compound (64) was prepared by heating methylene iodide with triethylphosphite. It had infra-red maxima at ν_{max} (film) 1630, 1250, 1040, 980 840cm^{-1}. The n.m.r. spectrum showed a multiplet at τ5.9 (8 ethoxy methylene protons) and a triplet at τ7.7 (2 methylene protons attached to phosphorous, J = 21 cps). The compound (64) on condensation with butyraldehyde gave (65), having a complex n.m.r. absorptions between τ3.00 and 4.84 (2 vinyl protons), a multiplet at τ6.02 (4 ethoxy methylene protons) and a complex at τ7.85 (2 methylene protons adjacent to double bond) in the n.m.r. spectrum. The reaction of cyclohexanone with the compound (65) proved unsuccessful.

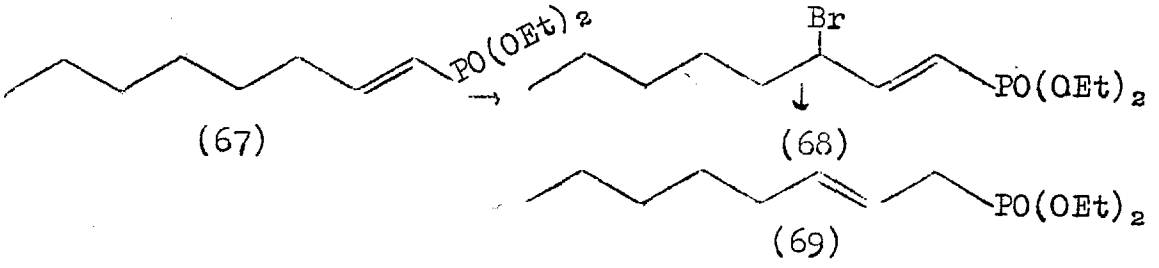
Finally, Diethyl oct-1-ene phosphonate[33] (67), a model vinyl phosphonate for our present investigation was selected. The compound (67) was prepared starting from oct-1-ene. An adduct was made by treating oct-1-ene with phosphorouspentachloride, and the product on alcoholysis yielded diethyl 2-chloro-octyl phosphonate (66), ν_{max} (film) 1260, 1040, 980cm^{-1}; the n.m.r. spectrum showed a multiplet at τ5.96 (4 ethoxymethylene protons and one other proton on carbon bearing chlorine atom)

and a pair of doublets at τ7.66 and 7.97 (2 methylene protons on carbon attached to phosphorous; one of the signals of each further split into two, J = 19 cps). The compound (66) on treatment with sodium ethoxide in ethanol gave diethyl oct-1-ene phosphonate (67), ν_{max} 1625, 1250, 1040, 975cm^{-1}. The n.m.r. spectrum showed a complex between τ2.75 and 4.84 (2 vinyl protons), a multiplet at τ5.98 (4 ethoxy methylene protons) and a broad signal at τ7.76 (2 methylene protons adjacent to double bond). Attempts to condense diethyl oct-1-ene phosphonate (67) with cyclohexanone in the presence of different bases, e.g. sodium hydride in 1,2-dimethoxy-ethane, sodium hydride in dimethylformamide at 80°C and methyl lithium in ether did not lead to any diene products.

The above reactions of the vinyl phosphonates thus conclusively prove that they do not condense with carbonyl compounds to form olefins. The reason for their inertness towards the carbonyl compounds must be due to non-formation of the anion. Why they should be so weakly acidic we are unable to explain.

It has been mentioned earlier in this text, that allyl phosphonate, on treatment with a base, was isomerised to the vinyl phosphonate. It then appeared inetesting to us to see whether a vinyl phosphonate could be

converted to an allyl one. We, therefore, undertook the work of converting vinyl octene phosphonate (67) to the corresponding allyl octene phosphonate (69). This was successfully achieved through the following series of reactions.



The compound (67) was refluxed with N-bromo-succinimide in carbontetrachloride to yield diethyl 3-bromo-oct-1-ene phosphonate (68) showing ν_{max} (film) 1633, 1255, 1040, 980cm^{-1} in its infra-red spectrum. The n.m.r. spectrum showed a pair of doublets at τ3.82 and 4.40 (1 vinyl proton), a complex multiplet at τ 3.34 (1 vinyl proton), multiplet at τ5.9 (4 ethoxy methylene protons and one proton on carbon bearing bromine atom). The bromo-phosphonate (68) was then treated with zinc and acetic acid and reduction formed diethyl oct-2-ene phosphonate (69), ν_{max} (film) 1628, 1250, 1040, 975cm^{-1}. The n.m.r. spectrum of (69) showed a triplet (each signal being split into doublet) at τ4.52 (2 vinyl protons), multiplet at τ5.98 (4 ethoxy

methylene protons) and a broad signal between τ7.25 and 8.1 (4 methylene protons adjacent to double bond).

Synthesis of Cross-conjugated Compounds.

Though our ultimate object in synthesising the fulgenic ester (13) was achieved, it may be recalled that our attempts to prepare diethyl 1-carboethoxy-pent-1-ene phosphonate (18) which might be a useful compound for the synthesis of the fulgenic ester (13) were unsuccessful. However, compounds of this type were expected to be useful for the synthesis of cross-conjugated compounds in general and, since there are no satisfactory methods for their preparation, we continued this investigation.

As it was found very difficult to dehydrogenate the saturated phosphonate ester, as mentioned earlier in this text, unsaturated phosphonates were this time chosen as the starting compounds; the idea being the introduction of a carboethoxy group into the unsaturated phosphonate unit.

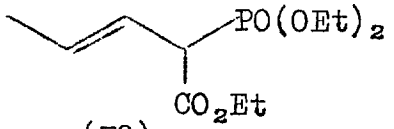
Allyl phosphonate (41) was first used for this purpose. It was hoped to condense it with ethyl-chloroformate, diethyl carbonate or ethyl phenyl carbonate to yield unsaturated phosphonate ester, but the reactions did not yield the desired compound. On the other hand

an interesting reaction with diethyl carbonate was noticed which will be discussed later on in this text.

However, a successful synthesis of the unsaturated phosphonate ester diethyl 1-carboethoxy-but-2-enyl phosphonate (70) was achieved by reacting diethyl carbonate with the anion of crotyl phosphonate, using methyllithium as base at -20°C. The compound (70) had infra-red



(51)



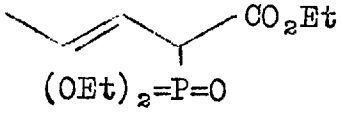
(70)

absorptions at ν_{max} (film) 1728, 1260, 1040, 980cm^{-1}. The n.m.r. spectrum showed multiplet at τ4.38 (2 vinyl protons) multiplet at τ5.90 (6 ethoxy methylene protons) a pair of doublet at τ6.3 (one proton on carbon attached to carboethoxy group), and a complex signal at τ8.34 (3 protons, methyl on double bond). The complexity of the latter signal is probably due to long-range coupling with the phosphorous. Elemental analysis of the compound was found to be consistent with $C_{11}H_{21}PO_5$, the molecular formula for (70).

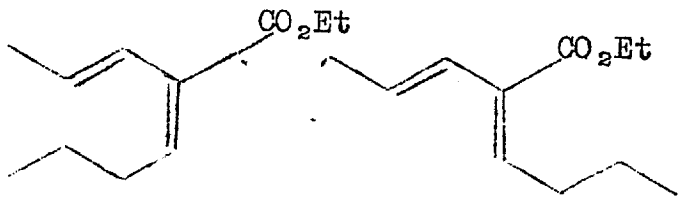
In the foregoing synthesis of the compound (70) a yield of 50% of the product was obtained and 30% of unreacted crotyl phosphonate was recovered. In order to

effect the complete reaction of this unreacted crotyl phosphonate with diethyl carbonate and thereby increasing the yield of the compound (70), the reaction was carried out under different experimental conditions. The use of excess of diethyl carbonate as well as that of excess of methyl lithium at different temperature in no way increased the yield of the compound (70), and in all cases ~30% of the crotyl phosphonate remained unreacted. The presence of this unreacted phosphonate in the reaction mixture may probably be due to protonation of the crotyl phosphonate anion by the phosphonate-ester formed during the reaction.

