SYNTHESIS OF POLYENES VIA PHOSPHONIUM YLIDS

H.J. Bestmann

Institut für Organische Chemie der Universität Erlangen-Nürnberg
D-8520 Erlangen, Henkestr. 42

Summary

The mechanism of the Wittig reaction is discussed on the basis of recent experimental
results. Our observations allow us to predict the stereochemistry of olefines formed by
carbonyl olefination with phosphorus ylids or phosphonate anions .
Deuterium or tritium may be incorporated into the resulting olefines. Synthetic routes to
"symmetric" carotenoids by oxidative dimerisation and the synthesis of "unsymmetric" polyenes
using polymeric carriers are discussed. Two approaches to ene-yne-compounds via phosphorus
ylids are presented.

Wittig's carbonyl olefination is a key reaction in preparative polyene chemistry [1] [2]. In
spite of the great importance of the Wittig reaction its mechanism remains unclear. The pre-
viously proposed mechanisms [3] [4] can not satisfactorily interpret the experimentally ob-
served stereochemistry. In the following the results of our investigations on the course of
the reaction between carbonyl compounds and alkylidenephosphoranes are reported. The conse-
quences of these investigations for the stereochemistry of polyene synthesis via the Wittig
reaction and the possibility of incorporating tritium and deuterium during the polyene
synthesis will be discussed.

Our studies indicate the following mechanism for the Wittig reaction [5]:
The oxaphosphetanes 3 are formed from ylid and aldehyde in a 2 + 2-cycloaddition giving
rise to a signal at δ = 60 - 70 ppm (H_3PO_4 as external standard) in the ^{31}P-NMR-spectrum [6].
The preliminary formation of the postulated [3] [4] [7] betain intermediate was not found in
any case. Kinetic studies also argue against a multistep process in the formation of 3 [8].
The transition state for the formation of 3 is unknown. Assuming that the ylid approaches
the carbonylgroup in an angle of 107°, the following conformation 9 should represent the
approaching complex [9].
The electrostatic attraction between the positively charged P-atom and the negatively charged
oxygen increases as the formation of the new C-C-bond is completed. A rotation around the new
C-C-bond takes place in such a manner that the P-O-bond forms simultaneously, giving 3.
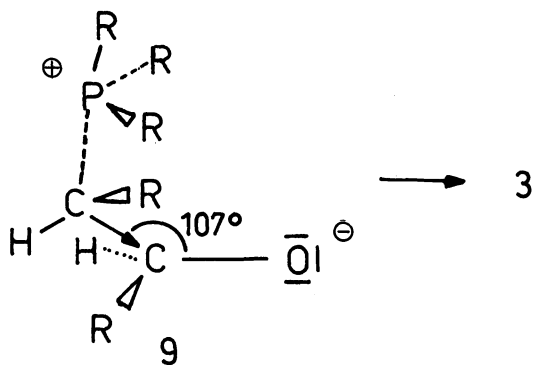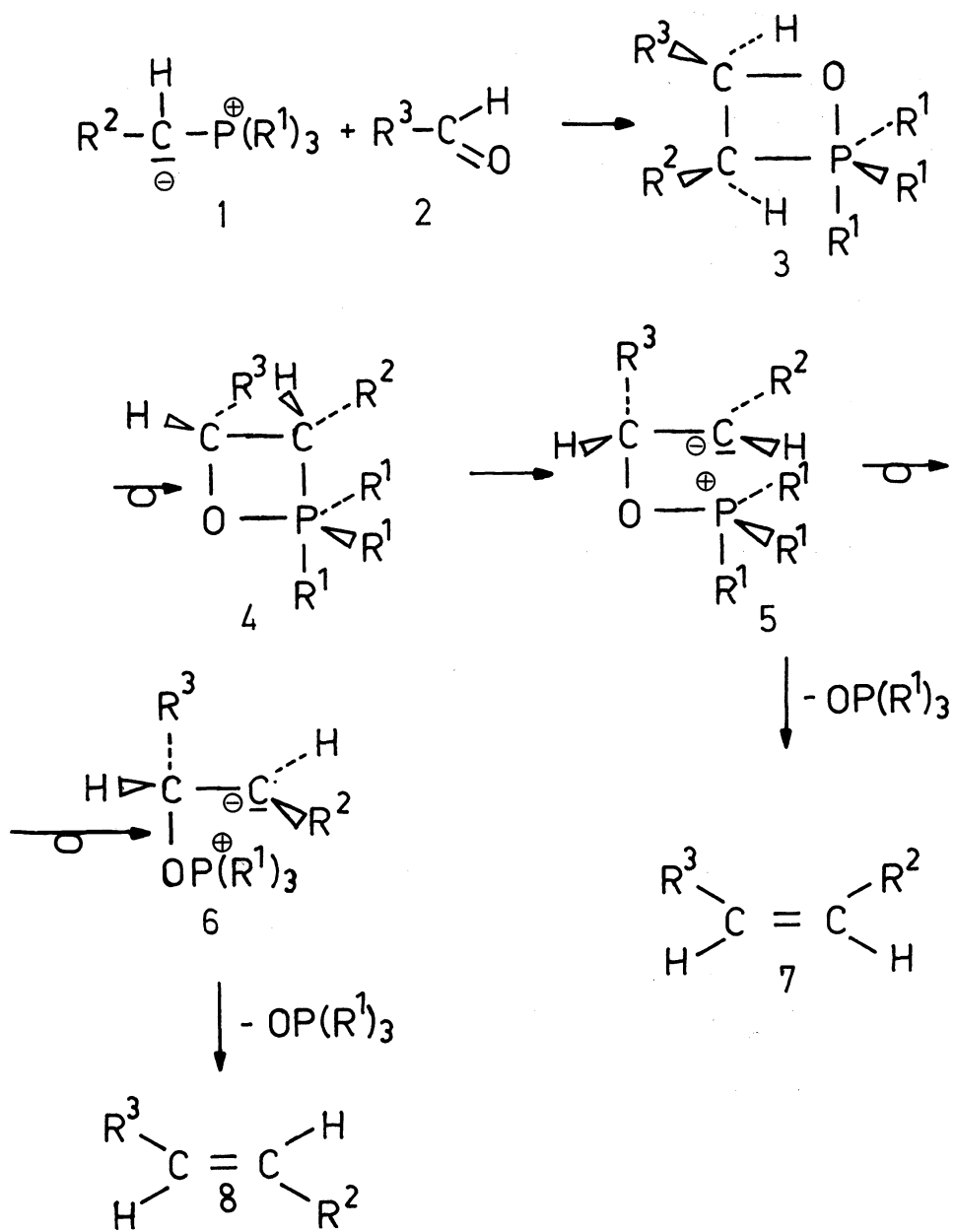
The arrangement of the ligands shown in 3, with axial oxygen, is based on the common rules governing the attack and the leaving of nucleophiles during the reciprocal formation of tetra- and penta-coordinated phosphorous compounds [10] as well as on the x-ray study of the adduct of hexaphenylcarbodiphosphorane with hexafluoracetone [11]. As the ^{31}P-NMR-spectra indicate oxaphosphetanes 5 are largely stable at temperatures below - 30°. The stability increases if R^1 = alkyl or cycloalkyl.

The breaking of the C-P-bond, which must take place in the course of the Wittig reaction can only be achieved if a rearrangement of the ligands (pseudorotation) takes place so that the C-P-bond becomes axial [12]. In the course of this rearrangement, or after the trigonalbipyra-midal structure 4 is formed, the C-P-bond collapses without a simultaneous opening of the C-O-bond, as it was previously assumed [3] [4]. The betain 5 is formed [13]. If R^2 is an electron donor and if the fixed ligands at the phosphorus are phenyl rings (R^1 = C_6H_5) the lifetime of 5 is very short; triphenylphosphineoxide is rapidly eliminated and Z-olefins 7 are formed. If however, R^2 is an electron acceptor (e.g. $COOCH_3$) the lifetime of 5 is prolonged. A rotation around the C-C-axis formed in the cycloaddition of 1 and 2 leads to the thermodynami-cally more stable conformational isomer 6, which splits off triphenylphosphineoxide yielding the E-olefin 8.

If the ligands R^1 are cyclohexyl groups the elimination of phosphineoxide from 5 is retarded so that a conformational change into 6 is possible [14]. As a consequence the proportion of the E-isomer in the reaction product increases markedly [15].
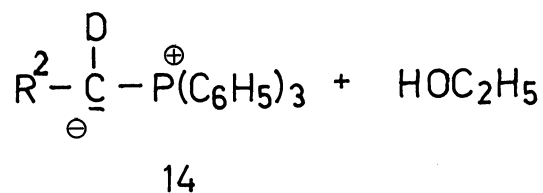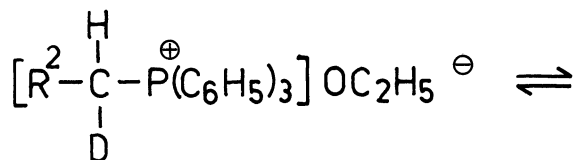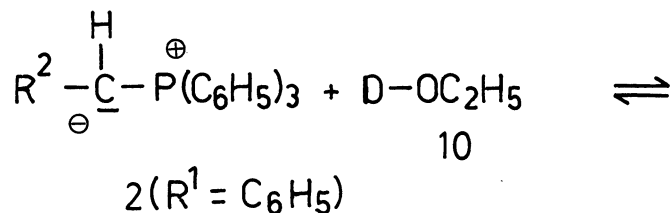
If the two components 1 (R^2=alkyl) and 2 are mixed together at -78° and ethanol is added, an increase in formation of the E-olefin is observed. If deuterated ethanol 10 is used, deuterium is incorporated into the molecule, the labeling being more extensive in the E-isomer than in the Z-isomer.

