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Mechanistic and synthetic aspects of the reaction of γ-halogeno-α,β-unsaturated ketones and esters with simple trialkyl phosphites

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Phosphorylation of different γ-halogeno-α,β-unsaturated ketones, ketoesters and diesters **11a**–**h** with simple trialkyl phosphites gives 1,3-dienylphosphates **14**, cyclopropylphosphonates **15**, ketovinylphosphonates **17** and other products depending on the nature and number of activating groups and halogen atoms in the substrate. Most likely the reaction proceeds *via* oxaphospholene **23** which is in equilibrium with pseudorotamer **24** and an open, dipolar form **22**. Dipolar form **33** is a likely intermediate when two activating groups are present.

Introduction

The presence of several electrophilic centers and an excellent leaving group in γ-halogeno-α,β-unsaturated ketones **1a** and esters **1b** suggests that they will react with strongly nucleophilic trialkyl phosphites in different and potentially competing ways. A survey of the literature revealed that only a few such reactions have been described so far. Trichlorobutenone **2a** and trichloropentenone **2b** subjected to phosphorylation with simple alkyl phosphites gave the corresponding 1,3-dienyl phosphates **3a** and **3b**.[1,2] The stereochemistry of these compounds was not determined. Similar treatment of chlorobutenones **4a** and **4b** with tributyl phosphite yielded the phosphonates **5a** and **5b** respectively.[3] Unfortunately, their structure was assigned exclusively on basis of ^{31}P NMR spectra. It was also reported that the reaction of trichlorodiketone **6a**, trichloroketoester **6b** or trichlorodiester **6c** with trialkyl phosphites gave the corresponding vinylphosphonates **7a**–**c**.[4] Finally, it has just been shown that the treatment of bromodiesters **8a** (R^1, R^2 = alkyl) with trialkyl phosphites initiates a Michael induced ring closure reaction (MIRC) leading to functionalized cyclopropylphosphonates **9**, whereas bromodiesters **8b** (R^1 = H, R^2 = H or alkyl) gave rise to aliphatic phosphonates **10** *via* Arbuzov reaction.[5] Presented data, in particular the diversity of the products, show the complex chemistry involved in these transformations. Obviously there is a need for more systematic investigations, to gain some insight into the mechanistic details of this type of reaction.

In this paper we describe our studies on the reactivity of different γ-halogeno α,β-unsaturated ketones, ketoesters and diesters **11a**–**h** with simple alkyl phosphites. Furthermore, we make an attempt to rationalize the obtained results by mechanistic considerations.

Results and discussion

The halogeno ketones **11a**–**d**, ketoesters **11e**,**f** and diesters **11g**,**h** used in this work are listed in Table 1. All these compounds were either known and prepared as described or obtained using standard methodologies (see Experimental section). The selected starting materials were than heated, neat or dissolved in benzene, with a slight excess of trimethyl or triisopropyl phosphite for 1–3 h. Detailed reaction conditions are given in Table 1. The effectiveness of the phosphorylation was monitored by ^{31}P NMR spectroscopy and/or TLC. When the reaction was completed, the resulting products were purified and, in many cases, separated by distillation or chromatography

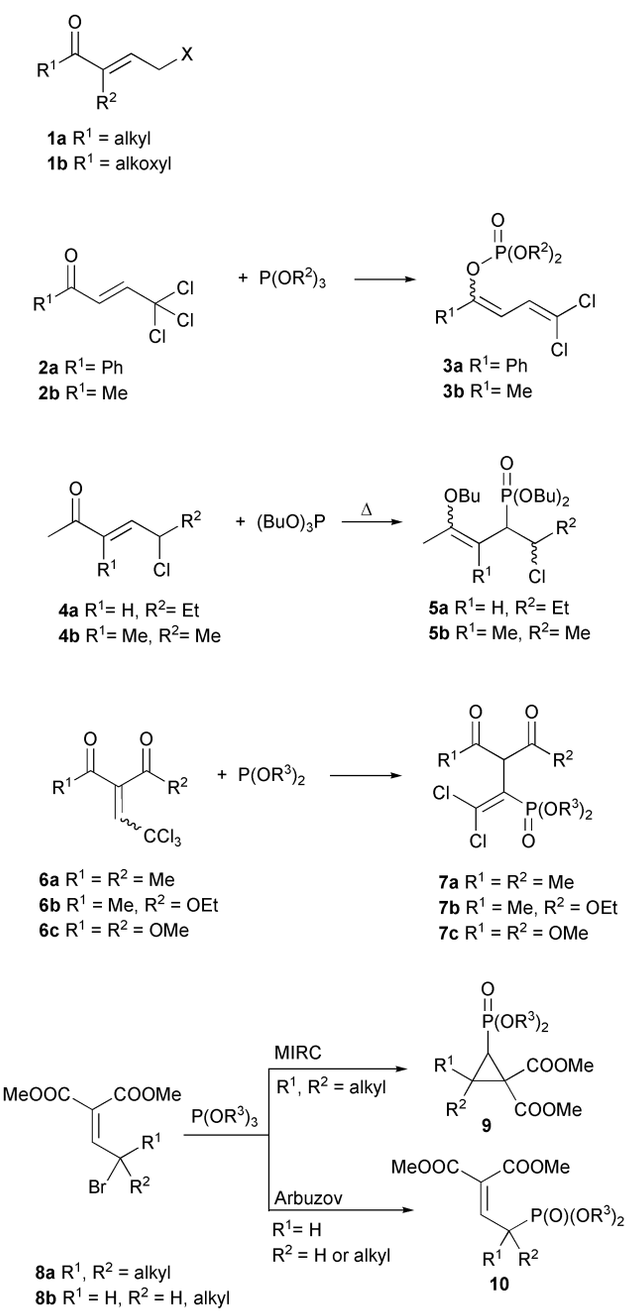

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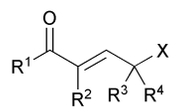
Table 1 Structures of γ-halogenated α,β-unsaturated ketones, ketoesters and diesters **11a**–**h** and the reaction conditions