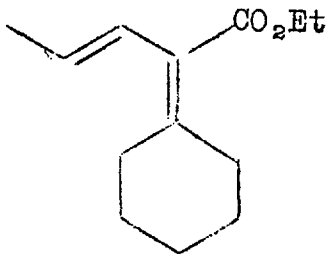
Condensation of diethyl 1-carboethoxy-but-2-enyl phosphonate with butyraldehyde in the presence of sodium hydride in tetrahydrofuran at room temperature gave a mixture of two isomeric compounds 70(a) and 70(b), Fig. IX, which have cross-conjugated systems in the molecules. The mixture had ν_{max} (film) 1715, 1640, 1625, 1240, 1220, 970cm^{-1}, and the ultra-violet spectrum λ_{max} 235mμ (ϵ5,950). The n.m.r. spectrum showed triplets at τ3.3 and 3.5 (one vinyl proton, cis and trans to carboethoxy group), a complex at τ4.15 (2 vinyl protons), a multiplet at τ5.86 (2 carboethoxy methylene protons), a triplet at τ7.80 (2 methylene protons adjacent to



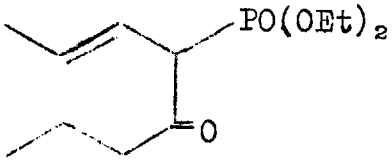
(70)



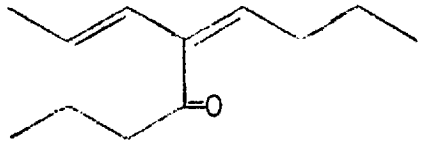
(70.a) (70.b)



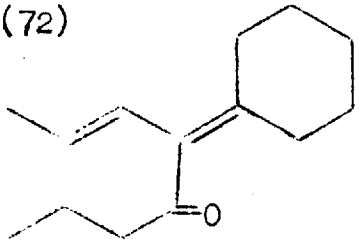
(71)



(72)



(73)



(74)

Fig. IX.

double bond) and signals at τ8.20 probably due to methyl on double bond.

The compound (70) was again utilised in a condensation with cyclohexanone in the presence of sodium hydride in tetrahydrofuran at 60°C to yield a cross-conjugated compound (71), showing λ_{max} 230, 290mμ. The n.m.r. spectrum showed a complex at τ4.52 (2 vinyl protons), a multiplet at τ5.90 (2 carboethoxy methylene protons), broad complex at τ7.75 (4 methylene protons adjacent to double bond) and a complex at τ8.35 (3 protons, methyl on double bond).

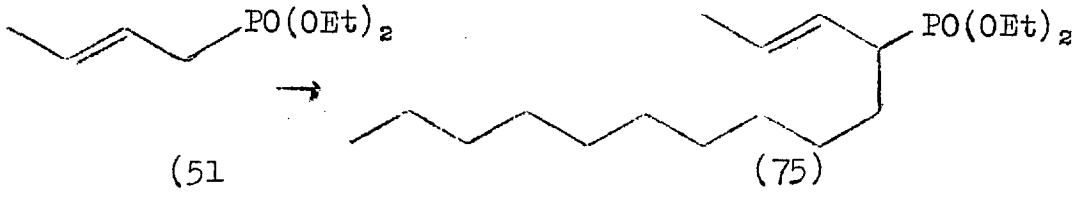
The second suitable phosphonate, selected for the preparation of cross-conjugated compounds was (72), the synthesis of which is discussed later in this text. Condensation of (72) with butyraldehyde in the presence of sodium hydride in tetrahydrofuran at room temperature led to the formation of the compound (73), having infra-red spectrum ν_{max} (film), 1690, 1670, 1610, 970cm^{-1} and ultra-violet spectrum λ_{max} 232mμ (ε5,040). The n.m.r. spectrum showed a complex between τ3.4 to 4.8 (3 vinyl protons) a multiplet at τ7.6 (4 methylene protons adjacent to carbonyl and double bond), and a triplet at τ8.25 (3 protons, methyl on double bond). The compound (72) was also condensed with cyclohexanone in the presence

of sodium hydride in tetrahydrofuran at 60°C to yield (74) having absorption at 247, 252mμ in the ultraviolet spectrum. The n.m.r. spectrum was not informative as it showed signs that decomposition was taking place.

Other Reactions of Unsaturated Phosphonates.

Hitherto, we have been concerned with investigating the condensation-reactions of unsaturated phosphonates with carbonyl compounds to yield 1:3 dienes. Next, we wish to discuss some reactions of phosphonate carbanions with other compounds, not yielding 1:3 dienes.

Unsaturated phosphonates, like saturated phosphonates, could easily be alkylated[34]. Crotyl phosphonate was condensed with n-decyl bromide to form diethyl 1-decyl-but-2-ene phosphonate (75)



(51 (75)

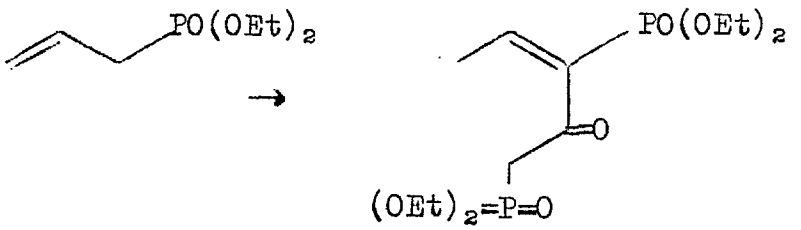
by the use of methyl lithium as base. The compound (75) had the infra-red spectrum ν_{max} (film) 1630, 1240, 1090,

980cm^{-1}. The n.m.r. spectrum showed a complex at τ4.72 (2 vinyl protons), a multiplet at τ5.98 (4 ethoxy methylene protons), a broad signal at τ7.35 (one proton on carbon containing the phosphonate group), a triplet at τ8.3 (3 protons, methyl on double bond). Elemental analysis was found to be consistent with $C_{18}H_{37}PO_3$, the molecular formula for (75).

Unsaturated phosphonates could be condensed with esters to form the unsaturated keto-phosphonate which was used for the synthesis of cross-conjugated compounds. Condensation of crotyl phosphonate with ethylbutyrate in the presence of methyl lithium in ether at -20°C, yielded the unsaturated keto-phosphonate (72), ν_{max} (film) 1710, 1630, 1250, 1030, 980cm^{-1}. The n.m.r. spectrum of this compound showed a complex at τ4.38 (2 vinyl protons), a multiplet at τ5.98 (4 ethoxy methylene protons and one proton adjacent to carbonyl group), a multiplet at τ7.49 (2 methylene protons adjacent to carbonyl) and a triplet at τ8.35 (3 protons, methyl on double bond). The analytical data conformed to the molecular formula $C_{12}H_{23}PO_4$.

As mentioned earlier, crotyl phosphonate condensed with diethylcarbonate to form unsaturated phosphonate ester (70) which was found to be a useful compound in the