$$R^3 \diagdown C = C \diagup D \qquad + \quad HOC_2H_5 \quad + \quad OP(R^1)_3$$
$$H \diagup \qquad \diagdown R^2$$

$$13 \qquad\qquad\qquad 10$$
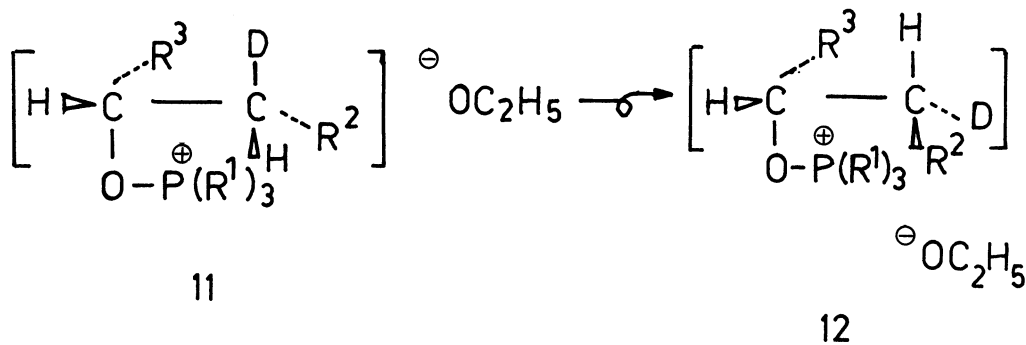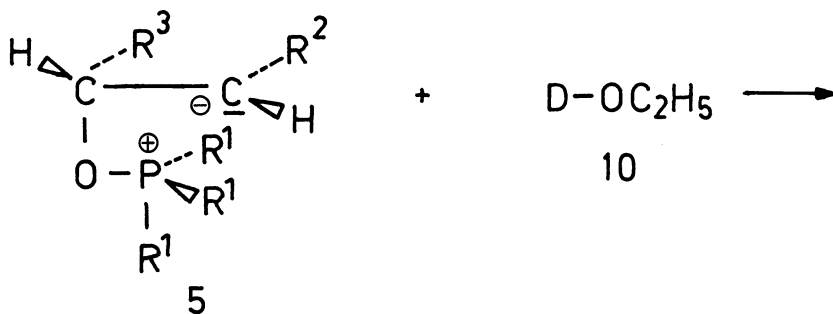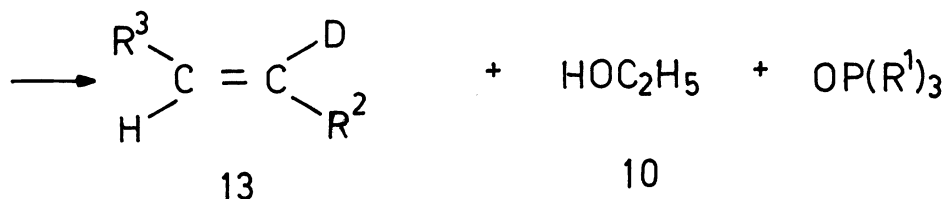
We suggest that the betain 5 reacts with 10 to give 11, whereby the incorporation of deuterium occurs preferentially from the backside of the original P-C-bond. The phosphonium alcoholate 11 may undergo a conformational rearrangement to give 12, from which 13 is formed by an anti-elimination.

In principle the incorporation of deuterium may also be explained by the fact that 3 dissociates into 1 and 2. In an equilibrium between 2 and 10 deuterium is than incorporated, with formation of 14 [16].

$$R^2 - \overset{\overset{\displaystyle H}{|}}{\underset{\ominus}{C}} - \overset{\oplus}{P}(C_6H_5)_3 \quad + \quad D-OC_2H_5 \qquad \rightleftharpoons$$

$$2\,(R^1 = C_6H_5) \qquad\qquad 10$$

$$\left[R^2 - \overset{\overset{\displaystyle H}{|}}{\underset{|}{C}} - \overset{\oplus}{P}(C_6H_5)_3 \right] OC_2H_5{}^{\ominus} \quad \rightleftharpoons$$
$$D$$

$$R^2 - \overset{\overset{\displaystyle D}{|}}{\underset{\ominus}{C}} - \overset{\oplus}{P}(C_6H_5)_3 \quad + \quad HOC_2H_5$$

$$14$$

However, the preferential incorporation of deuterium into the E-olefin and the following experimental results argue against this mechanism.

If one oxidizes the ylid 2 ($R^1=C_6H_5$) with the adduct 15 of triphenylphosphine and ozone [17] at -78° and adds 10, the resulting olefin 16 contains only one deuterium atom, which is incorporated at step 5. If the deuterium exchange were accomplished by the equilibrium 2⇌14 olefins with 2 deuterium atoms should also be formed.

We will now discuss the consequences of these results for the synthesis of deuterium labelled olefins, specially polyenes.

$$2 \; R^2 - \underset{\ominus}{\overset{H}{\underset{|}{C}}} - \overset{\oplus}{P}(C_6H_5)_3 \quad \xrightarrow[\substack{2) \; DOC_2H_5 \\ 10}]{\substack{1) \; O_3 \; \underset{15}{P}(OC_6H_5)_3/-78° }} \quad R^2 - \overset{H}{\underset{|}{C}} = \overset{D}{\underset{|}{C}} - R^2$$
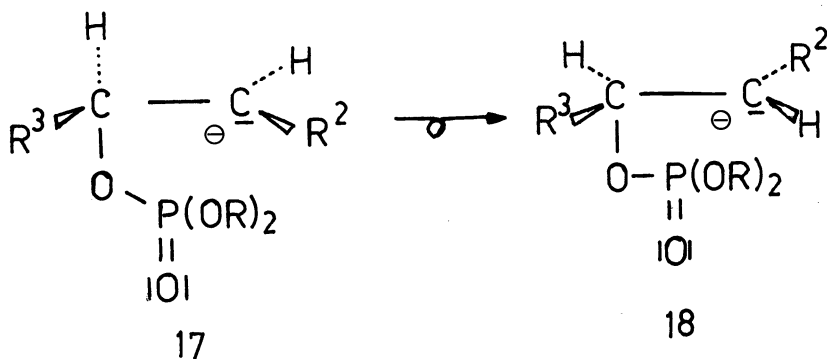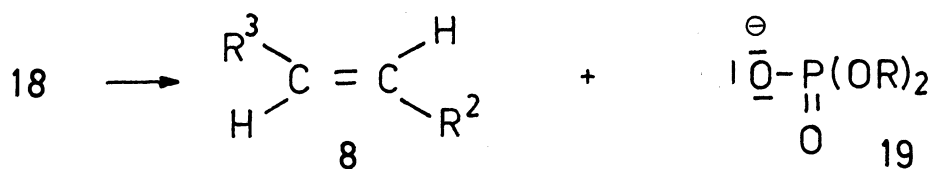
$$2\,(R'=C_6H_5) \qquad\qquad\qquad 16$$

$$+ \quad OP(C_6H_5)_3 \quad + \quad OP(OC_6H_5)_3$$
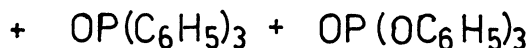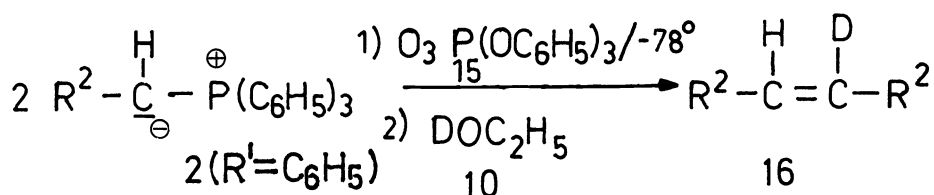
The following rules for the Wittig reaction with alkylidenephosphoranes result:
If electron donating groups (e.g. alkylgroups) are attached to the ylid C-atom, Z-olefines
are obtained stereoselectively. Working at low temperature we could achieve a Z-stereoselec-
tivity of 98%. In these experiments the use of sodium bis(trimethylsilyl)amide as a base to
generate the ylids from the corresponding phosphonium salts proved to be very successful [18].
Electron withdrawing groups at the ylid C-atom (e.g. ester groups) give rise to E-stereo-
selectivity. If the C-atom in α-position to the phosphorane is connected with a polyene
system mixtures of Z and E conformations at the newly formed C=C-double bond result.
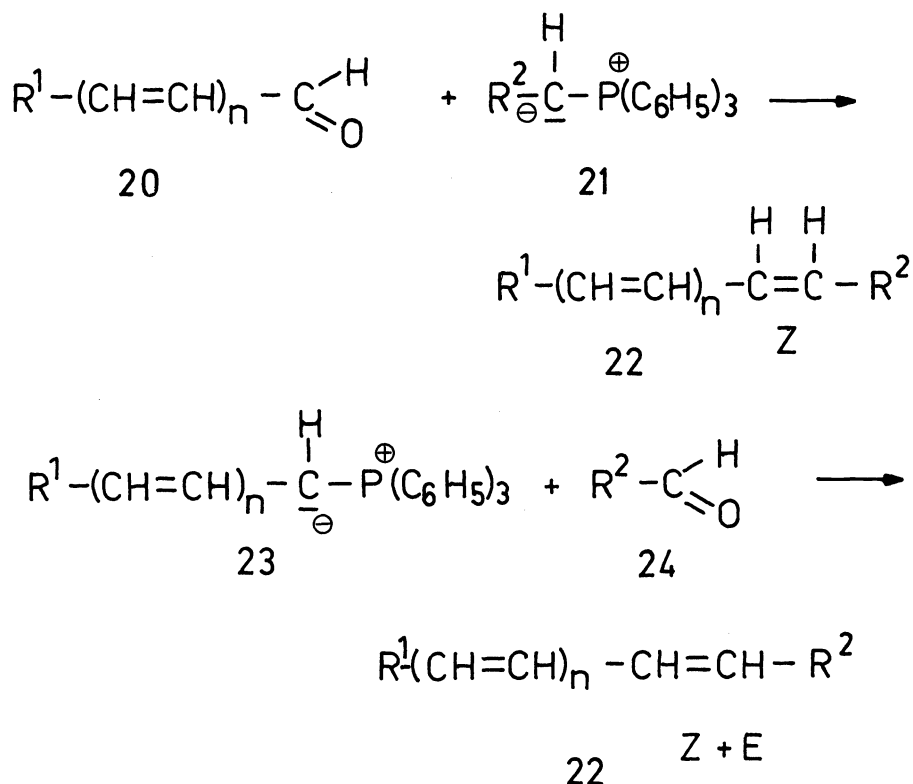
In all cases the proportion of the formed E-isomer increases if alcohol is added after the
reactants 1 and 2 have been mixed together at low temperature or if the reaction is carried
out in the presence of alcohol from the beginning. In the latter case however, the total
yields are smaller if ylids with R^2=alkyl-groups are used. The E-olefin is also formed on a
larger scale if higher temperatures are used or if the triphenylphosphonio group is substi-
tuted for a trialkyl- or tricycloalkylphosphonio group.