							Reaction conditions		
11	R^1	R^2	X	R^3	R^4	*E*/*Z*	Solvent	Reaction temperature/°C	Reaction time/h
a	Me	H	Cl	Me	Me	>95/5	Neat	140	3
b	Me	H	Cl	Cl	Me	>95/5	Neat	110	3
c	Me	H	Cl	Cl	Cl	>95/5	Neat	100	2
d	Me	H	Br	Br	Me	>95/5	Benzene	Reflux	2
e	Me	COOMe	Cl	Cl	Cl	50/50	Benzene	Reflux	1
f	Me	COOMe	Br	Me	Me	45/55	Benzene	Reflux	1.5
g	OEt	COOEt	Br	Me	Me	—	Benzene	Reflux	3
h	OMe	$P(O)(OEt)_2$	Br	Me	Me	>95/5	Benzene	Reflux	1

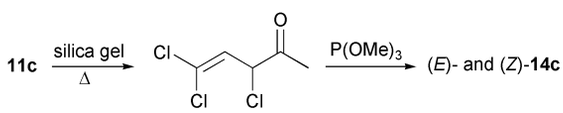


11a-h

techniques. Their structures, yields and proportional contributions to particular, crude reaction mixtures (in parentheses), are shown on Scheme 1.

Phosphorylation of the halogeno ketones **11a**–**d** with trimethyl phosphite was not chemoselective and yielded rather complex mixtures of different compounds. The only components of these mixtures representing the same structural pattern were 1,3-dienyl phosphates **14a**–**d**. The remaining isolable products of the reaction performed with **11a** were identified as ketophosphonate **12** and oxaphosphole **13**, while phosphorylation of **11b** provided additionally cyclopropylphosphonate **15a** and furylphosphonate **16**. In all cases, ^{31}P NMR spectra of the crude reaction mixtures revealed weak signals in the range of 19 to 32 ppm attributed to unisolatable byproducts. The treatment of ketoesters **11e**,**f** with trimethyl phosphite resulted in their clean conversion to the completely enolyzed ketovinylphosphonates **17a** and **17b** respectively. Finally, the reaction of diesters **11g**,**h** with trimethyl and triisopropyl phosphites afforded the corresponding cyclopropanecarboxylates **15b**,**c** and **15d**, in excellent to moderate yields.

All structural and configurational assignments are based on the analysis of ^1H, ^{13}C and ^{31}P NMR spectra. Assigning the stereochemistry of the double bonds in 1,3-dienyl phosphates **14a**–**d** was one of the main challenges. The reactions leading to **14a** and **14c** were fully stereoselective and each of these compounds was obtained as a single stereoisomer. Unfortunately, their ^1H NMR spectra were not conclusive enough for unequivocal stereochemical assignments. The lack of spectral data for the remaining stereoisomers made the comparison of the potentially diagnostic chemical shifts of H-2 protons impossible. To overcome this difficulty we decided to prepare both isomers of 1,3-dienyl phosphate **14c** using a different synthetic approach. Thermally induced and silica gel catalyzed allylic rearrangement[6] of the ketone **11c** provided the chloroketone **18** whose subsequent Perkow reaction with trimethyl phosphite gave the desired mixture of (*E*)- and (*Z*)-buta-1,3-dienyl phosphate **14c** in a 1 : 1 ratio. Analysis of the ^1H NMR spectrum of this mixture revealed the expected difference in chemical shifts of the H-2 protons in (*E*)- and (*Z*)-**14c** (6.41 ppm and 6.03 ppm, respectively), resulting from the deshielding effect of the *cis* oriented phosphate group.[7] The H-2 proton in 1,3-dienyl phosphate **14c** had a chemical shift at 6.03 ppm proving the *Z* configuration of this compound. On the basis of the similarity of the spectral data, *Z* stereochemistry was also assigned to the C-1 double bond of the 1,3-dienyl phosphate **14a**. The phosphates **14b** and **14d** were obtained as a mixture of two out of four possible stereoisomers in a ratio close to 1 : 1. The attempted separation of the mixture was not successful. As expected, the *Z* configuration of the C-1 double bond in **14b** and **14d** was confirmed by characteristic chemical shifts and coupling constants in their ^1H NMR spectra, similar to those recorded for the phosphates **14a**,**c**. Consequently, *E* as well as *Z* configuration was assigned to C-3 double bond in these compounds.