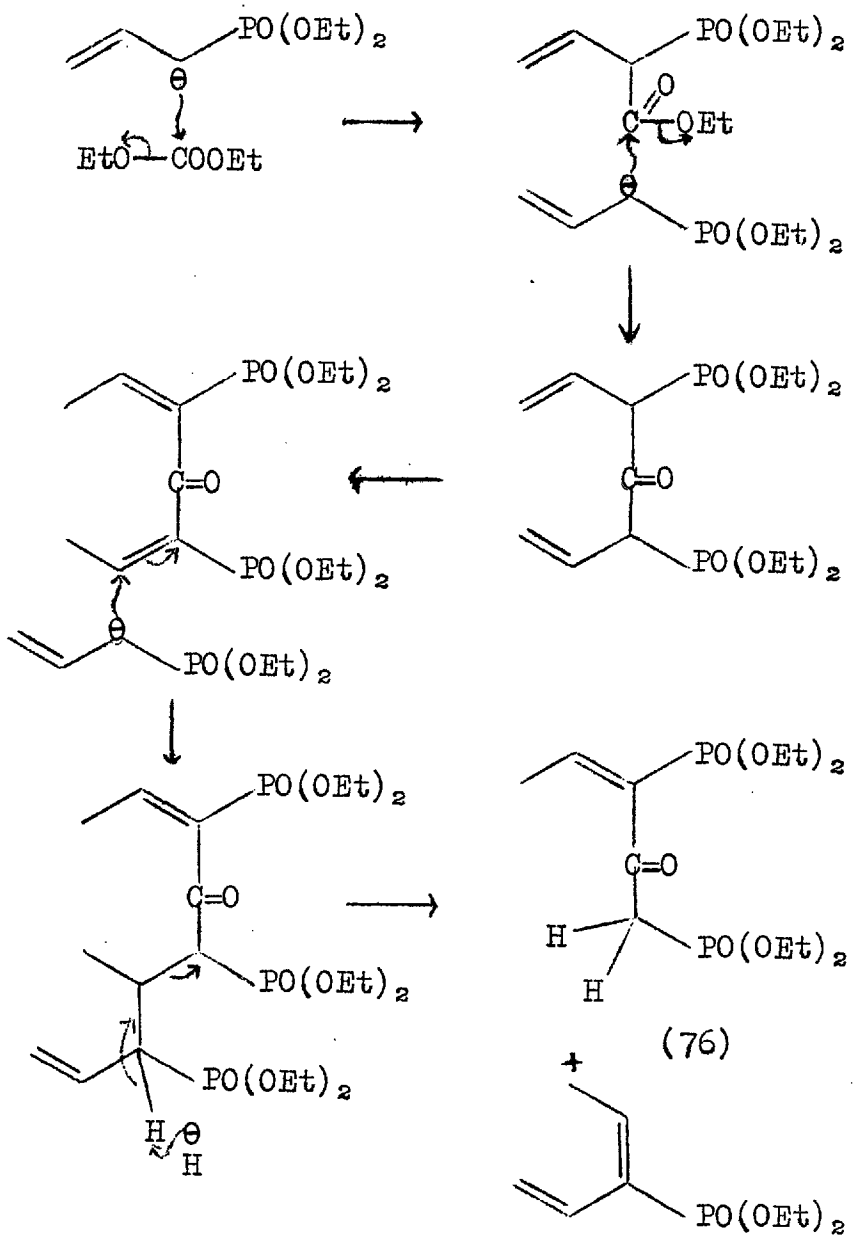
synthesis of cross-conjugated compounds. Allyl phosphonate, on the other hand, condensed with diethyl-carbonate in the presence of sodiumhydride in 1,2-dimethoxyethane to yield an unexpected compound



(41 (76)

tentatively identified as (76).

The compound (76) had infra-red absorptions at ν_{max} 1630, 1235, 1035, 975cm^{-1}. The n.m.r. spectrum of the compound showed a complex between τ4.00 and 5.00 (1 vinyl proton), a multiplet at τ6.00 (8 ethoxy methylene protons), a complex at τ8.07 (5 protons; 3 protons of methyl on double bond and 2 methylene protons adjacent to carbonyl group). The mass spectrum of the compound showed molecular-ion peak at 356, and also showed peaks at 219, 205 and 177 which may be due to loss of $-PO(OEt)_2$, $-CH_2PO(OEt)_2$ and $-COCH_2PO(OEt)_2$ groups respectively. A possible mechanism for the formation of the compound (76) is given below.


PO(OEt)2
EtO
COOEt
OEt
O
C=O
H
(76)

Conclusions.

From the previous work we can say that allyl phosphonates can be used for 1,3-diene synthesis, but in the case of simple compounds the Wittig method is probably superior. However, this method does offer some promise for the synthesis of cross-conjugated carbonyl systems although the reaction with ketones is notably slower than that with aldehydes and the reaction with α-ketoesters fails probably due to the phosphonate anion abstracting a proton from the α-ketoester, rather than condensing with the carbonyl group; only unreacted phosphonate and condensation products of the α-keto-ester can be isolated.

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EXPERIMENTAL SECTION.

Melting points were determined on a Kofler block and are uncorrected.

Ultraviolet spectra, unless otherwise stated, were recorded in cyclohexane solution, on a Unicam S.P.800 instrument. Infrared spectra were recorded on a Unicam S.P.200 instrument.

Nuclear magnetic resonance spectra were kindly recorded by Mrs. Boston on a Varian A.60. Micro-analyses were performed by the staff of the Micro Analytical Laboratory, Imperial College.

The purity of all compounds was checked by thin layer chromatography (Silica-gel GF_{254}).

Work up of reactions by extractive procedures involved the drying of the organic phase with anhydrous magnesium sulphate, except where otherwise stated, and evaporation of the solvent in reduced pressure.

The ε value presented against U.V. data for the compound refers to the absorption maximum underlined.

Attempted Synthesis of 2-(1-butenyl)-3-methyl maleic anhydride.

Ethyl pyruvate (5).

Pyruvic acid (freshly distilled, 29.4gm.) was dissolved in absolute ethanol (59ml.) and carbontetrachloride (A.R.78ml.), and the mixture refluxed overnight under a column topped with a continuous chloroform extraction apparatus. Additional ethanol (7ml.) was added and the mixture refluxed for further 30 minutes. After cooling, the solution was washed with water, aqueous sodium bicarbonate solution (1%), water, dried by anhydrous magnesium sulphate, and the solvents removed in vacuum to yield an oil. The oil on distillation in an atmosphere of nitrogen gave ethyl pyruvate[1] (27.5gm.), b.p. 149-152°.

Diethyl Carboethoxyethylphosphonate (6).

Ethyl 2-bromopropionate (45gm.) and triethylphosphite (freshly distilled, 42gm.) were heated together on a metal bath at 150° for 3 hours in an atmosphere of nitrogen.

Distillation in vacuum gave diethyl carboethoxy-

ethylphosphonate[2] (38.5gm.), b.p. 70-72°, 0.07 mm.Hg., ν_{max} (film) 1735, 1275, 1070cm^{-1}.

Condensation of ethylpyruvate with diethyl carboethoxyethylphosphonate (7) and (8).

A solution of diethyl carboethoxyethylphosphonate (6.486gm.) in dry 1,2-dimethoxyethane (10ml.) was added dropwise to a stirred slurry of sodiumhydride (50%, 1.3082gm.) in dry 1,2-dimethoxyethane (50ml.). The mixture was stirred at room temperature for one hour and then treated with a solution of ethylpyruvate (freshly distilled, 3.162gm.) in dry 1,2-dimethoxyethane (10 ml.). The resulting yellow mixture was stirred at room temperature for 24 hours. It was then diluted with water and extracted with ether to yield an oil (4.72 gm.)

The oil (1.5gm.) was chromatographed on silica-gel (M.F.C. 100gm.), eluting first with benzene when the mineral oil, present in sodium hydride, was removed. It was then eluted with benzene containing an increasing proportion of chloroform to yield two fractions which were separated easily. One of these fractions was proved to be diethyl pyrocinchonate[3] (7) (1.1gm.), b.p. 73-75°, 3 mm.Hg.; ν_{max} (film) 1725, 1635cm^{-1}.

The second fraction was proved to be diethyl 2:3-dimethylfumarate (8) (85mg.), ν_{max} (film), 1725, 1635cm^{-1}.

2:3-dimethylfumaric acid (9).

Diethyl 2:3-dimethylfumarate (85mg.) was refluxed with 2(N) NaOH (25ml.), for 4 hours. The solution was then cooled and the mixture acidified with 6(N)H_2SO_4. The solid obtained was 2:3-dimethylfumaric acid[4], m.p. 231°.

2:3-dimethyl-maleic anhydride (10).

Sodium hydroxide (2N, 50ml.) was added to diethyl-pyrocinchonate (1.1gm.) dissolved in ethanol (5ml.) and the mixture was refluxed for 5 hours. The solution was cooled, acidified with 6(N) sulphuric acid and extracted with ether to give the solid 2:3 dimethyl maleic anhydride[5] recrystallised from ether, m.p.95° (lit.m.p.96°), ν_{max} (nujol) 1840, 1780cm^{-1}.

Bromination of 2:3-dimethyl-maleic anhydride

2-(1'-bromo-methyl)-3-methyl-maleic anhydride (11).

N-bromo-succinimide (184mg.) was added to 2:3-dimethyl-maleic anhydride (130mg.) dissolved in dry carbontetrachloride (25ml.), and the mixture refluxed. A few crystals of benzoyl peroxide were added to initiate the reaction. The reaction was complete after 2 hours. It was then cooled, filtered and solvents removed to yield an oil (163mg.). The n.m.r. spectrum showed it to be the bromo-compound (11), contaminated with some starting material. However, the separation was not effected at this stage.

Reaction of the bromo-anhydride (11) with triethyl-phosphite.

2-(1'-diethyl-phosphono-methyl)-3-methyl maleic anhydride (12)

Triethylphosphite (freshly distilled, 134mg.) was added to the above impure sample of bromo-anhydride (163mg.) and the mixture was heated at 140°C. for 3 hours in an atmosphere of nitrogen. After that the mixture was vacuumed off to yield an oil (178mg.), which was resolved by preparative thin layer chromatography (silica-gel GF_{254}, 72gm.; water 108ml.) employing a solvent system

containing benzene 30 parts, ether 5 parts and formic acid 3 parts (mixture made V/V), to yield the pure compound (12), (66mg.), ν_{max} (film) 1760, 1645, 1250, 1050cm^{-1}. The n.m.r. spectrum confirmed the formation of the compound (12).