According to Horner, Wadworth and Emmons PO-activated olefination proceeds in a E-stereo-
selective fashion. In this case we also assume the same mechanism as discussed above. The
opening of the C-P-bond yielding the betain 18 results when the intermediates analogous to
3 and 4 have been formed. The elimination of the phosphate ester anion 19 takes place
slower than that of the triphenylphosphinoxide. In a conformational rearrangement 17 is con-
verted to 18, which decomposes into the E-olefin 8 and 19.

$$\underset{17}{\overset{H}{\underset{\substack{R^3 \nearrow C \\ | \\ O \searrow P(OR)_2 \\ \| \\ |O|}}{}} \underset{\ominus}{} \overset{H}{\underset{R^2}{C}}} \quad \xrightarrow{\;\sigma\;} \quad \underset{18}{\overset{H}{\underset{\substack{R^3 \nearrow C \\ | \\ O - P(OR)_2 \\ \| \\ |O|}}{}} \underset{\ominus}{} \overset{R^2}{\underset{H}{C}}}$$

$$18 \longrightarrow \begin{matrix} R^3 \\ \diagdown \\ H \diagup \end{matrix} C = C \begin{matrix} \diagup H \\ \diagdown R^2 \end{matrix} \qquad + \qquad | \overset{\ominus}{\underline{O}} - \underset{\underset{O}{\|}}{P}(OR)_2$$

$$\qquad\qquad\qquad\qquad\qquad 8 \qquad\qquad\qquad\qquad\qquad\qquad\qquad 19$$

For the synthesis of polyenes the following consequences result:

$$R^1-(CH=CH)_n - C\overset{\diagup H}{\underset{\diagdown O}{}} \qquad + \qquad R^2 \overset{H}{\underset{\ominus}{\underline{C}}} - \overset{\oplus}{P}(C_6H_5)_3 \longrightarrow$$

$$\qquad\qquad 20 \qquad\qquad\qquad\qquad\qquad 21$$

$$R^1-(CH=CH)_n - \overset{H}{\underset{}{C}}=\overset{H}{\underset{}{C}} - R^2$$

$$\qquad\qquad\qquad 22 \qquad\qquad Z$$

$$R^1-(CH=CH)_n - \overset{H}{\underset{\ominus}{C}} - \overset{\oplus}{P}(C_6H_5)_3 \quad + \quad R^2 - C\overset{\diagup H}{\underset{\diagdown O}{}} \longrightarrow$$

$$\qquad\qquad 23 \qquad\qquad\qquad\qquad 24$$

$$R^1(CH=CH)_n - CH=CH - R^2$$

$$\qquad\qquad 22 \qquad\qquad Z + E$$

Conjugated unsaturated aldehydes 20 react with alkylidene triphenylphosphoranes 21 forming the new Z-double bond in the polyene 22. On the other hand reaction of polyene ylids 23 with aldehydes 24, in which R^2 may also be a polyene chain, leads to a mixture of polyenes 22 having E- and Z-configuration at the resulting double bond. If one works in a protic solvent, e.g. alcohol, the proportion of the E-isomer increases. PO-activated olefination shows high E-stereoselectivity.
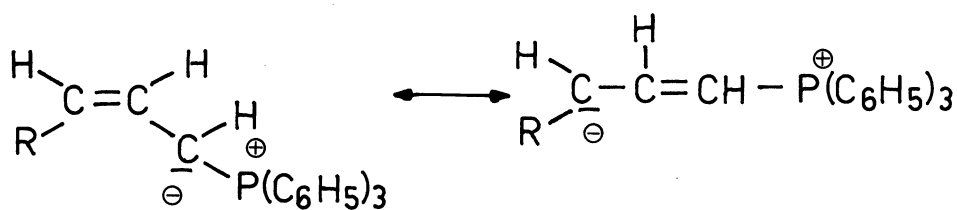
It is widely held, that alkylidene triphenylphosphoranes 25 do not isomerize at the C=C double bond in ß,γ -position next to the phosphorous [19]. The ylids 25 may be represented by the mesomeric forms 25a and 25b.

In the equilibrium reaction of 25 with TOC_2H_5 we found that tritium is incorporated at the α- as well as at the γ-position. Our studies showed also that in the reaction of 25 with halogen compounds an attack at the γ-position takes place [20]. From these results one would expect, that 25b could be easily converted into the conformer 26b, thus leading to the iso-merisation of 25⇌26. Our studies proved, that such E,Z-isomerisations take place with ylids 25, the extent of isomerisation being more than 59% [21] [22]. During the working at low temperature one of the isomers 25 or 26 may cristallise preferably. If the Wittig reaction is

$$\text{R}-\text{C(H)}=\text{C(H)}-\overset{\ominus}{\text{C}}(H)-\overset{\oplus}{\text{P}}(C_6H_5)_3 \longleftrightarrow \text{R}-\overset{\ominus}{\text{C}}(H)-\underset{H}{\text{C}}=\text{CH}-\overset{\oplus}{\text{P}}(C_6H_5)_3$$

25a   b   25 b

$$\underset{R}{\overset{H}{}}\text{C}=\text{C(H)}-\overset{\ominus}{\text{C}}(H)-\overset{\oplus}{\text{P}}(C_6H_5)_3 \longleftrightarrow \underset{R}{\overset{H}{\overset{\ominus}{\text{C}}}}-\underset{H}{\text{C}}=\text{CH}-\overset{\oplus}{\text{P}}(C_6H_5)_3$$
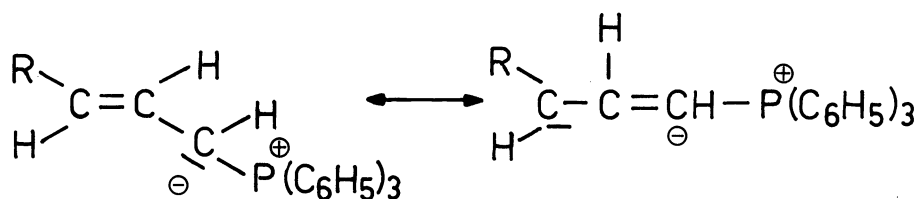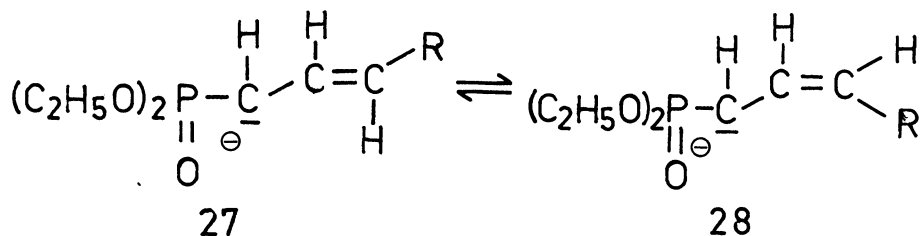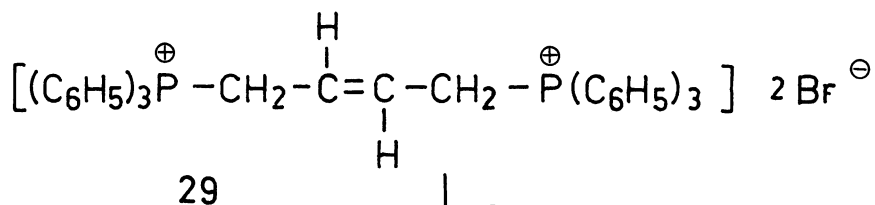
26a   26 b

carried out under such conditions Z- or E-selectivities may result.
Similar isomerisations were observed using the corresponding phosphonate anions [22] (27 ⇌ 28).