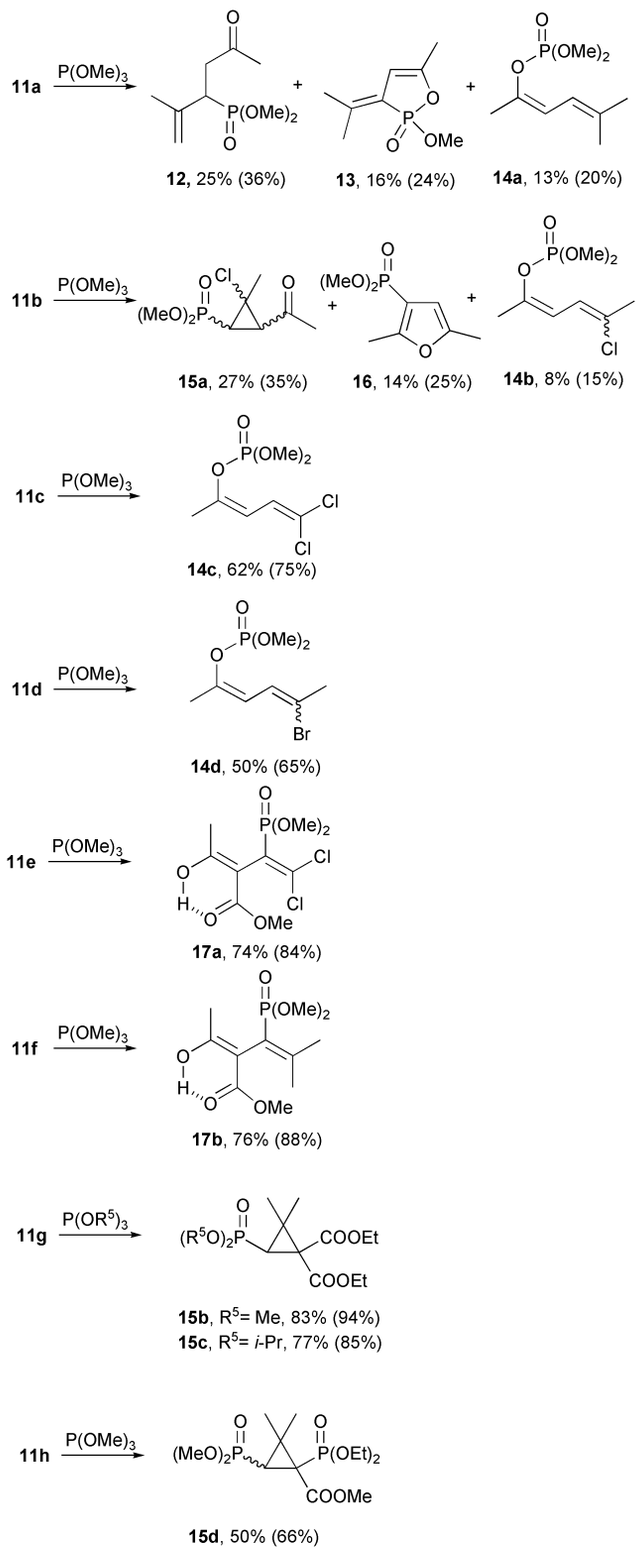


18

Cyclopropylphosphonate **15a** was formed as a single diastereoisomer. Its structure was readily elucidated using ^1H, ^{13}C and ^{31}P NMR spectroscopy but the stereochemistry remained undetermined. Signals of the protons in the cyclopropane ring were not resolved enough to have diagnostic value. On the other hand, cyclopropanecarboxylate **15d** was obtained as a mixture of isomers in a 95 : 5 ratio, as calculated from the ^{31}P NMR spectrum of the crude product. Column chromatography afforded a pure major isomer and a mixture of isomers in an 83 : 17 ratio. Analysis of the NMR spectra of these materials confirmed their structures and showed that the major isomer has *c*-3,*r*-1 configuration. Among others, $^3J_{PH\text{-}3}$ coupling constants were diagnostic[8] (14.8 Hz and 5.3 Hz for *c*-3,*r*-1 and *t*-3,*r*-1 isomer, respectively).

The presented results, especially the diversity of the products formed, reveal the very complex nature of the performed reactions and their sensitivity to even small structural changes in the reactants. The formation of 1,3-dienyl phosphates **14a**–**d** could not be explained by any of the two mechanisms postulated for the classical Perkow reaction[9] (Scheme 2) *i.e.* the initial attack by the phosphite at the carbonyl carbon to form the adduct **19**, followed by migration of the phosphonium group from carbon to oxygen to yield Perkow intermediate **20** (path a) or the initial attack of the phosphite on the "positive" γ- halogen substituent to produce a halogeno-phosphonium enolate ion-pair **21**, which rearranges affording the same **20**. Dealkylation of the Perkow intermediate **20** would give the final products **14a**–**d**. None of these mechanisms explained the fully diastereoselective formation of the C-1 double bond of *Z* configuration in 1,3-dienyl phosphates **14a**–**d** or the origin of the other obtained products.