Condensation of 2-(1'-diethylphosphono-methyl)-3-methyl maleic anhydride with propionaldehyde.

The phosphonate-anhydride (66mg.) dissolved in dry 1,2-dimethoxyethane (2ml.) was added to a stirred slurry of sodium hydride (50%, 12mg.) dissolved in dry dimethoxyethane (5ml.). Propionaldehyde (freshly distilled, 15mg.) also dissolved in dimethoxyethane (2ml.) was then added to it and the mixture stirred for 2 hours. The reaction mixture was then diluted with water and extracted with ether to yield a gum, shown to be a mixture of many compounds by thin layer chromatography.

Synthesis of propyl fulgenic ester.

2-Bromo-Hexanoic acid (20).

Phosphorous trichloride (0.74ml.) was added with caution to distilled hexanoic acid (50.2gm.). Dry bromine (washed with concentrated sulphuric acid, 24.4ml.) was then added drop by drop to this mixture. When the addition of bromine was complete, the mixture was heated on steam-bath overnight. The mixture on distillation in vacuum gave 2-bromo-hexanoic acid[6] (54.5gm.), b.p.76-80°, 0.1mm.Hg.

Ethyl 2-Bromo-Hexanoate (21).

2-bromo-hexanoic acid (64gm.) was dissolved in absolute enthanol (50ml.) and sodium dried benzene (75ml.). Concentrated sulphuric acid (0.6ml.) was added to the mixture and the solution was refluxed overnight under a column topped with a Dean and Stark apparatus. After that, another (10ml.) of ethanol was further added and the mixture refluxed for 30 minutes more. The solution was then cooled, washed with water, aqueous sodium bicarbonate solution 10%, water, dried and the solvents removed to yield an oil. Distillation in vacuum gave ethyl 2-bromo-hexanoate[7] (75gm.), b.p. 70-74°, 2.5mm.Hg.

Diethyl 1-carboethoxypentylphosphonate (22).

Triethylphosphite (5.25gm., freshly distilled) was added to ethyl 2-bromo-hexanoate (7.07gm.) and the mixture was heated at 140° for 3 hours in an atmosphere of nitrogen. The reaction mixture on distillation under vacuum gave diethyl 1-carboethoxypentylphosphonate (6.3gm.), b.p. 110°, 0.7mm.Hg. The infra-red spectrum of the compound had ν_{max} (film) 1730, 1259, 1059, 1036, 976cm^{-1}.

Attempted Preparation of diethyl 1-carboethoxypent-1-ene phosphonate (18) from diethyl 1-carboethoxypentylphosphonate.

Several reagents were tried to dehydrogenate diethyl 1-carboethoxypentylphosphonate, but with no successful results. Selenium dioxide in acetic acid, and 2:3-dichloro-5:6-dicyano-p-benzoquinone in benzene did not give the expected compound (18); on the other hand the starting material was obtained.

Tosylazide[8], added to the sodium salt of diethyl 1-carboethoxypentylphosphonate, did not react to give the compound (18).

Diethyl 1-carboethoxy-1-benzoyloxypentylphosphonate (23).

Diethyl 1-carboethoxypentylphosphonate (0.56gm.) dissolved in 1,2-dimethoxyethane(3ml.) was added drop by drop to a stirred slurry of sodium hydride (60%, 0.080gm.) suspended in dimethoxyethane (25ml.). The mixture was stirred for 1 hour. Benzoyl peroxide (0.484gm.) dissolved in dimethoxyethane (5ml.) was then added to the mixture, when a ppt. of sodium benzoate was formed. The mixture was heated at 70° overnight and then worked up as usual to yield an oil (0.60gm.). The oil was resolved by preparative thin layer chromatography using silica plates to yield the compound (23), ν_{max} (film) 1725, 1595, 1275, 1036cm^{-1}. The n.m.r. spectrum proved the formation of the compound (23).

Attempted preparation of diethyl 1-carboethoxypent-1-enephosphonate from the pyrolysis of diethyl 1-carboethoxy-1-benzoyloxypentylphosphonate.

Diethyl 1-carboethoxy-1-benzoyloxypentylphosphonate was heated on a metal bath (Bath temperature 160°) when a liquid was distilled, b.p. 105-110°, 0.25mm.Hg. The liquid was proved to be the starting material (23).

Diethyl 1-carboethoxy-1-bromo-pentylphosphonate (24).

Diethyl 1-carboethoxypentylphosphonate (0.7548gm.) dissolved in dimethoxyethane (5ml.) was added to a stirred slurry of sodium hydride (53.3%, 0.122gm.) suspended in dimethoxyethane (25ml.). Bromine (0.43gm.) dissolved in dimethoxyethane (5ml.) was then added[9] to it and the mixture stirred for 2 days. The reaction mixture after usual work-up yielded an oil (0.486gm.), which on distillation under vacuum gave the compound (24), ν_{max} (film) 1720, 1260, 1030, 976cm^{-1}.

Attempted dehydrobromination of Diethyl 1-carboethoxy-1-bromo-pentylphosphonate.

Pot-t-butoxide in t-butanol as well as Lithium chloride in dimethylformamide were tried on (24) to get diethyl 1-carboethoxypent-1-enephosphonate, but without any success. In both the cases the starting material was recovered.

2-Hydroxy-Hexanoic acid (25).

Sodium carbonate (40gm.) was added cautiously to 2-bromo-hexanoic acid (35.5gm.), suspended in water (150ml.) and the resulting mixture was refluxed for 1½ hours. The solution was cooled and acidified with 50% sulphuric acid with caution. The mixture was continuously extracted with ether to give a solid, crystallised from ether-petroleum ether (b.p. 40-60°), as 2-hydroxy-hexanoic acid[10] (14.5gm.), m.p.60-62°, ν_{max} (chloroform) 3800-2250, 1715cm^{-1}.

Ethyl 2-Hydroxy-Hexanoate (26).

A mixture of 2-hydroxy-hexanoic acid (14.5gm.), absolute ethanol (18ml.) and sodium dried benzene (28ml.) was added with concentrated sulphuric acid (0.2ml.). The resulting solution was refluxed overnight under a column topped with Dean and Stark apparatus. After cooling, the solution was successively washed with water, aqeous sodium bicarbonate solution (1 %), and water. Removal of the solvent and distillation gave ethyl 2-hydroxy-hexanoate[11] (11gm.), b.p. 64-66°, 2.5mm.Hg., ν_{max} (film) 3560, 1723cm^{-1}.

Ethyl 2-Keto-Hexanoate (27).

Chromic acid (21ml.; prepared from 17.5gms. of chromium trioxide in 50ml. of water and 14.8ml. of concentrated sulphuric acid) was added dropwise to ethyl 2-hydroxyhexanoate (9gm.) dissolved in acetone (A.R. 156ml.). The mixture was stirred for 2 hours. It was then filtered, diluted with water (235ml.) and after the addition of sodium metabisulphite extracted with ether to yield an oil accompanied by water. The water was separated and the oil dried.

Distillation in vacuum gave ethyl 2-keto-hexanoate[12] (4.5gm.), b.p. 62-65°, 2.5mm.Hg.; ν_{max} (film) 1740, 1723cm^{-1}.

Diethyl 1-carboethoxy-1-hydroxy-pentylphosphonate (28).

Ethyl 2-keto-hexanoate (1.70gm.) and diethylphosphite (1.49gm.) were added to a solution of sodium-ethoxide (74mg.) in ethanol (5ml.). The resulting mixture was stirred overnight. It was then worked up in the usual way to yield an oil.

Distillation in vacuum gave diethyl 1-carboethoxy-1-hydroxypentylphosphonate (2.23gm.), b.p. 100-104°, 0.07mm.Hg.; ν_{max} (film) 3475, 1740 shoulder, 1260, 1059, 1036, 980cm^{-1}.

(Found: C, 48.49; H, 8.34; $C_{12}H_{25}O_6P$ requires C, 48.65; H. 8.44%).

Attempted dehydration of diethyl 1-carboethoxy-1-hydroxypentylphosphonate to form diethyl 1-carboethoxy pent-1-enephosphonate (18).