$$(C_2H_5O)_2\overset{\text{O}}{\underset{\ominus}{\text{P}}}-\overset{H}{\underset{\ominus}{\text{C}}}-\underset{H}{\overset{H}{\text{C}}}=\text{C}\underset{\text{H}}{\overset{R}{}} \rightleftharpoons (C_2H_5O)_2\overset{\text{O}}{\underset{\ominus}{\text{P}}}-\overset{H}{\underset{\ominus}{\text{C}}}-\underset{}{\overset{H}{\text{C}}}=\text{C}\underset{R}{\overset{H}{}}$$
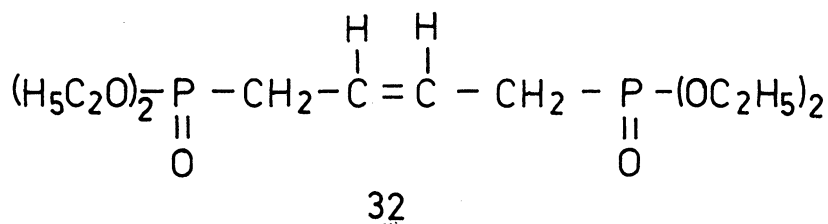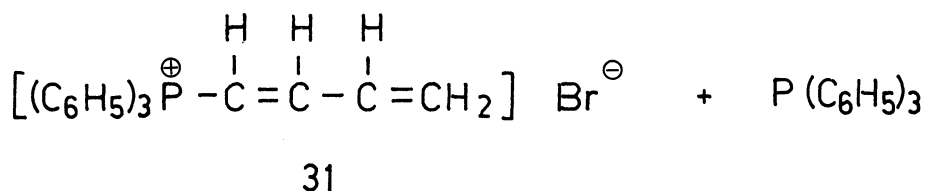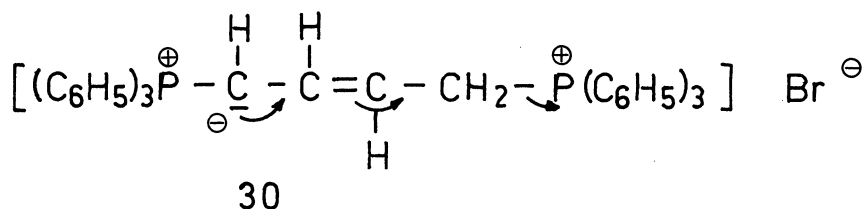
27   28

As a consequence we have to realize that during polyene synthesis using building blocks of the type 25 or 27 stereomutations may take place.

The corresponding bis-ylid may not be synthesized from the bis-phosphonium salt 29 because the intermediately formed monoylid 30 undergoes rapid elimination of triphenylphosphine, yielding the phosphoniumsalt 31. This reaction also occurs if the triphenylphosphonio group in 29 is substituted by another good leaving group [23].
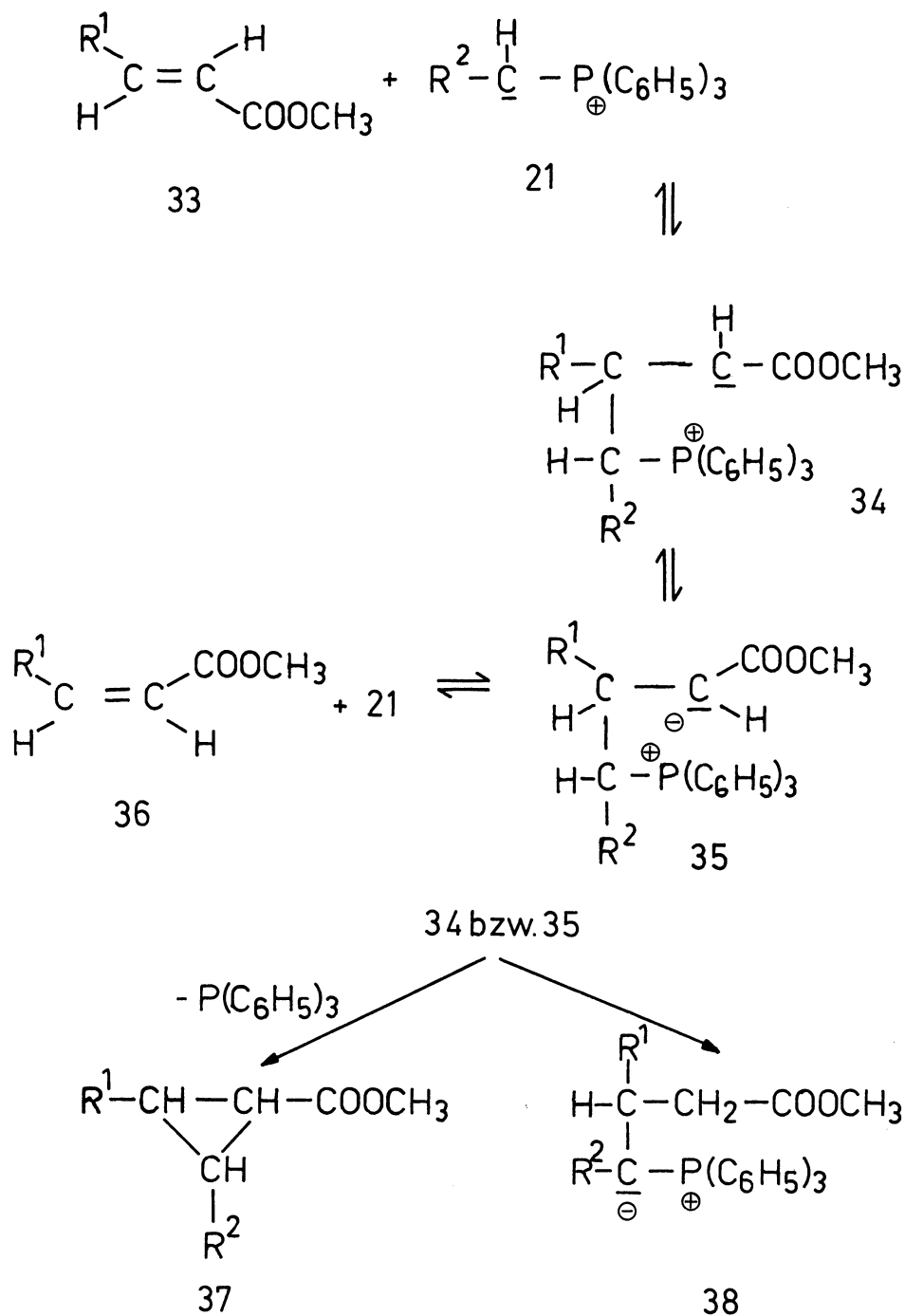
$$[(C_6H_5)_3\overset{\oplus}{P}-CH_2-\overset{\overset{\displaystyle H}{|}}{C}=\overset{\overset{}{\underset{\underset{\displaystyle H}{|}}{}}}{C}-CH_2-\overset{\oplus}{P}(C_6H_5)_3]\ 2\ Br^{\ominus}$$

29

Base

$$[(C_6H_5)_3\overset{\oplus}{P}-\underset{\ominus}{\overset{\overset{\displaystyle H}{|}}{C}}-\overset{\overset{\displaystyle H}{|}}{C}=\overset{\underset{\underset{\displaystyle H}{|}}{}}{C}-CH_2-\overset{\oplus}{P}(C_6H_5)_3]\quad Br^{\ominus}$$

30

$$[(C_6H_5)_3\overset{\oplus}{P}-\overset{\overset{\displaystyle H}{|}}{C}=\overset{\overset{\displaystyle H}{|}}{C}-\overset{\overset{\displaystyle H}{|}}{C}=CH_2]\ Br^{\ominus}\quad+\quad P(C_6H_5)_3$$

31

$$(H_5C_2O)_2\overset{\overset{\displaystyle }{||}}{\underset{\displaystyle O}{P}}-CH_2-\overset{\overset{\displaystyle H}{|}}{C}=\overset{\overset{\displaystyle H}{|}}{C}-CH_2-\overset{\overset{\displaystyle }{||}}{\underset{\displaystyle O}{P}}-(OC_2H_5)_2$$

32

When 29, or a similar triphenylphosphonium salt with two triphenylphosphonio groups separated by a conjugated polyene chain, is reacted with base in the presence of carbonyl compounds a double Wittig reaction takes place in poor yield [1]. If however, the two triphenylphosphonio groups in 29 are substituted by cyclohexyl groups the elimination rate is retarded so that the Wittig reaction becomes competitive and bisolefinations may be carried out in good yields under appropriate conditions [24].

The dianion resulting from the bisphosphonate 32 may also be used successfully for olefinations under appropriate conditions [1].
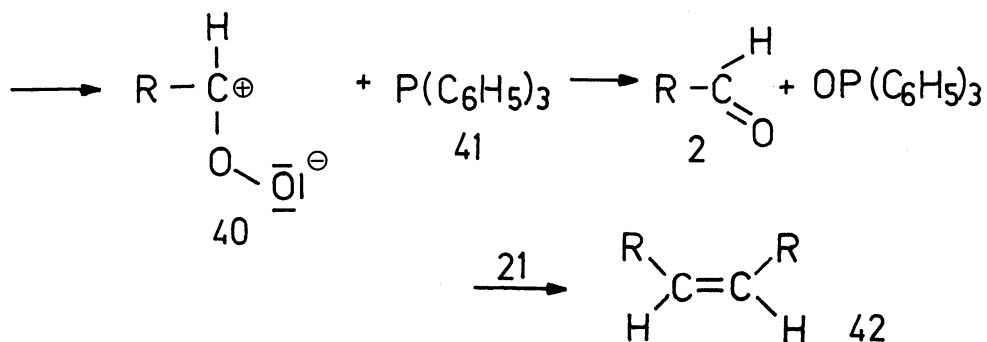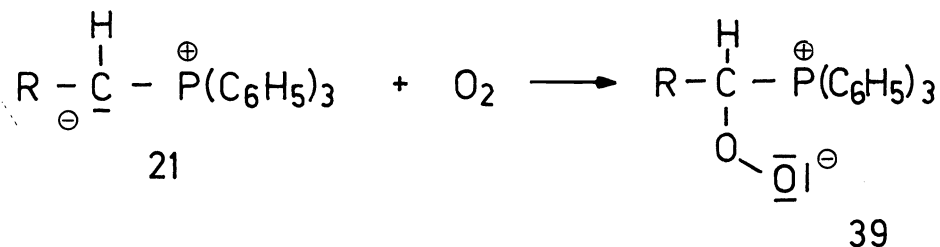
Some years ago we showed that ylids 21 may react with olefins (e.g. 33) having electron withdrawing groups at the C=C-bond, yielding betains 34. 34 undergo a conformational change, forming 35, which dissociate into the Z-isomers 36 and 21. Z,E-isomerisation may also occur in the interaction of ylids and compounds with activated C=C-double bonds.