On the other hand Ramirez[10] and Gorenstein[11] demonstrated that alkyl phosphites are readily added to conjugated enones such as **11a**–**d** to give oxaphospholene **23** (Scheme 3). The oxaphospholenes of this type were shown to be in an equilibrium with pseudorotamer **24** and also a dipolar structure **22**. We believe that all the results obtained for halogenoenones **11a**–**d**, including stereochemistry of phosphates **14a**–**d** can be rationalized if we assume such an equilibrium. Dipolar structure **22** can react *via* path a, b or c. Thus, intramolecular C- or O- alkylation leads to cyclopropylphosphonium chloride **25** or dihydrofuranylphosphonium chloride **26** (path a or b respectively). Simple dealkylation of **25** gives cyclopropylphosphonate **15a** whereas aromatization of **26** to furanylphosphonium chloride **30** followed by dealkylation provides furylphosphonate **16**. Path c begins with proton exchange in **22** and the formation of



Scheme 1

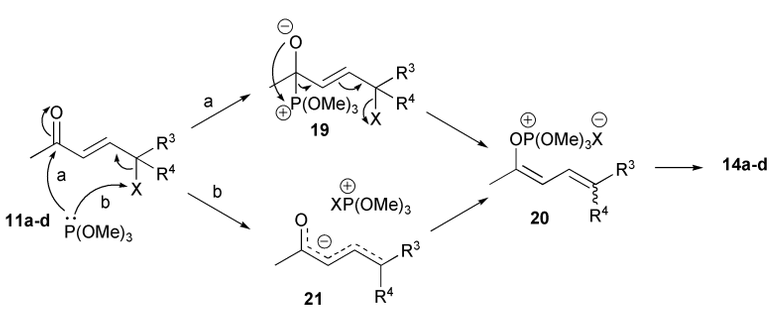
ylide **27**. Elimination of HCl from **27** with subsequent dealkylation of vinylphosphonium chloride **31** and deconjugation of the double bond provides allylphosphonate **12**. Such deconjugative isomerization is not unusual. The tendency of the double bond to occupy an allylic rather than vinylic position in alkenylphosphonates is well documented.[12] The formation of the oxaphosphole **13** can be explained by the reaction sequence starting with the dissociation of the P–O bond in oxaphospholene **23** to give phosphonium methoxide **28**. The elimination of HCl from **28** and dealkylation of the thus formed vinylphosphonium chloride **32** yields **13**. Finally, the fully diastereoselective formation of (1*Z*)-1,3-dienyl phosphates **14a–d** can be easily rationalized if we assume a simultaneous dissociation of the P–C bond and the elimination of halogenide anion from oxaphospholene **24** followed by dealkylation of phosphonium halogenide **29**.

It is difficult to comment on the actual proportions of the products formed in phosphorylations of **11a** and **11b** because too many steric as well as electronic factors are involved in each transformation. The efficient formation of phosphates **14c** and **14d** from chloroketones **11c** and **11d** respectively, can be, however, rationalized. We believe that high chemoselectivity of the first reaction can be explained by the presence of the electronegative CCl_3 group in oxaphospholane **23** (R^3, R^4 = Cl) which increases apicophilicity[10] of the C-3 carbon atom and shifts the equilibrium towards pseudorotamer **24**. Also, the effective formation of phosphate **14d** from bromoketone **11d** can be justified by the fact that bromide is a better leaving group than chloride, which facilitates the elimination of bromonium anion from pseudorotamer **24** (X = Br) to give **29**.

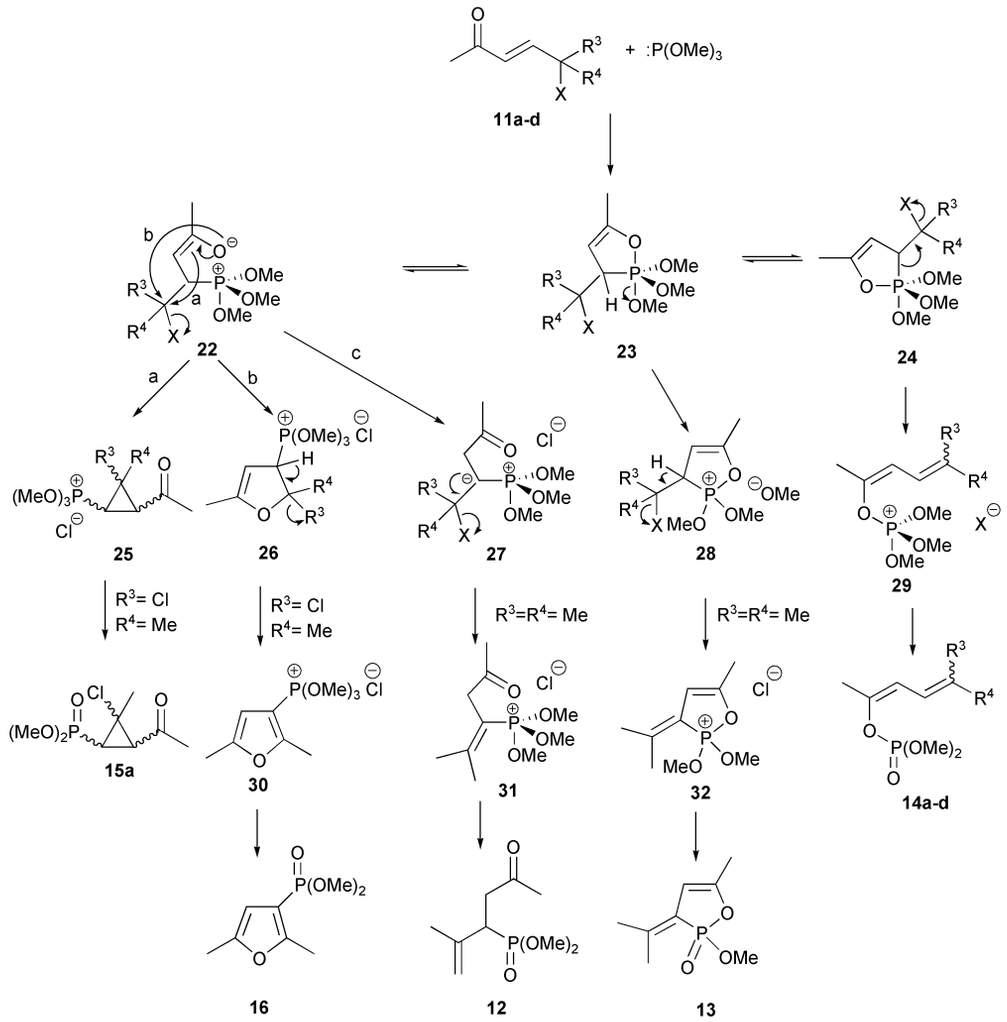
The reaction of highly activated ketoesters **11e**,**f** and diesters **11g**,**h** with alkyl phosphites also fits the presented reaction pattern. The presence of the second activating group in these compounds favors the formation of dipolar adducts **33e–h**, by stabilizing the enolate anion (Scheme 4). Further transformations of these adducts follow the reaction sequences, analogous to paths a and c from Scheme 3. C-Alkylation provides cyclopropylphosphonates **15b–d** (MIRC), whereas elimination of hydrogen halogenide gives vinylphosphonates **17a**,**b** (Scheme 4, path a and c respectively). Full chemoselectivity of these reactions can be rationalized assuming that competition between path a and c originates from different rates of cyclization and elimination reactions. The rate of elimination depends directly on the acidity of the hydrogen atom geminal to the phosphonium group. Ketones stabilize negative charge in the enolate ion better than esters, so the acidity of this hydrogen is higher in adducts **33e**,**f** formed from ketoesters **11e**,**f** than in adducts **33g**,**h** originated from diesters **11g**,**h**. We believe that this difference in acidity is the main reason why the former adducts are stabilized by elimination of hydrogen halogenide and the latter undergo cyclization.