The following reagents were tried on diethyl 1-carboethoxy-1-hydroxypentylphosphonate with no successful results, the material being recovered unchanged in almost all cases.

Phosphorous oxychloride-pyridine, thionyl chloride-pyridine, phosphorous pentoxide-benzene, boric acid, p-toluenesulphonic acid, polyphosphoric acid, Iodine, concentrated sulphuric acid, formic acid and borontrifluoride in ether.

Phosphorous oxychloride (2ml.) was added dropwise to the compound (28) 150mg., dissolved in pyridine (5ml.) at 0°. The mixture was left overnight at room temperature and then worked up as usual to yield ethyl 2-chlorohexanoate[13] (30mg.), identical with the authentic sample.

Diethyl 1-carboethoxy-1-chloro-pentylphosphonate (30).

Phosphorous pentachloride (3gm.) was added to cooled diethyl 1-carboethoxy-1-hydroxypentylphosphonate (4.05gm.) dissolved in carbontetrachloride (10ml.). The resulting mixture was refluxed for 5 hours and then worked up in the usual manner to yield an oil.

Distillation in vacuum gave the compound (30), b.p. 98°, 0.1mm.Hg.; ν_{max} 1740, 1260, 1060cm^{-1}.

Attempted dehydrochlorination of (30).

Refluxing the compound (30) with zinc in acetic acid as well as with lithium carbonate in dimethylformamide, failed to give the compound (18). On the otherhand, the starting material was recovered unchanged.

Diethyl Carboethoxymethylphosphonate (31).

Diethyl carboethoxymethylphosphonate, prepared as described by Freeman and Speziale[14], had b.p. 88°, 0.3mm.Hg.; ν_{max} (film) 1733, 1276, 1035cm^{-1}.

Ethyl hex-2-en-oate (32).

Butyraldehyde (3.6gm., freshly distilled) was condensed with the anion from diethyl carboethoxymethylphosphonate (11.2gm.) and sodium hydride (50%; 2.4gm.) in 1,2-dimethoxyethane in the usual way to yield ethyl hex-2-en-oate[15] (4.6gm.), b.p. 78-80°, 60mm.Hg., ν_{max} (film) 1725, 1655cm^{-1}.

Reaction of Phosphorouspentachloride with ethyl hex-2-en-oate.

An adduct[16] was formed by heating phosphorous pentachloride (2.25gm.) with ethyl hex-2-en-oate (1gm.) at 110° for 6 hours. The adduct on refluxing with ethanol (25ml.) gave a mixture of compounds which after separation through preparative thin layer chromatography (silica-gel, plates) was resolved into two main components. The minor component was proved to be triethylphosphite (80mgs.). The major product could not be assigned to any structure.

Diethyl 2-p-tosyl-3-methylmaleate (35).

p-toluene sulphonylchloride (1.063gm.) was added to diethyl oxalopropionate (1.13gm.), dissolved in pyridine (10ml.) and the mixture was stirred overnight. The reaction mixture was worked up in the usual manner to yield a viscous oil (0.63gm.).

Distillation in a microheating block gave diethyl 2-p-tosyl-3 methylmaleate, ν_{max} 1720, 1645, 1590, 1290, 1190cm^{-1}. The n.m.r. spectrum confirmed the formation of the compound.

(Found: C, 53.80; H, 5.75; $C_{16}H_{20}O_7S$ requires C, 53.93; H, 5.61%).

Attempted condensation of Diethyl 2-p-tosyl-3 methyl-maleate (35) with the sodium salt of diethylphosphite to form diethyl 2-diethylphosphono-3 methyl-maleate.

Diethyl 2-p-tosyl-3 methyl-maleate (470mgs.) was added to a stirred solution of the sodium salt of diethyl-phosphite, prepared from diethylphosphite (183mg.) and sodium hydride (53.3%, 61mg.) in dimethylformamide. The mixture was stirred overnight and it gave back the starting material unchanged on working up in the usual way.

Again, the compound (35) on treatment with the sodium salt of diethylphosphite (prepared[17] by metallic sodium and diethylphosphite in ether) in dimethylformamide also did not react.

Diethyl oxalo-bromo-propionate (36).

Bromine (3.42gm.) was added dropwise to a solution of diethyl oxalopropionate (4.32gm.) in carbontetrachloride (A.R.25ml.). The resulting mixture was refluxed for 4 hours.

Distillation in vacuum gave the compound (36), b.p. 60-64°, 0.05mm.Hg. The compound was confirmed by its n.m.r. spectrum.

Reaction of Diethyl oxalo-bromo-propionate (36) with diethylphosphite.

A mixture of diethyl oxalo-bromo-propionate (0.78gm.) and diethylphosphite (0.38gm.) was added to a solution of sodiethoxide (19mg.) in ethanol (5ml.). The solution was stirred overnight. On working up the mixture in the usual way, the starting material was recovered unchanged.

1,4-diethyl 2-hydroxy-2 diethylphosphono-3-methyl succinate (37).

A mixture of diethyl oxalopropionate (12.48gm.) and diethylphosphite (8.53gm.) was added to a solution of sodiumethoxide (0.42gm.) in ethanol (10ml.). The reaction mixture was stirred overnight at room temperature and then worked up in the usual manner to yield an oil (12.5gm.).

Distillation in vacuum gave Diethyl 2-hydroxy-2-diethylphosphono-3-methyl succinate (9.8gm.), b.p. 112-116°, 0.06mm.Hg.; ν_{max} (film) 3480, 1740, 1640, 1270, 1040cm^{-1}

(Found: C, 45.94; H, 7.35; $C_{13}H_{25}O_8P$ requires C, 45.88; H, 7.35%).

Dehydration of Diethyl 2-hydroxy-2-diethylphosphono-3-methyl succinate by phosphorous oxychloride and pyridine.

A solution of diethyl 2-hydroxy-2-diethylphosphono-3-methyl succinate (500mg.), in dry pyridine (6ml.) was treated with phosphorous oxychloride (4ml.). The solution was left to stand at 0° overnight. It was then diluted with water and extracted with ether to yield an oil (125mg.), ν_{max} (film) 1725, 1625, 1265, 1040cm^{-1}. The n.m.r. spectrum showed the oil containing 50% of (34).

Ethyl Citraconate (38).

Citraconic acid (13.6gm.) was esterified with ethanol (85ml.) and concentrated sulphuric acid (1ml.) in benzene (125ml.). The mixture after working up in the usual way was distilled to give ethyl citraconate[18] (12.5gm.), b.p. 71.5°/0.6mm.Hg.; ν_{max} (film) 1725, 1649cm^{-1}.

Diethyl 2,3-dibromo-2 methyl succinate (39).

Diethyl citraconate (12.5gm.) and bromine (11gm.) in carbon tetrachloride (150ml., Analar), were irradiated at room temperature with a tungsten lamp for 3 hours, when the solution became colourless. Distillation in vacuum gave diethyl 2,3-dibromo-2 methyl succinate[19] (18.5gm.), b.p. 109-111°/1.4mm.Hg., ν_{max} (film) 1740cm^{-1}.

Diethyl 2-bromo citraconate (40).

Diethyl 2,3-dibromo-2 methyl succinate (18.5gm.) and pyridine (9gm.) were heated at 120° for 30 minutes. The mixture was cooled, acidified with dilute sulphuric acid (2N), added with a large volume of water and then extracted with ether. The ethereal extract, after washing with

sodium bicarbonate and water, was dried to give a colourless liquid.

Distillation gave diethyl 2-bromocitraconate (9.5gm.), b.p. 94-96°/0.7mm.Hg.; ν_{max} (film) 1725, 1625cm^{-1}.

(Found: C, 41.10; H, 5.05; $C_9H_{13}BrO_4$ requires C, 40.77; H, 4.94%).

Reaction of Diethyl 2-bromo-citraconate with triethylphosphite to form vinyl (34) and allyl (33) phosphonates.

Diethyl 2-bromocitraconate (6gm.) was heated with triethylphosphite (7.5gm.) at 150° for 18 hours.

Distillation gave a mixture of vinyl (34) and its isomeric allyl (33) phosphonate (3.5gm.), b.p. 108°/0.03mm. Hg.; ν_{max} (film) 1725, 1625, 1265, 1040cm^{-1}.

(Found: C, 48.22; H, 6.95; $C_{13}H_{23}PO_7$ requires C, 48.44; H, 7.19%).

Diethyl cis- and trans-propylfulgenates (13.C), (13.t).