$$R^1\!-\!CH = CH(H)(COOCH_3) \quad + \quad R^2\!-\!\underset{H}{\overset{H}{C}}\!-\!\overset{\oplus}{P}(C_6H_5)_3$$

33   +   21

$$\Updownarrow$$

$$R^1\!-\!\underset{H}{C}\ -\ \underset{|}{\overset{H}{C}}\!-\!COOCH_3$$
$$H\!-\!\underset{R^2}{\overset{|}{C}}\ -\ \overset{\oplus}{P}(C_6H_5)_3 \qquad 34$$

$$\Updownarrow$$

$$R^1\!-\!CH = CH(COOCH_3)(H) \quad + \quad 21 \quad \rightleftharpoons$$

36

$$R^1\!-\!\underset{H}{C}\ -\ \underset{\ominus}{C}(COOCH_3)(H)$$
$$H\!-\!\underset{R^2}{\overset{|}{C}}\ -\ \overset{\oplus}{P}(C_6H_5)_3 \qquad 35$$

$$34\ bzw.\ 35$$

$$-P(C_6H_5)_3 \nearrow \qquad \searrow$$

$$R^1\!-\!CH\!-\!CH\!-\!COOCH_3$$
$$\underset{\underset{R^2}{|}}{\diagdown CH\diagup}$$

37

$$H\!-\!\underset{\underset{\ominus}{|}}{\overset{\overset{R^1}{|}}{C}}\!-\!CH_2\!-\!COOCH_3$$
$$R^2\!-\!C\ -\ \overset{\oplus}{P}(C_6H_5)_3$$

38

The betains 34 and 35 may also stabilize by splitting off triphenylphosphine yielding cyclo-propanes 37 or may rearrange into 38 by a proton transfer [25] [26] [27]. In agreement with this finding our detailed studies show that in the course of Wittig reactions Z,E-rearrangements may also happen at the original C=C-double bonds if unsaturated aldehydes 20 are used.

This can be largely avoided if the reaction is carried out at low temperature and if there is
no excess of ylid (e.g. by adding the ylid slowly to the aldehyde solution). If the product
of a Wittig reaction is an unsaturated ester and if the ylid is used in excess cyclopropanes
37 may result. These undesirable side reactions in some cases become important for prepara-
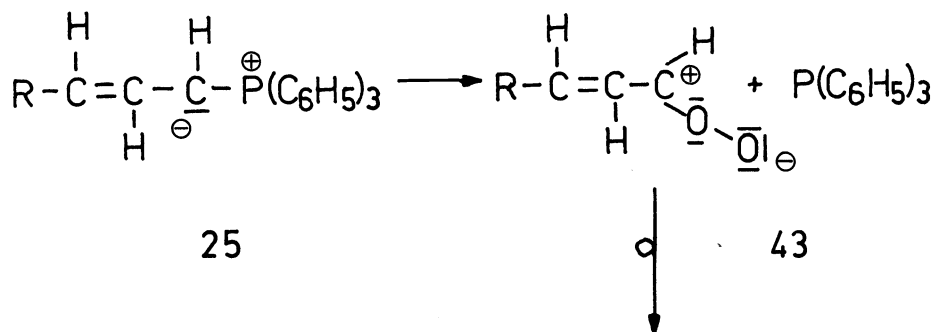tive applications [28].

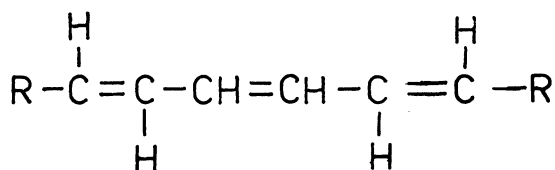We have shown, that ylids 21 react with oxygen to give olefins 42 [29].

$$R - \overset{\overset{\displaystyle H}{|}}{\underset{\ominus}{\overset{}{C}}} - \overset{\oplus}{P}(C_6H_5)_3 \quad + \quad O_2 \longrightarrow R - \overset{\overset{\displaystyle H}{|}}{\underset{O_{\diagdown \overline{O}|^{\ominus}}}{\overset{}{C}}} - \overset{\oplus}{P}(C_6H_5)_3$$

$$\qquad\qquad\qquad 21 \qquad\qquad\qquad\qquad\qquad\qquad 39$$

$$\longrightarrow R - \overset{\overset{\displaystyle H}{|}}{\underset{O_{\diagdown \overline{O}|^{\ominus}}}{\overset{}{C}\oplus}} \quad + \quad P(C_6H_5)_3 \longrightarrow R - \overset{H}{\underset{O}{\overset{\diagup}{C}}} \quad + \quad OP(C_6H_5)_3$$

$$\qquad\qquad 40 \qquad\qquad\qquad\qquad 41 \qquad\qquad\qquad 2$$

$$\qquad\qquad\qquad\qquad \overset{21}{\longrightarrow} \quad \overset{R}{\underset{H}{\diagdown}}C=C\overset{R}{\underset{\diagdown H}{\diagup}} \quad 42$$
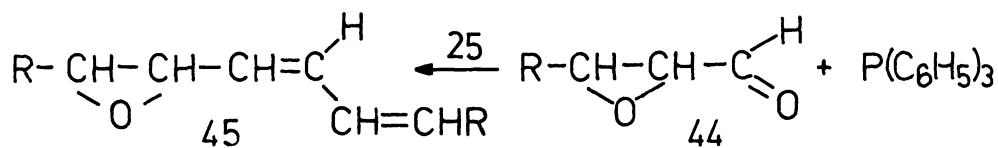
We discuss the following mechanism:

39 is formed from 21 and oxygen and then decomposes into 40 and triphenylphosphine 41. 40
has also been suggested as intermediate product during the ozonolysis of olefins. 40 and tri-
phenylphosphine give triphenylphosphinoxide and the aldehyde 2, which reacts with one mole of
not yet oxidized 21 to give the olefin 42. In agreement with this mechanism the end product
of the autoxidation always contains triphenylphosphine 41.

If allylidene triphenylphosphoranes 25 are used to synthezise polyolefins 46 in the autoxi-
dation the yield of triphenylphosphine increases and epoxy products 45 are also formed [24].

$$R-\overset{\overset{\displaystyle H}{|}}{C}=\overset{\overset{\displaystyle H}{|}}{\underset{\displaystyle H}{C}}-\overset{}{\underset{\ominus}{\overset{}{C}}}-\overset{\oplus}{P}(C_6H_5)_3 \longrightarrow R-\overset{\overset{\displaystyle H}{|}}{C}=\overset{}{\underset{\displaystyle H}{C}}-\overset{}{\underset{\overset{\displaystyle |}{\underset{\overline{O}|\ominus}{O}}}{\overset{\diagup H}{C}\oplus}} \quad + \quad P(C_6H_5)_3$$

$$\qquad\qquad\qquad 25 \qquad\qquad\qquad\qquad\qquad\qquad\qquad 43$$

$$R-\underset{\underset{45}{O}}{CH}-CH-CH=C\overset{H}{\underset{CH=CHR}{\Big\langle}} \xleftarrow{25} R-\underset{\underset{44}{O}}{CH}-CH-C\overset{H}{\underset{O}{\Big\langle}} + P(C_6H_5)_3$$

$$R-\overset{H}{\underset{H}{C}}=C-CH=CH-\overset{H}{C}=\overset{H}{\underset{H}{C}}-R$$

$$46$$

We assume, that the intermediate product 26 rearranges in an inter- or intramolecular reaction to give the epoxyaldehyde 44, which reacts with 25 to yield 45.

The oxidation of axerophthylidene triphenylphosphorane 47 leads to a reaction mixture which containes, besides ß-carotene 48, the compounds mutachrome 49, aureochrome 50 and triphenylphosphine [24) 30)].

$$47$$

$$\downarrow O_2$$

$$48$$

$$49$$
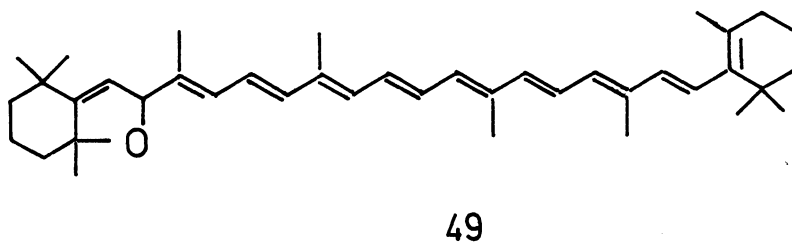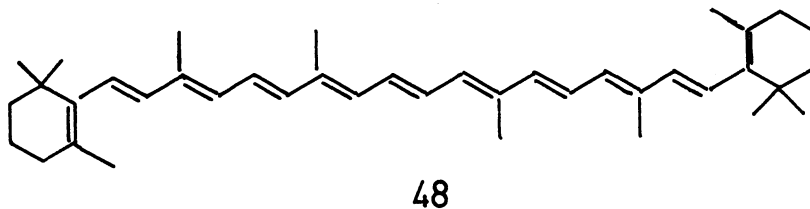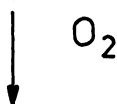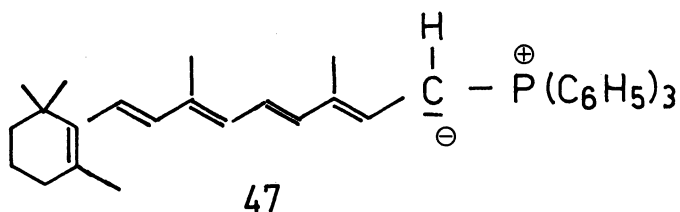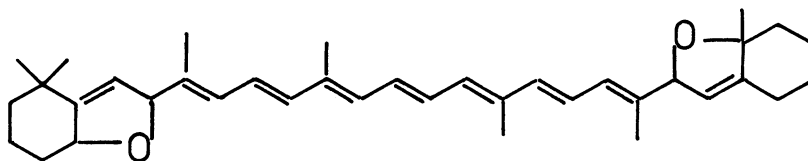
50