Conclusions

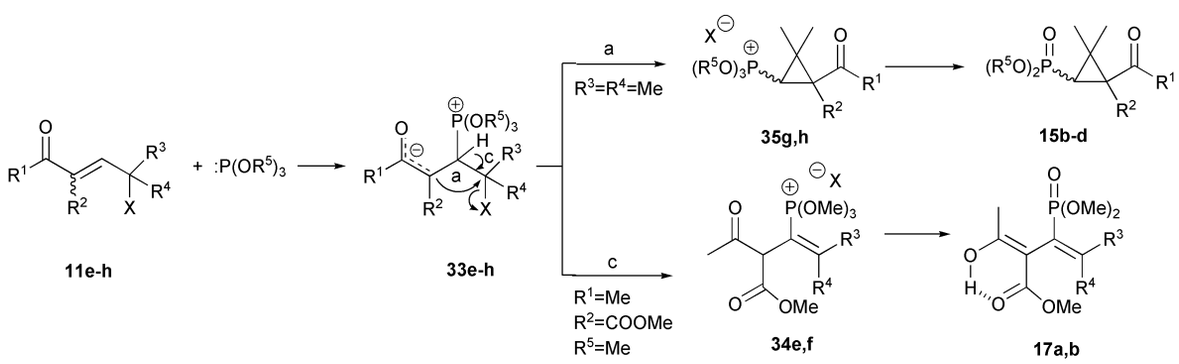
The phosphorylation of selected γ-halogeno α,β-unsaturated ketones and esters **15a**,**h** with simple trialkyl phosphites gave a variety of organophosphorus compounds, which were isolated



Scheme 2



Scheme 3



Scheme 4

and characterized. Also, the consistent mechanistic scheme explaining the formation of all products, including their stereochemistry was proposed. We believe that initial addition of the ketones **15a**–**d**, bearing only one activating group, to trialkyl phosphites gives an intermediate, which can exist as oxaphospholenes **23** and **24**, and also as an open, dipolar form **22**. Presence of the second activating group, as in ketoesters **15e**,**f** and diesters **15g**,**h**, favors the formation of dipolar intermediate **33**. The actual outcome of the reaction depends on the position of the equilibrium between these three forms as well as the rate of their further transformations. Such structural features as the number and nature of both the halogen atoms and the activating groups play a key role in the reactivity pattern of the specific substrate. We also believe the investigated reactions to be of synthetic interest due to the formation of a variety of highly functionalised organophosphorus compounds such as 1,3-dienylphosphates **14**, ketovinylphosphonates **17** or phosphorylated cyclopropanecarboxylates **15** in high yields.

Experimental

^{1}H NMR (250 MHz), ^{13}C NMR (62.9 MHz) and ^{31}P NMR (101 MHz) spectra were recorded on a Bruker DPX-250 spectrometer with TMS as an internal standard and 85% H_3PO_4 as an external standard, respectively. ^{31}P NMR spectra were recorded using broadband proton decoupling. The coupling constants (*J*) values are given in Hz. Column chromatography was performed on FLUKA® silica gel (230–400 mesh). TLC was carried out on 0.25 mm thick Merck 60 F_{254} silica gel plates.