The mixture of vinyl and allyl phosphonates (1.3gm.) dissolved in dry tetrahydrofuran (20ml.) was added to a stirred slurry of sodium hydride (53.3%; 182mg.) in

tetrahydrofuran (40ml.). The mixture was stirred for 1 hour and then butyraldehyde (freshly distilled, 1.32gm.) dissolved in tetrahydrofuran (20ml.) was added. The reaction mixture was stirred for 24 hours at 50° and then worked up as usual to yield an oil which was purified by preparative thin layer chromatography, eluting with chloroform-benzene (1:1) to give cis- and trans- diethyl-propylfulgenates (1:1 mixture), (0.560gm.), b.p. 90-95°/0.05mm., ν_{max} (film) 1723, 1643, 1625cm^{-1}.

(Found: C, 64.96; H, 8.46; $C_{13}H_{20}O_4$ requires C, 64.98; H, 8.39%).

Synthesis of 1:3 dienes.

Allyl phosphonate (41).

Allyl bromide (22.8gm.) was added to triethylphosphite (freshly distilled, 31.3gm.) and the mixture was heated at 160° for 3 hours in an atmosphere of nitrogen. The resulting liquid on distillation gave allyl phosphonate[20,21] (26.2gm.), b.p. 52°, 0.15mm.Hg.; $n_D^{22.5}$ 1.413; ν_{max} (film) 1630, 1258, 1038cm^{-1}.

Isomerisation of allyl phosphonate to vinyl phosphonate. (Diethyl propenylphosphonate)(42).

Allyl phosphonate (3.26gm.) was added dropwise to a stirred slurry of sodium hydride (60%, 0.733gm.) in dry 1,2-dimethoxyethane (20ml.). The mixture was stirred overnight and then worked up in the usual way to yield an oil (0.80gm.).

Distillation in vacuum gave Diethyl propenylphosphonate[22,23] (0.53gm.), b.p. 50-56°, 0.3mm.Hg.; ν_{max} (film) 1635, 1240, 1040, 980cm^{-1}. The compound was confirmed by its n.m.r. spectrum.

(Found: C, 46.90; H, 8.69; $C_7H_{15}O_3P$ requires C, 47.19; H, 8.42%).

Allylidine Cyclohexane (43).

Sodium hydride (53.3%, 1.146gm.) was added to a mixture of allyl phosphonate (4.25gm.) and cyclohexanone (2.34gm.) dissolved in dry 1,2-dimethoxyethane (40ml.). The reaction was complete within 2 hours. The mixture was then diluted with water and extracted with ether to yield an oil (3.5gm.).

Distillation under reduced pressure gave allylidine cyclohexane[24] (1gm.), b.p. 80°/35mm.Hg.; ν_{max} (film) 1645, 1605, 995, 905cm^{-1}; λ_{max} (cyclohexane) 237mμ; (ϵ29,170).

(Found: C, 88.63; H, 11.54; C_9H_{14} requires C, 88.53; H, 11.47%).

Improved method of preparing allylidine cyclohexane.

Allyl phosphonate (5gm.) and cyclohexanone (2.76gm.) dissolved in dimethoxyethane (10ml.), were added to a stirred slurry of oil-free sodium hydride (50%, 1.35gm.; oil removed by washing with petrolether) suspended in dry 1,2-dimethoxyethane (40ml.), at -10°C. The temperature was maintained at -10°C. for 3 hours and the mixture was then worked up in the usual way to yield an oil (2.50gm.).

Distillation under vacuum gave pure allylidine cyclohexane (1.65gm.), identical to the above sample.

Purification of the oil through column chromatography.

The oil (1.55gm.) obtained by the above method, was run into an alumina column (60gms., grade III) eluted with benzene. A rapid elution gave the pure allylidine cyclohexane (0.4gm.). Later on, an identified solid (0.20gm.) and the vinyl phosphonate (0.30gm.) were also obtained from the column. The solid m.p. 85-87°, crystallised from ethanol-petrol and sublimed at 55°/ 0.35mm.Hg., had ν_{max} (nujol) 3340, 1645, 1465, 1380, 980, 855cm^{-1}; λ_{max} (cyclohexane) 237, 244, 251mμ (ε22,400). The mass spectrum of the compound showed the molecular weight 202, and elemental analysis gave C = 81.5% and H = 10.9%.

Preparation of allylidine cyclohexane using different basic media.

Allyl phosphonate (1gm.) and cyclohexanone (0.55gm.) were added to a stirred slurry of potassium-t-butoxide (64mg.) in D.M.F. (10ml.) and the mixture was stirred overnight. Normal work-up of the mixture gave a product (·35gm.) which on distillation gave allylidine cyclohexane (0.10gm.), identical to the previous sample.

1-Phenyl 1:3-Butadiene (44).

A mixture of allyl phosphonate (5gm.) and benzaldehyde (freshly distilled, 3gm.) was added to a stirred slurry of sodium hydride (53.3%, 1.43gm.) in dry 1,2-dimethoxyethane (40ml.). The resulting solution was stirred and then worked up to yield an oil.

Distillation under reduced pressure gave 1-phenyl 1:3-butadiene[25,26,27] (1.1gm.), b.p. 100°/20mm.Hg.; ν_{max} (film) 1630, 1603, 1015, 915, 760, 700cm^{-1}; λ_{max} (cyclohexane) 205, 208, 219, 226, 233, 280, 306mμ (ε29,800).

(Found: C, 92.50; H, 7.45; $C_{10}H_{10}$ requires C, 92.30; H, 7.7%).

1,1-diphenyl 1:3-butadine (45).

Sodium hydride (50%, 1.114gm.) was added to a solution of allyl phosphonate (4gm.) and benzophenone (1gm.) dissolved in dry 1,2-dimethoxyethane (40ml.). The mixture was stirred and the reaction was complete within 3 hours. It was then worked up in the usual manner to yield a viscous oil. The oil was chromatographed in a silica-gel column, eluting with petrol ether (40-60°), when the oil present in sodium hydride was removed. Later on, elution with benzene gave 1,1-diphenyl 1:3-butadine (110mg.),

a solid m.p. 34-35°; ν_{max} (nujol) 1645, 1610, 1590, 915, 765, 700cm^{-1}. λ_{max} (cyclohexane) 285mμ (ε9,500).

(Found: C, 92.99; H, 6.96; $C_{16}H_{14}$ requires C, 93.2; H, 6.8%).

1-phenyl 1-methyl 1:3-butadiene (46), (47).

Reaction of allyl phosphonate (4gm.) with acetophenone (1gm.) under the identical condition as applied in the case of the compound (45), yielded after chromatography, a liquid having ν_{max} (film) 1640, 1608, 1590, 915cm^{-1} and λ_{max} (cyclohexane) 260mμ. The n.m.r. spectrum showed the liquid to be a mixture of cis and trans 1-phenyl 1-methyl 1:3-butadiene (46) and (47).

1:3-Heptadiene (48).

Sodium hydride (50%, 1.1gm.) was added to a mixture of allyl phosphonate (4gm.) and butyraldehyde (1.62gm.), dissolved in dry 1,2-dimethoxyethane (40ml.), kept at -10°C. The mixture, maintained at that temperature, was stirred for 4 hours and then left overnight at room temperature. The resulting solution, after working up gave a liquid which on distillation yielded 1:3-heptadiene[28] (0.3gm.), b.p. 70°, 6cm.Hg., ν_{max} (film) 1640, 1600, 1010, 960cm^{-1},

λ_{max} 228mμ (ϵ21,600).

(Found: C, 87.64; H, 12.69; C_7H_{12} requires C, 87.50; H, 12.5%).

1,1-diethyl 1:3-butadiene (49).

(a) Reaction of allyl phosphonate (4gm.) with diethyl ketone (2gm.) under the identical condition as applied in the case of the compound (48), yielded a liquid which on distillation gave 1,1-diethyl 1:3 butadiene (100mg.), b.p. 50°/13c.m.Hg.; ν_{max} (film) 1640, 1595, 995, 900cm^{-1}.

(Found: C, 87.45; H, 12.64; C_8H_{14} requires C, 87.27; H, 12.73%).

(b) The mixture of allyl phosphonate (4gm.) and diethyl ketone (2gm.), was added to a solution of potassium-t-butoxide (2.52gm.) in dimethylformamide (40ml.) and stirred for 3 hours. Work up as usual and distillation gave 1,1-diethyl 1:3 butadiene (70mg.), b.p. 50°/13cm.Hg.; identical with the above compound.