Also in this case we assume that an intermediate analogous to 43 is formed, leading in an intermolecular or intramolecular epoxidation followed by a rearrangement, to 49 and 50 respectively. The yields of carotene derivatives in the course of the autoxidation as well as the periodate method [31b) 32)] are not very satisfactory. Much higher yields of ß-carotene are obtained by the oxidation of 47 with the adduct 15 of ozone and triphenylphosphite. 48 is obtained in 75% yield [17)]. No mutachrome 49 and aureochrome 50 are formed. Oxidation with 15 may be carried out at -78°. ^{31}P-NMR-studies show, that oxygen is obviously not transferred as singlet oxygen from 15 to 47 [17)].
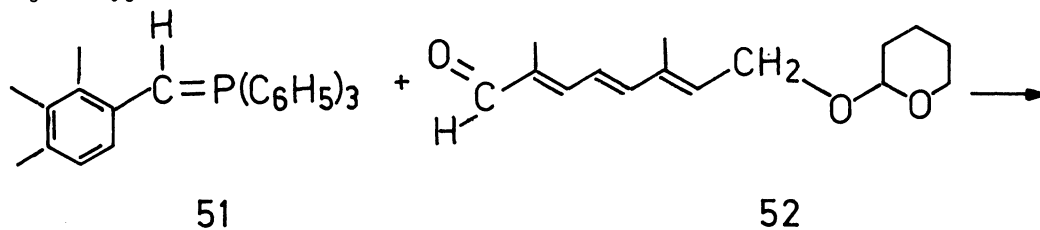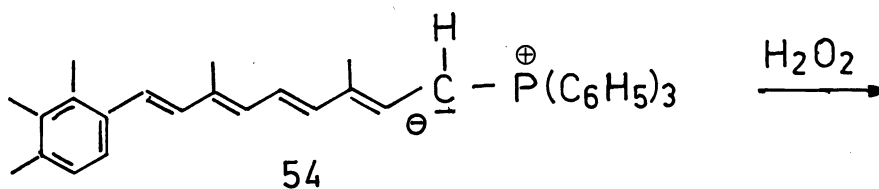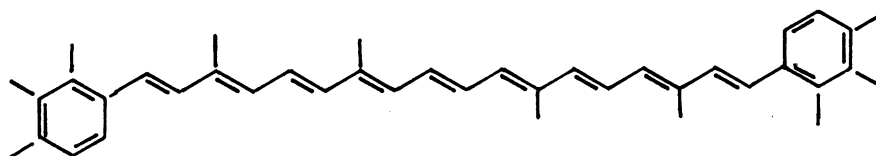

51   **52**
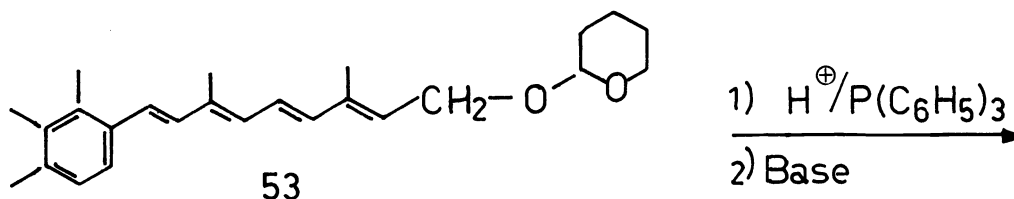
53

1) $H^{\oplus}/P(C_6H_5)_3$

2) Base

54

H_2O_2

55

The recently found oxidation of polyene ylids by hydroperoxide is of special interest for the synthesis of symmetrical carotenoids [32]. β-carotene is formed from 47 and perhydrol in water in 80% yield. The application of this method in the course of the synthesis of renierapurpurin 55 underlines the importance of the Wittig reaction for carotenoid synthesis [33].

The Wittig reaction of the ylid 51 and the aldehyde 52 yields the compound 53. Treatment of 53 with acid in the presence of triphenylphosphine gives rise to the formation of the corresponding phosphonium salt, which may be converted into the ylid 54 by base. If the ylid is generated with aqueous sodium carbonate in the presence of 50% hydroperoxide the carotenoid 55 is formed in 73% yield.

The above results concerning the course of the Wittig reaction enable us to incorporate tritium or deuterium in a selectivity during the synthesis of polyenes. If in the course of a Wittig reaction the two reactants are mixed together at -75° and if after ca. 15-20 minutes tritium- or deuterium-labelled alcohol is added, the isotope is incorporated at the C-atom which was α to the phosphorus atom before the Wittig reaction (Ylid-C-atom).

If deuteroethanol 10 is added to the reaction mixture of the oxidation of 47 with 15 at -78°, 15 minutes after the components have been mixed together, the monodeuterated β-carotene 56 (rate of incorporation 68%) can be isolated. If, however, the labelled alcohol (e.g. 10) is added to the ylid solution 47 before the oxidation is carried out, then isotope exchange at the ylid-C-atom takes place. The subsequent oxidation by 15 yields the bisdeuterated β-carotene 57 and 56 [34].

56

57
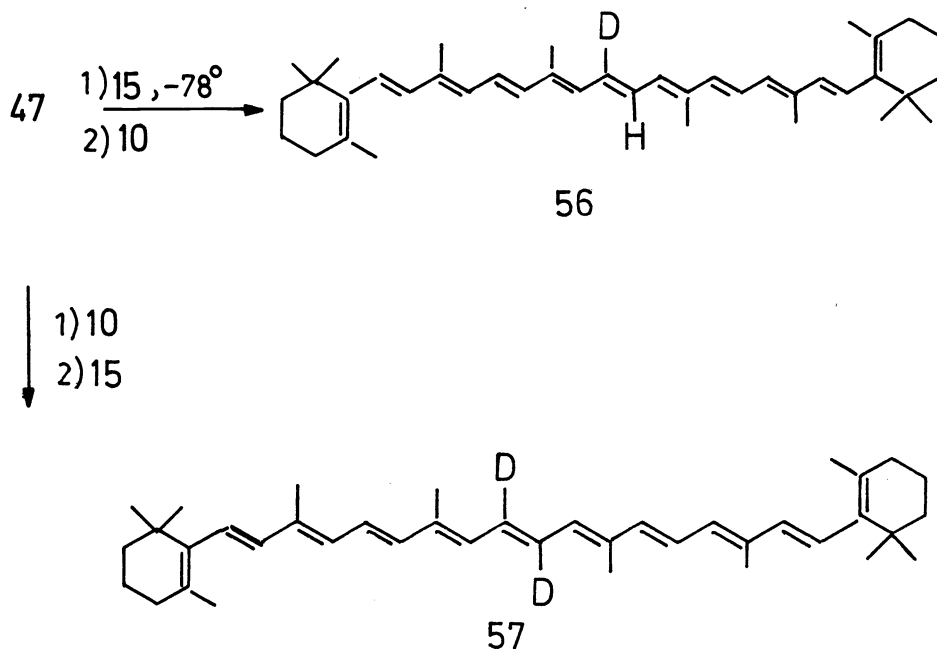
It could be proved by mass spectroscopy [34] [35] [36] that the deuterium atoms in 56 and 57 are only incorporated at the 15,15'-bond. In the case of 56 the molecular ion $M^+ = 537$ is observed, 57 shows $M^+ = 538$. From both compounds only undeuterated xylol is split off, whereas the fragment dimethylcyclodecapentaene from 56 contains one and that from 57 contains two deuterium atoms [36].