Compounds **11a**,[13] **11b**,[14] **11c**[14] and **11g**[15] were prepared as described.

(*E*)-5,5-Dibromo-3-hexen-2-one (11d)

This compound was obtained by applying the procedure described for **11a**[13] and using 2,2-dibromopropanal[16] and diethyl 2-oxopropylphosphonate. (68%), mp 36–37 °C (after purification by column chromatography, eluent: AcOEt–benzene 1 : 1) (Found: C, 28.3; H, 3.3; Br, 62.2. C_6H_8BrO requires C, 28.2; H, 3.15; Br, 62.4%); $\delta_H(CDCl_3)$ 2.75 (3H, s, COMe), 3.12 (3H, s, CBr_2Me), 6.58 (1H, d, *J* 16.0, 3-H), 7.48 (1H, d, *J* 16.0, 4-H).

Methyl 3-oxo-2-(2,2,2-trichloroethylidene)butanoate (11e)

This compound was obtained as a mixture of *E* and *Z* isomers in a 1 : 1 ratio, by applying the procedure described for the corresponding ethyl ester,[17] from methyl acetoacetate and trichloroacetic aldehyde. (51%), bp 88–90 °C/0.1 mmHg (Found: C, 34.3; H, 2.8; Cl, 43.5. $C_7H_7Cl_3O_3$ requires C, 34.25; H, 2.9; Cl, 43.3%); $\delta_H(CDCl_3)$[21] 2.38 and 2.46 (3H, s, COMe), 3.85 (3H, s, OMe), 7.15 and 7.18 (1H, s, C=CH).

Methyl 3-oxo-2-(2-bromo-2-methylpropylidene)butanoate (11f)

This compound was obtained as a mixture of *E* and *Z* isomers in a ~1 : 1 ratio, by standard allylic bromination[18] of methyl 3-oxo-2-(2-methylpropylidene)butanoate.[19] It was used in the next step without purification. Purity ~97%, estimated from the ^{1}H NMR spectrum; $\delta_H(CDCl_3)$[21] 1.91 and 1.95 (6H, s, Me_2C), 2.32 (3H, s, MeCO), 2.45 (3H, s, MeCO), 3.78 and 3.85 (3H, s, OMe), 6.95 and 7.03 (1H, s, CH).

(*E*)-Methyl 4-bromo-2-(diethoxyphosphoryl)-4-methyl-2-pentenoate (11h)

This compound was obtained by standard allylic bromination[18] of methyl 2-(diethoxyphosphoryl)-4-methyl-2-pentenoate.[20] It was used in the next step without purification. Purity ~97%, estimated from the ^{1}H NMR spectrum; $\delta_H(CDCl_3)$ 1.35 (6H, t, *J* 6.5, CH_2CH_3), 1.96 (6H, s, CMe_2), 3.83 (3H, s, OMe), 3.99–4.26 (4H, m, CH_3CH_2), 6.89 (1H, d, $^3J_{PH}$ 19.5, 3-H); $\delta_P(CDCl_3)$ 12.54.

General procedure for the reaction of γ-halogenated α,β-unsaturated ketones and esters 11a–h with trialkyl phosphites

A mixture of halogenated ketone or ester **11** (5.0 mmol) and alkyl phosphite (7.5 mmol), neat or in benzene (10 mL) was stirred and heated under an argon atmosphere at the temperature and for the time given in the Table 1. Progress of the reaction was monitored by ^{31}P NMR spectroscopy. Then the excess of alkyl phosphite was evaporated under vacuum and the residue was analyzed using the ^{31}P NMR technique. The crude product was purified by distillation or column chromatography and separated, if necessary, using column chromatography. The eluents for chromatographic purification are given below.

Dimethyl 1-(1′-methylethenyl)-3-oxobutylphosphonate (12)

Eluent: AcOEt–benzene = 6 : 4, R_f = 0.16 (275 mg, 25%) (Found: C, 49.2; H, 7.8; P, 14.3. $C_9H_{17}O_4P$ requires C, 49.1; H, 7.8; P, 14.1%); $\delta_H(CCl_4)$ 2.31 (3H, d, *J* 1.0, CH_3C=), 2.52 (3H, s, COMe), 3.09–3.22 (2H, m, 2-H), 3.66 (1H, ddd, *J* 21.1, 8.5, 5.3, 1-H), 4.10 (6H, d, *J* 11.0, 2 × OMe), 5.18 (1H, dd, *J* 2.1, 1.0, =CH), 5.40 (1H, d, *J* 2.1, =CH); $\delta_C(CDCl_3)$ 21.34 (d, $^3J_{CP}$ 2.4, CH_2=*CMe*), 31.53 (C-4), 37.55 (d, $^2J_{CP}$ 3.7, C-2), 43.79 (d, $^1J_{CP}$ 139.2, C-1), 51.86 (d, $^2J_{CP}$ 5.9, P[OMe]$_2$), 115.12 (d, $^3J_{CP}$ 11.9, C-2′), 139.4 (d, $^2J_{CP}$ 9.0, C-1′), 210.45 (d, $^3J_{CP}$ 14.7, C-3); $\delta_P(CCl_4)$ 30.1.