Allylidine Cholestane (50).

Allyl phosphonate (0.9gm.) and cholestanone (0.30gm.) dissolved in dimethoxyethane, were added to a slurry of sodium hydride (60%, 0.20gm.) in dimethylformamide (25ml.).

The mixture was heated at 80° overnight and then worked up as usual to yield on oil. The oil was purified in preparative thin layer chromatography, to give allylidine cholestane, m.p. 52-53°; ν_{max} (film) 1640, 1590, 1010, 900cm^{-1} and λ_{max} 234, 241, 249mμ.

Crotyl Phosphonate (51).

Freshly distilled crotyl bromide (13.5gm.) was added with triethylphosphite (distilled, 16.6gm.) and the mixture heated at 150° for 2 hours in an atmosphere of nitrogen.

Distillation gave Crotyl phosphonate[29] (16.5gm.), b.p. 56°, 0.35mm.Hg.; ν_{max} (film) 1640, 1256, 1036, 976cm^{-1}.

1-Cyclohexylidine-2-butene (52).

(a) Crotyl phosphonate (1.92gm.) dissolved in dry 1,2-dimethoxyethane (5ml.) was added dropwise to a slurry of sodium hydride (60%, 0.40gm.) in dimethoxyethane (40ml.). After some time the solution became clear. Cyclohexanone (0.98gm.) dissolved in dimethoxyethane (5ml.) was then added to it and the mixture was stirred overnight.

Work up as usual gave an oil 1.38gm. which on distillation yielded 1-cyclohexylidine-2-butene[30] (0.2gm.), b.p. 82-83°, 20mm.Hg. The yield was diminished to a great extent on distillation.

(b) Crotyl phosphonate (0.48gm.) was added to a stirred slurry of oil-free sodium hydride (60mg.) in dry 1,2 dimethoxyethane (25ml.). After some time, cyclohexanone (0.25gm.) was added and the mixture stirred overnight. Work up as usual gave an oil 0.351gm. which was chromatographed in an alumina column eluting with petroleum ether (40-60°), to yield 1-cyclohexylidine-2-butene 0.230gm. Later on, a gummy material (30mg.) was obtained from the column.

The compound had ν_{max} (film) 1645, 1610, 970cm^{-1} and λ_{max} 235, 241, 249mμ (ε21,168).

(Found: C, 88.10; H, 11.57; $C_{10}H_{16}$ requires C, 88.23; H, 11.77%).

Geranyl Bromide (54).

Phosphorous tribromide (10gm.) was added dropwise to a solution of geraniol (freshly distilled, 15.4gm.) in dry ether (150ml.), kept at 0°. When the addition was complete the mixture was refluxed for 2½ hours.

The resulting solution was cooled, added to ice-cold water and then extracted with ether. The ethereal extract was washed with saturated sodium bicarbonate solution, water and then dried. Distillation gave geranyl bromide[31] (12.5gm.), b.p. 52-56°, 0.25mm.Hg.

Geranyl Phosphonate (55).

Geranyl bromide (11.22gm.) and triethylphosphite (distilled, 9.6gm.) were heated at 160° for 3 hours.

Distillation gave geranyl phosphonate (11.5gm.), b.p. 107-109°, 0.3mm.Hg., ν_{max} (film) 1650, 1630, 1250, 1035, 965cm^{-1}.

Geranylidine Cyclohexane (56).

Sodium hydride (60%, 0.12gm.) was made oil-free by washing with petroleum ether several times and then the slurry was made in dimethylformamide. Geranyl phosphonate (0.822gm.) and cyclohexanone (0.294gm.) were then added to the slurry and the mixture was heated at 80° for 2 hours. Work up as usual gave an oil (0.40gm.) which was chromatographed in a silica-gel column, eluting with benzene, to yield geranylidine cyclohexane (0.14gm.), ν_{max} (film) 1605, 1440, 980, 850cm^{-1}, λ_{max} 243, 251,

259mμ (ε38000).

(Found: C, 87.86; H, 12.20; $C_{16}H_{26}$ requires C, 88.00; H, 12.00%).

Bromination of allyl phosphonate (57).

Bromine (19.2gm.) was added dropwise to a cooled solution of allyl phosphonate (21.3gm.) in ethanol (50ml.). The mixture was stirred overnight and then worked up as usual.

Distillation gave the dibromo compound (57) 34.55gm., b.p. 113-120°/0.5mm.Hg., ν_{max} (film) 1245, 1030, 975cm^{-1}.

Monobromo-allyl and vinyl phosphonates (58a), (58b).

The dibromo phosphonate (57), 8.7gm., was added to a solution of sodium ethoxide (1.75gm.) in ethanol (40ml.) and the mixture was stirred for 3 days. It was worked up in the usual way and then distilled to yield a mixture of monobromo allyl and vinyl phosphonates, (4gm.) b.p. 90-94°, 0.4mm.Hg., ν_{max} (film) 1632, 1240, 1040, 980cm^{-1}.

The n.m.r. spectrum showed the mixture to be of 1:1 ratio.

Ethoxy-allyl phosphonate (59).

The dibromo phosphonate (57), 10.5gm., was added to a solution of sodium ethoxide (4.5gm.) in ethanol (60ml.) and the mixture was refluxed for 6 hours. Normal work up and distillation gave ethoxy allyl phosphonate[32] (59), 3.5gm., b.p. 65-68°, 0.8mm.Hg., ν_{max} (film) 1658, 1380, 1250, 1040, 980cm^{-1}.

(Found: C, 48.55; H, 8.54; $C_9H_{19}PO_4$ requires C, 48.64; H, 8.55%).

Condensation of bromo-phosphonates (58.a), (58.b) with Cyclohexanone (60).

Condensation of the bromo phosphonates (1.028gm.) with cyclohexanone (0.392gm.) in the presence of sodium hydride (60%, 0.160gm.) and dimethoxyethane (25ml.) by the normal procedure gave a liquid which was purified in preparative thin layer chromatography to yield the diene (60), 46 mg., λ_{max} 248, 253, 262mμ.

Condensation of ethoxy phosphonate (59) with cyclohexanone (61).

The mixture containing ethoxy phosphonate (0.42gm.), cyclohexanone (0.19gm.) and sodium hydride (60%, 80mg.) in dimethoxyethane (25ml.) was heated at 70° for 5 hours.

Work up as usual gave a liquid which was purified in preparative thin layer chromatography to yield the diene (61), (10mg.), λ_{max} 228, 254, 264mμ. The compound decomposed rapidly.

Diethyl 1-hydroxy propyl phosphonate (62).

Propionaldehyde (distilled, 4gm.) and diethyl-phosphite (9.6gm.) were added to a solution of sodium ethoxide (0.47gm.) in ethanol (10ml.). The mixture was stirred overnight and then extracted continuously with ether to give a liquid, which was distilled to yield diethyl 1-hydroxy propyl phosphonate (5.1gm.), b.p. 90-94°, 0.25mm.Hg.; ν_{max} (film) 3300, 1210, 1030, 970cm^{-1}.

Diethyl 1-acetoxy-propyl phosphonate (63).

Acetic anhydride (excess, 5ml.) was added to a solution of diethyl 1-hydroxy propyl phosphonate (1.48gm.) in pyridine (5ml.) and the mixture stirred for 12 hours. It was refluxed for another 2 hours and then worked up as usual.

Distillation gave diethyl 1-acetoxy-propyl-phosphonate (1.1gm.), b.p. 66-68°, 0.25mm.Hg.; ν_{max} (film) 1740, 1225, 1040, 980cm^{-1}.

Pyrolysis of (63).

Diethyl 1-acetoxy-propyl phosphonate (250mg.) was heated to 190° on a metal bath for 3 hours and then distilled to give diethyl propenyl phosphonate (42), 50mg., b.p. ~170°; ν_{max} (film) 1635, 1240, 1040, 980cm^{-1}.

Attempted condensation of diethyl propenyl phosphonate with cyclohexanone.

The mixture of diethyl propenyl phosphonate (0.47gm.) and cyclohexanone (0.26gm.) added to the stirred slurry of sodium hydride (60%, 0.107gm.) was stirred overnight. Work up as usual yielded a liquid shown to be the mixture of the starting materials unchanged.

Tetraethyl methane diphosphonate (64).

Methylene iodide (26.7gm.) was added to triethyl phosphite (distilled, 34gm.) and the mixture was heated at 160°. During the reaction ethyl iodide formed was distilled off. The residual mixture was further heated at 170° for 2 hours.