While the oxidative dimerisation proved to be quite successful for the synthesis of symmetric carotinoids, there was developed a procedure using an insoluble polymeric carrier [37] for the synthesis of unsymmetrical polyenes via the Wittig reaction.
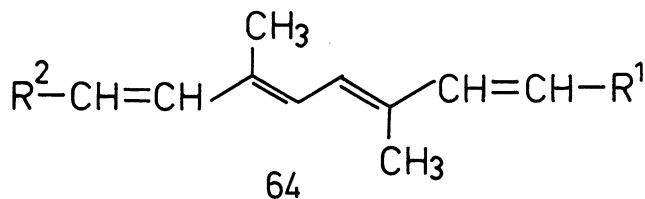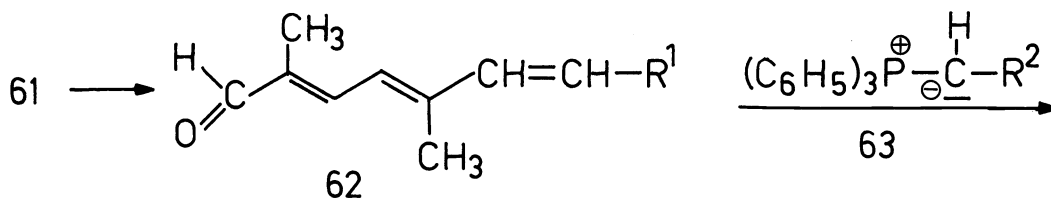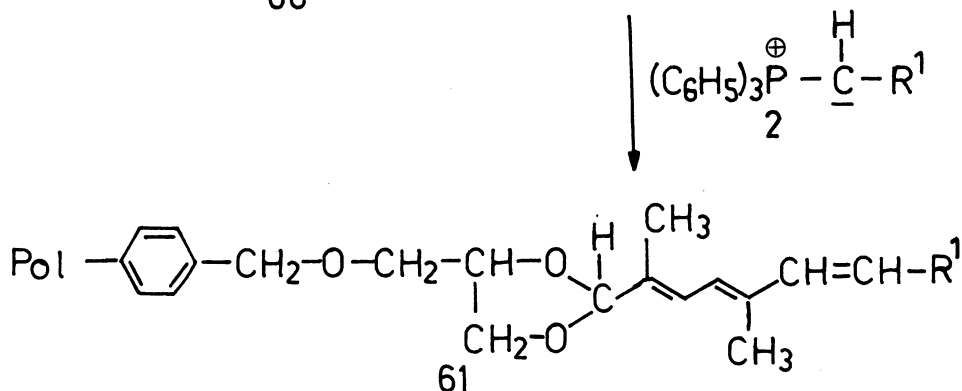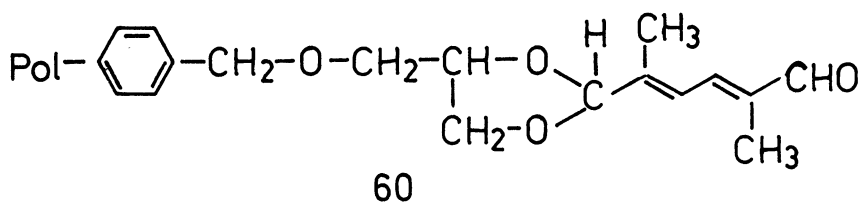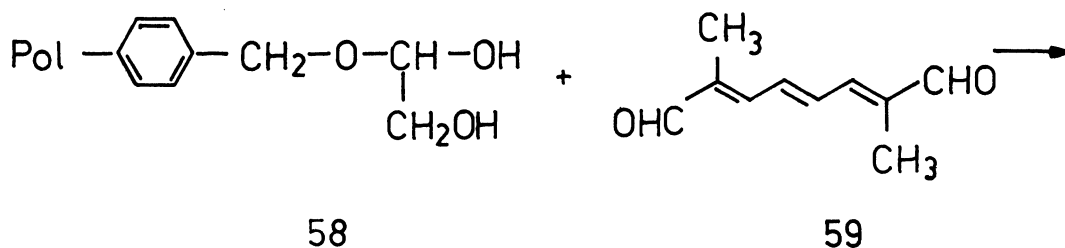
The common polymers 58 react with the conjugated bisaldehyde 59 yielding the carrier linked monoacetal 60, which is olefinated by an ylid 2 (R^1 may be also a conjugated polyene chain) giving rise to the formation of the carrier linked acetal 61. Hydrolysis of 61 leads to 58 and the aldehyde 62 which produces with another ylid 63 the unsymmetric polyene 64.

Recently we developed two synthetic approaches for /enes-ynes which should be of interest also for carotenoid synthesis in the future. The reaction of 2 moles ketenylidenetriphenyl-phosphorane 65 [38] with one mole of halide 66, yields 1,3-cyclobutanedione derivatives 67, from which the open chained bisphosphoranes 68 are formed with sodium methanolate.

$$2 \ (C_6H_5)_3 \overset{\oplus}{P} - \overset{\ominus}{C} = C = O \quad + \quad R^1 - Br \quad \longrightarrow$$
$$\qquad\qquad\qquad 65 \qquad\qquad\qquad\qquad 66$$

$$\left[(C_6H_5)_3 \overset{\oplus}{P} - \overset{\overset{R^1}{|}}{\underset{|}{C}} - C \overset{O}{\diagup} \atop O \overset{\diagdown}{=} C - \overset{\ominus}{C} \diagdown \overset{\oplus}{P}(C_6H_5)_3 \right] Br^{\ominus} \quad \overset{Na|\overset{\ominus}{O}CH_3}{\longrightarrow}$$
$$\qquad\qquad\qquad 67$$

$$R^1 - \overset{\ominus}{\underset{(C_6H_5)_3\overset{P}{\oplus}}{C}} - \overset{}{\underset{O}{C}} - \overset{\ominus}{\underset{\overset{P}{\underset{\oplus}{(C_6H_5)_3}}}{C}} - \overset{\overset{O}{||}}{C} - OC_2H_5 \qquad\qquad R^2_2C\overset{\diagup H}{\underset{\diagdown O}{}} \longrightarrow$$
$$\qquad\qquad\qquad 68$$

$$68 \overset{2}{\longrightarrow} \quad R^2 - CH = \overset{\overset{R^1}{|}}{C} - \overset{}{\underset{O}{C}} - \overset{\ominus}{\underset{\overset{\oplus}{P}(C_6H_5)_3}{C}} - \overset{\overset{O}{||}}{C} - OC_2H_5 \qquad\qquad \longrightarrow$$
$$\qquad\qquad\qquad 69$$

$$R^2 - CH = \overset{\overset{R^1}{|}}{C} - C \equiv C - COOC_2H_5$$
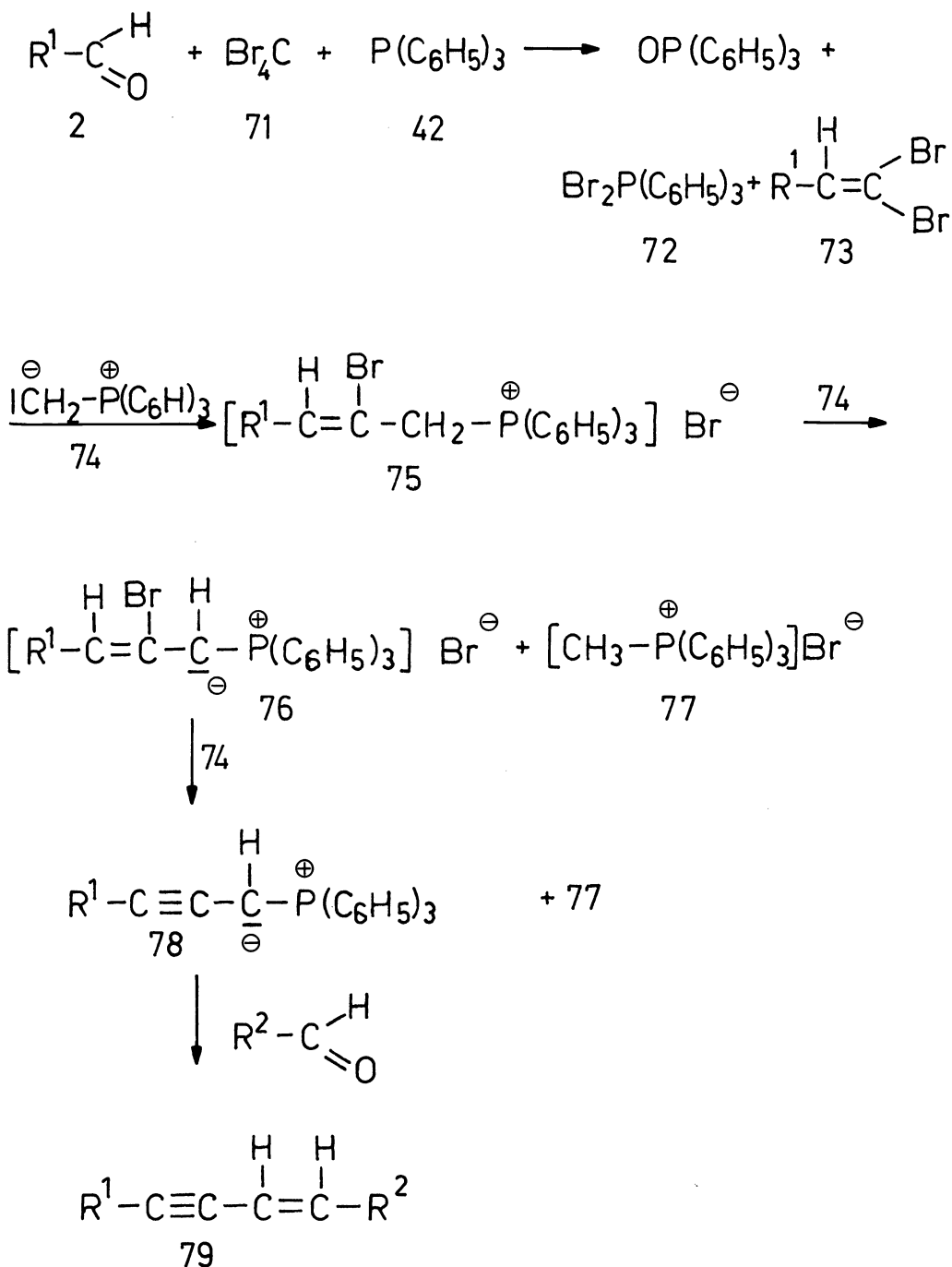$$\qquad\qquad 70$$
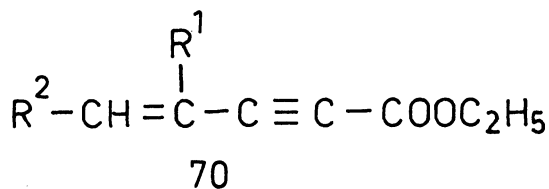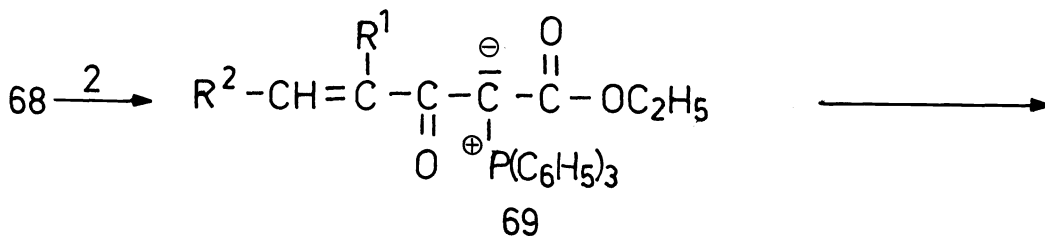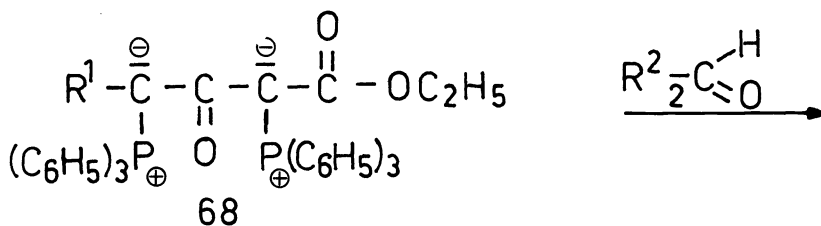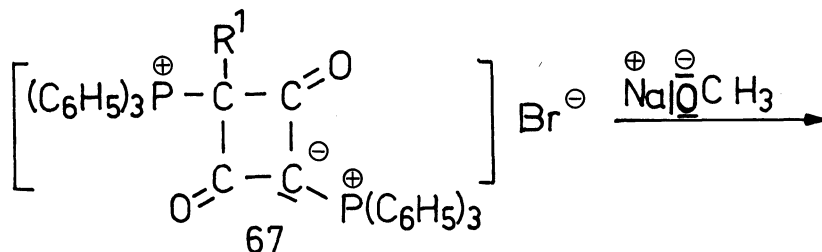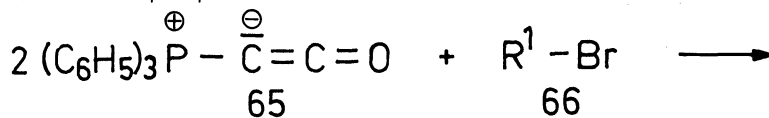
The ylid function of 68 which has two adjacent carbonyl groups is much more reactive than the ylid function which has only one neighboring carbonyl group. Reaction of 68 with aldehydes therefore leads to the formation of phosphoranes 69 [38] [39] which on heating split off tri-phenylphosphineoxide yielding ene-yne-ester 70 [40].