3-Isopropylidene-2-methoxy-5-methyl-3*H*-[1,2]oxaphosphole-2-oxide (13)

Eluent: AcOEt–benzene = 6 : 4, R_f = 0.33 (150 mg, 16%) (Found: C, 51.25; H, 7.0; P, 16.7. $C_8H_{13}O_3P$ requires C, 51.1; H, 7.0; P, 16.5%); $\delta_H(CDCl_3)$ 1.89 (3H, d, *J* 1.5, 5-Me), 2.01 (3H, s, MeC=C), 2.10 (3H, d, *J* 3.0, MeC=C), 3.66 (3H, d, *J* 12.0, OMe), 5.74 (1H, dq, *J* 31.0 and 1.5, 4-H); δ_C ($CDCl_3$) 19.74 (d, $^3J_{CP}$ 8.1, C=C*Me*), 20.27 (d, $^3J_{CP}$ 18.6)/24.92 (d, *J* 7.0) (C=C*Me*$_2$), 51.07 (d, $^2J_{CP}$ 5.4, OMe), 102.94 (d, $^2J_{CP}$ 7.3, C-4), 119.11 (d, $^1J_{CP}$ 187.2, C-3), 153.35 (d, $^2J_{CP}$ 13.9, C=*C*Me$_2$), 154.62 (d, $^2J_{CP}$ 8.4, C-5); $\delta_P(CCl_4)$ 29.8.

Dimethyl (*Z*)-1,4-dimethylpenta-1,3-dienyl phosphate (14a)

Eluent: AcOEt–benzene = 6 : 4, R_f = 0.39 (143 mg, 13%) (Found: C, 49.0; H, 7.8; P, 14.3. $C_9H_{17}O_4P$ requires C 49.1; H, 7.8; P, 14.1%); $\delta_H(CDCl_3)$ 2.18 (3H, d, *J* 0.8, 5-H), 2.25 (3H, d, *J* 0.7, 4-Me), 2.53 (3H, d, *J* 1.0, 1-Me), 4.30 (6H, d, *J* 11.5, 2 × OMe), 6.12 (1H, dq, *J* 11.0 and 1.0, 2-H), 6.54 (1H, br d, *J* 11.0, 3-H); $\delta_C(CDCl_3)$ 19.40/24.52 (C=*CMe*$_2$), 22.08 (d, $^3J_{CP}$ 5.3, C=C*Me*), 53.92 (d, $^2J_{CP}$ 5.1, 2 × OMe), 108.63 (d, $^3J_{CP}$ 5.3, C-2), 130.56/138.25 (C-3, C-4), 139.58 (d, $^2J_{CP}$ 10.1, C-1); $\delta_P(CDCl_3)$ −4.23.

Dimethyl 4-chloro-1-methylpenta-1,3-dienyl phosphate (14b)

Eluent AcOEt–benzene = 6 : 4, R_f = 0.33 (96 mg, 8%) (Found: C, 40.0; H, 5.7; Cl, 14.5; P, 12.6. $C_8H_{14}ClO_4P$ requires C, 39.9; H, 5.9; Cl, 14.7; P, 12.9%); mixture of (1*Z*,3*E*) and (1*Z*,3*Z*) isomers in 1 : 1 ratio; $\delta_H(CDCl_3)$[21] 1.98 (3H, d, *J* 0.8, 4-Me), 2.07 (3H, d, *J* 0.8, 4-Me), 2.14 (3H, d, *J* 1.0, 1-Me), 2.18 (3H, d, *J* 1.0, 1-Me), 3.78 (6H, d, *J* 11.5, 2 × OMe), 3.8 (6H, d, *J* 11.5, 2 × OMe), 5.42 (1H, dq, *J* 11.0 and 1.0, 2-H), 5.72 (1H, dq, *J* 11.0 and 1.0, 2-H), 6.32 (1H, br d, *J* 11.0, 3-H), 6.40 (1H, br d, *J* 11.0, 3-H); $\delta_P(CDCl_3)$[21] −4.10, −4.14.

(*Z*)-Dimethyl 4,4-dichloro-1-methylbuta-1,3-dienyl phosphate (14c)

Bp 100–102 °C/0.4 mmHg (lit.[2] 115–116 °C/1 mmHg) (809 mg, 62%) (Found: C, 32.2; H, 4.20; Cl, 27.3; P, 11.7. $C_7H_{11}Cl_2O_4P$ requires C, 32.2; H, 4.25; Cl, 27.2; P, 11.9%); $\delta_H(CDCl_3)$ 2.55 (3H, d, *J* 1.0, 1-Me), 4.18 (6H, d, *J* 11.0, 2 × OMe), 6.02 (1H, dd, *J* 11.0 and 1.0, 2-H), 7.00 (1H, d, *J* 11.0, 3-H); $\delta_C(CDCl_3)$ 22.24 (d, $^3J_{CP}$ 5.3, C=C*Me*), 53.87 (d, $^2J_{CP}$ 5.1, 2 × OMe), 110.52 (d, $^3J_{CP}$ 5.4, C-2), 127.32/130.38 (C-3, C-4), 146.41 (d, $^2J_{CP}$ 10.0, C-1); $\delta_P(CDCl_3)$ −4.83.