Distillation gave a number of products including tetraethyl methane diphosphonate[33], (2gms.) 135-140°, 0.3mm.Hg.

Diethyl pent-1-ene phosphonate (65).

Tetraethyl methanediphosphonate (222mg.) dissolved in dimethoxyethane (2ml.) was added dropwise to a stirred slurry of sodium hydride (50%, 37mg.) in dimethoxyethane (20ml.) when a clear solution was obtained. Butyraldehyde (distilled, 56mg.) dissolved in dimethoxyethane (2ml.) was then added to it and the mixture stirred for 20 hours. Work up of the mixture in the usual way gave a liquid which was purified in preparative thin layer chromatography to yield diethyl pent-1-ene phosphonate (23mg.), ν_{max} (film) 1630, 1250, 1040, 980, 840cm^{-1}. The n.m.r. spectrum proved the structure of the compound.

The condensation of this compound (65) with cyclohexanone under usual conditions failed and the starting material was recovered.

Diethyl 2-chloro-octyl phosphonate (66).

Octene-1 (8gm.) was added dropwise to a slurry of phosphorous pentachloride (15gm.) in dry benzene (50ml.) kept at 0°, and the mixture stirred for two days to form an adduct. Phosphorous pentoxide (4gm.) was then added to the adduct and the mixture was stirred at room

temperature (2 hours), at 35° (2 hours) and then at 55° for another 2 hours. It was filtered, solvent removed and distilled. The distillate (6.5gm.) added dropwise to ethanol (25ml.) was stirred for 8 hours.

Distillation gave diethyl 2-chloro-octyl phosphonate (4.6gm.), b.p. 106-108°, 0.3mm.Hg.; ν_{max} (film) 1260, 1040, 980cm^{-1}.

Diethyl oct-1-ene phosphonate (67).

Diethyl 2-chloro-octyl phosphonate (2.27gm.) was added to a solution of sodium ethoxide (0.55gm.) in ethanol (10ml.) and the mixture stirred overnight. Work up as usual gave diethyl oct-1-ene phosphonate[34] (1.52gm.), ν_{max} (film) 1625, 1250, 1040, 975cm^{-1}.

Attempted condensation of diethyl oct-1-ene phosphonate with cyclohexanone.

The reaction of diethyl oct-1-ene phosphonate (24.8mg.) with cyclohexanone (98mg.) in the presence of sodium hydride (60%, 40mg.) in dimethoxyethane under identical conditions gave a liquid shown to be a mixture of the starting materials.

Diethyl 3-bromo-oct-1-ene phosphonate (68).

N-bromosuccinimide (115mg.) was added to a solution of diethyl oct-1-ene phosphonate (124mg.) in carbontetrachloride (Analar, 10ml.), and the mixture was refluxed. A few crystals of benzoylperoxide were added to initiate the reaction. After 20 minutes when the reaction was complete, the mixture was cooled, filtered and the solvents removed to yield an oil which was purified by preparative thin layer chromatography, to give diethyl 3-bromo-oct-1-ene phosphonate (62mg.), ν_{max} (film) 1633, 1255, 1040, 980cm^{-1}.

Diethyl oct-2-ene phosphonate (69).

Zinc dust (A.R. 350mg.) was added to a cooled and stirred solution of diethyl 3-bromo-oct-1-ene phosphonate (112mg.) in acetic acid (A.R. 5ml.) and the mixture was stirred for 2 hours. It was filtered, added with water, extracted with ether and the ethereal layer washed with saturated sodium bicarbonate solution and water to yield an oil. Distillation gave diethyl oct-2-ene phosphonate (80mg.), (bath temperature 82°), 0.3mm.Hg.; ν_{max} (film) 1628, 1250, 1040, 975cm^{-1}.

Synthesis of Cross-conjugated Compounds

Diethyl 1-carboethoxy-but-2-enyl phosphonate (70).

Methyl lithium (1.67M, 6ml.) was injected into a solution of crotyl phosphonate (1.92gm.) in dry ether (25ml.) kept at -20°C. Pure and dry nitrogen gas was bubbled through the solution until the reaction was complete. After 5 minutes of the addition of methyl lithium, diethylcarbonate (1.2gm.) was added to the reaction mixture and stirred for 2 hours. The resulting solution was acidified with dilute hydrochloric acid and extracted with ether to yield a liquid (2gm.) which was purified by chromatography in a silica-gel column, eluting with ethyl acetate, to give diethyl 1-carboethoxy-but-2-enyl phosphonate (1.3gm.), distilled at 82°, 0.35mm.Hg.; ν_{max} (film) 1725, 1645, 1255, 1040, 980cm^{-1}.

(Found: C, 49.94; H, 7.85; $C_{11}H_{21}O_5P$ requires C, 49.99; H, 7.95%).

Further elution with ethyl acetate yielded unreacted crotyl phosphonate (290mg.).

Condensation of diethyl 1-carboethoxy-but-2-enyl phosphonate with butyraldehyde (70.a), (70.b).

Diethyl 1-carboethoxy-but-2-enyl phosphonate (264mg.) dissolved in dry tetrahydrofuran (2ml.) was added dropwise to a stirred slurry of sodium hydride (60%, 50mg.) in tetrahydrofuran (10ml.). After 20 minutes, butyraldehyde (72mg.) in tetrahydrofuran (2ml.) was added and the mixture stirred for 12 hours. Usual work up and then purification in preparative thin layer chromatography gave the diene ester (50mg.), ν_{max}(film) 1715, 1640, 1625, 1240, 1220, 970cm^{-1}, λ_{max} 235mμ (ε5950).

The n.m.r. spectrum showed a mixture (1:1) of isomeric compounds.

Condensation of diethyl 1-carboethoxy-but-2-enyl phosphonate with cyclohexanone (71).

Condensation of diethyl 1-carboethoxy-but-2-enyl phosphonate (264mg.) with cyclohexanone (98mg.) in the presence of sodium hydride (50mg.) in tetrahydrofuran at 60°C under the above procedure gave (71) 21mg., λ_{max} 230, 290mμ.

Condensation of crotyl phosphonate with ethyl butyrate (72).

The anion of crotyl phosphonate formed by the action of methyl lithium (6ml.) on crotyl phosphonate (1.92gm.), condensed with ethyl butyrate (1.2gm.) under the same procedure as described for (70), to yield the corresponding 0.95gm. of keto phosphonate (72), ν_{max} (film) 1710, 1640, 1245, 1030, 980cm^{-1}.

(Found: C, 55.08; H, 9.05; $C_{12}H_{23}O_4P$ requires C, 54.96; H, 8.77%)

Condensation of (72) with butyraldehyde (73).

The anion of the compound (72), (formed by treating keto phosphonate (262mg.) with sodium hydride (40mg.) in tetrahydrofuran) was condensed with butyraldehyde (72mg.) under the procedure as applied for (70.a) and (70.b), to form the diene 22mg. ν_{max} (film) 1690, 1670, 1610, 970cm^{-1}; λ_{max} 232mμ (ϵ5040).

Condensation of (72) with cyclohexanone (74).

Cyclohexanone (98mg.) was condensed with the anion of (72), formed by treating (72), (262mg.), with sodium hydride (40mg.) in tetrahydrofuran, in the manner as described in (71), to give (74), 20mg., λ_{max} 247, 252mμ.

Alkylation of Crotyl phosphonate with decylbromide (75).

The anion of crotyl phosphonate obtained by adding methyl lithium (1.5ml.) on crotyl phosphonate (480mg.), was condensed with decylbromide (550mg.) in the manner as described for (70), to give diethyl 1-decyl-but-2-enyl phosphonate (250mg.), ν_{max} (film) 1630, 1240, 1090, 980cm^{-1}.

(Found: C, 63.87; H, 11.27; $C_{18}H_{37}O_3P$ requires C, 64.09; H, 11.14%).

Reaction of allyl phosphonate (41) with diethylcarbonate (76).

Allyl phosphonate (468mg.), diethylcarbonate (311mg.) and sodium hydride (50%, 128mg.) in dimethoxyethane (20ml.), were stirred for 3 days. The mixture was worked up and extracted continuously with ether to yield a liquid which was distilled to give (76), 200mg., b.p. 70-75°, 0.2mm.Hg.; ν_{max} (film) 1630, 1235, 1035, 975cm^{-1}.

(Found: C, 42.85; H, 7.83; $C_{13}H_{26}P_2O_7$ requires C, 42.60; H, 7.1%).

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