If an aldehyd 2, tetrabromomethane 71 and triphenylphosphine 41 are mixed together, triphenyl-
phosphinoxide, the adduct 72 of triphenylphosphine and bromine and the 1,1-dihalo olefins 73
[41)] are formed.

The reaction of compound 73 with 3 moles methylene triphenylphosphorane 74 yield 2 moles
methyltriphenylphosphoniumbromide 77 which crystallises from the solution, and the ylids 78
[42)].

In the first instance from 73 and 74 the phosphonium salt 75 is formed, which then undergoes
a transylidation [42) 43)] with a second mole of 74 yielding 76 and a mole of 77. A third mole
of 74 removes HBr from 76 giving rise to the formation of a further mole of 77 and 78, which
can react with an aldehyde to give the ene-yne 79.

$$R^1-C\overset{H}{\underset{O}{\lessgtr}} \ + \ Br_4C \ + \ P(C_6H_5)_3 \ \longrightarrow \ OP(C_6H_5)_3 \ +$$

$$\quad 2 \qquad\qquad 71 \qquad\qquad 42$$

$$Br_2P(C_6H_5)_3 + \ R^1-\overset{H}{C}=C\overset{Br}{\underset{Br}{\lessgtr}}$$

$$\qquad 72 \qquad\qquad 73$$

$$\overset{\ominus}{I}CH_2-\overset{\oplus}{P}(C_6H)_3 \atop 74 \ \longrightarrow \ \left[R^1-\overset{H}{C}=\overset{Br}{C}-CH_2-\overset{\oplus}{P}(C_6H_5)_3\right] Br^{\ominus} \ \xrightarrow{74}$$

$$\qquad\qquad\qquad\qquad\qquad 75$$

$$\left[R^1-\overset{H}{C}=\overset{Br}{C}-\underset{\ominus}{\overset{H}{C}}-\overset{\oplus}{P}(C_6H_5)_3\right] Br^{\ominus} \ + \ \left[CH_3-\overset{\oplus}{P}(C_6H_5)_3\right]Br^{\ominus}$$

$$\qquad\qquad 76 \qquad\qquad\qquad\qquad 77$$

$$\bigg\downarrow 74$$

$$R^1-C\equiv C-\underset{\ominus}{\overset{H}{C}}-\overset{\oplus}{P}(C_6H_5)_3 \qquad\qquad + 77$$

$$\qquad 78$$

$$\bigg\downarrow \quad R^2-C\overset{H}{\underset{O}{\lessgtr}}$$

$$R^1-C\equiv C-\overset{H}{C}=\overset{H}{C}-R^2$$

$$\qquad\qquad 79$$

We carried out this reaction sequence starting from retinal 80.

80

+ 71   + 41

81

82

83

84
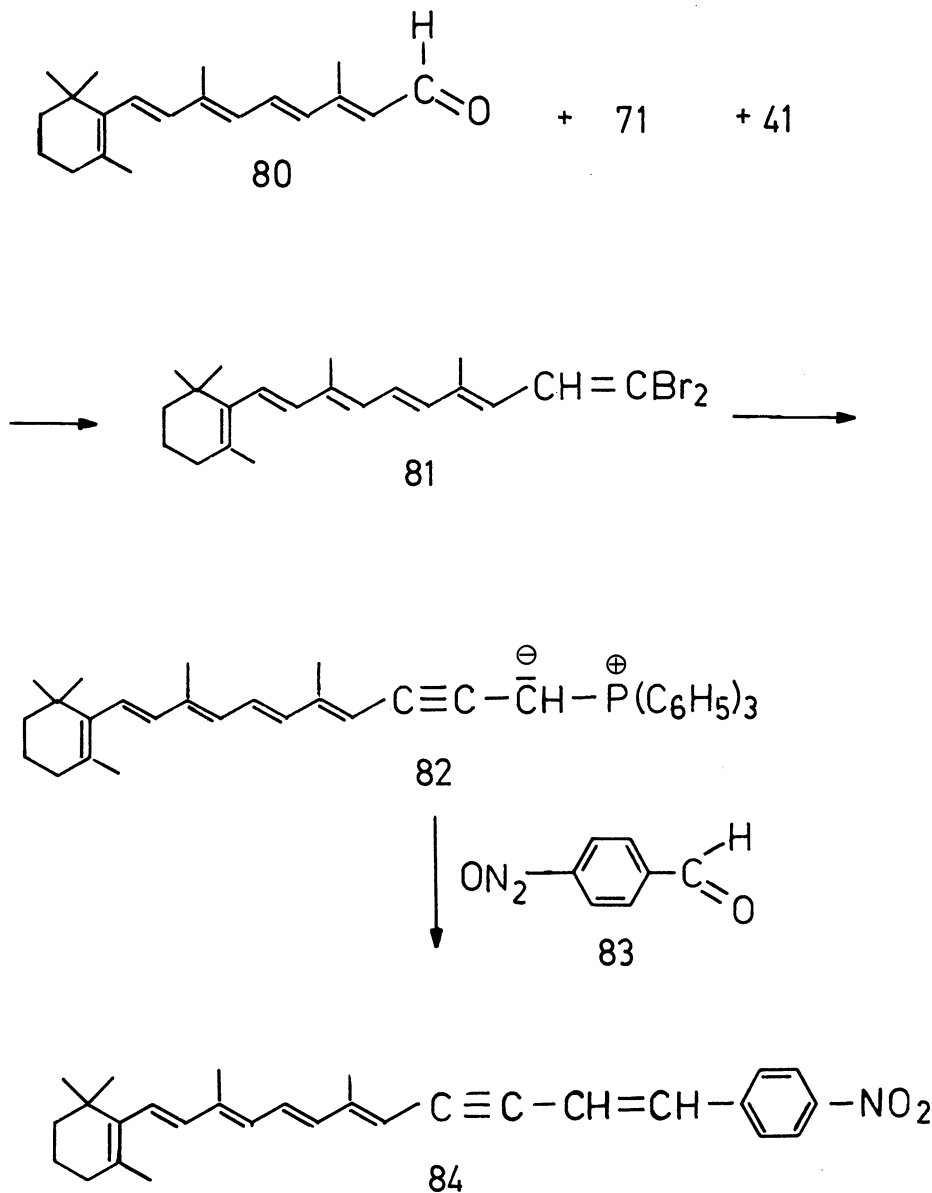
80 reacts with 71 and 41 to give the dibromocompound 81, which reacts with 3 moles of 74 to give the ylid 82 from which compound 84 is obtained upon the addition of p-nitrobenzaldehyde 83 [42].

Detailed results of our studies concerning the mechanism of the Wittig reaction make it possible to predict the stereochemistry of the end products and to project a stereoselective synthesis of polyenes. The selective incorporation of deuterium or tritium in the course of the Wittig reaction is possible. The reactions which lead to ene-ynes, show, that it is not only the reaction of phosphorus ylids with aldehydes or ketones which is of great importance for the chemistry of carotenoids but also the great variety of alkylidene phosphoranes reacting as nucleophilic components [26] [27] [39] [44] which may be usefully applied in the synthesis of polyenes.

The reported results of our team are based on the work of R. Armsen, W. Downey, H. Frey, Ch. Geismann, O. Kratzer, E. Maekawa, W. Rieck and J. Süß, to whom I want to express my gratitude for their enthusiastic cooperation.

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