Dimethyl 4-bromo-1-methylpenta-1,3-dienyl phosphate (14d)

Eluent AcOEt–benzene = 6 : 4, R_f = 0.38 (712 mg, 50%) (Found: C, 33.8; H, 5.0; Br, 28.15; P, 10.9. $C_8H_{14}BrO_4P$ requires C, 33.7; H, 4.95; Br, 28.0; P, 10.9%); mixture of (1*Z*,3*E*) and (1*Z*,3*Z*) isomers in a 65 : 35 ratio; $\delta_H(CDCl_3)$[21] (major isomer) 2.52 (3H, br s, 4-Me), 2.85 (3H, d, *J* 1.0, 1-Me), 4.25 (6H, d, *J* 11.5, 2 × OMe), 5.95 (1H, dd, *J* 10.0 and 1.0, 2-H), 6.80 (1H, d, *J* 10.0, 3-H), (minor isomer) 2.45 (3H, br s, 4-Me), 2.80 (3H, d, *J* 1.0, 1-Me), 4.21 (6H, d, *J* 11.5, 2 × OMe), 5.82 (1H, dd, *J* 11.0 and 1.0, 2-H), 6.92 (1H, d, *J* 11.0, 3H); $\delta_P(CDCl_3)$[21] (major isomer) −4.74, (minor isomer) −4.13.

Dimethyl 3-acetyl-2-chloro-2-methylcyclopropylphosphonate (15a)

Eluent AcOEt–benzene = 6 : 4, R_f = 0.25 (325 mg, 27%) (Found: C, 39.7; H, 5.8; Cl, 14.9; P, 12.7. $C_8H_{14}ClO_4P$ requires C, 39.9; H, 5.9; Cl, 14.7; P, 12.9%); $\delta_H(CDCl_3)$ 2.25 (3H, s, 3-Me), 2.48 (3H, s, C(O)Me), 3.15–3.31 (2H, m, 1-H, 3-H), 3.74 (3H, d, *J* 11.0, OMe), 3.77 (3H, d, *J* 11.0, OMe); $\delta_C(CDCl_3)$ 25.50 (d, $^3J_{CP}$ 4.7, CCl*Me*), 31.09 (CO*Me*), 32.44 (d, $^1J_{CP}$ 190.4, C-1), 34.38 (d, $^2J_{CP}$ 3.2, C-3), 45.23 (d, $^2J_{CP}$ 2.5, C-2), 52.04 (d, $^2J_{CP}$ 7.6)/52.31 (d, $^2J_{CP}$ 6.5) (P[OMe]$_2$), 211.85 (C=O); $\delta_P(CDCl_3)$ 25.32.

Diethyl 3-(dimethoxyphosphoryl)-2,2-dimethylcyclopropane-1,1-dicarboxylate (15b)

Bp 129–130 °C/0.5 mmHg (1.34 g, 83%) (Found: C, 48.6; H, 7.05; P, 9.7. $C_{13}H_{23}O_7P$ requires C, 48.45; H, 7.2; P, 9.6%);

δ_H($CDCl_3$) 1.16 (3H, d, $^4J_{PH}$ 1.5, 2-Me), 1.25 (6H, t, *J* 7.0, CH_2CH_3), 1.50 (3H, s, 2-Me), 1.65 (1H, d, $^2J_{PH}$ 2.0, 3-H), 3.64 (3H, d, $^3J_{PH}$ 11.0, OMe), 3.71 (3H, d, $^3J_{PH}$ 11.0, OMe), 4.15 (4H, q, $^3J_{PH}$ 7.0, CH_2CH_3); δ_C($CDCl_3$) 13.32/13.52 (2 × OCH_2CH_3), 19.98 (d, $^3J_{CP}$ 5.6)/21.84 (d, $^3J_{CP}$ 2.9) (CMe_2), 27.23 (d, $^1J_{CP}$ 188.2, C-3), 29.51 (d, $^2J_{CP}$ 2.9, C-2), 43.55 (d, $^2J_{CP}$ 2.9, C-1), 51.53 (d, $^2J_{CP}$ 5.9)/52.18 (d, $^2J_{CP}$ 7.5) ($P[OMe]_2$), 60.84/61.55 (2 × CH_2CH_3), 164.88 (d, $^3J_{CP}$ 7.5)/166.96 (d, $^3J_{CP}$ 4.4) (2 × C=O); δ_P($CDCl_3$) 23.87.

Diethyl 3-(diisopropoxyphosphoryl)-2,2-dimethylcyclopropane-1,1-dicarboxylate (15c)

Bp 105–106 °C/0.05 mmHg (1.45 g, 77%) (Found: C, 53.9; H, 8.2; P, 8.0. $C_{17}H_{31}O_7P$ requires C, 54.0; H, 8.3; P, 8.2%); δ_H($CDCl_3$) 1.12 (3H, d, $^4J_{PH}$ 1.5, 2-Me), 1.24 (6H, t, *J* 7.0, 2 × CH_2CH_3), 1.26 (12H, d, *J* 6.5, 2 × $CH[CH_3]_2$), 1.50 (3H, s, 2-Me), 1.63 (1H, $^2J_{PH}$ 2.3, 3-H), 3.98–4.25 (4H, m, 2 × CH_2CH_3), 4.49–4.83 (2H, m, 2 × $CH[CH_3]_2$); δ_C($CDCl_3$) 13.41/13.65 (2 × OCH_2CH_3), 19.23 (d, $^3J_{CP}$ 5.6)/22.01 (d, $^3J_{CP}$ 2.9) (CMe_2), 24.53/24.75/24.92/25.04 (d, $^3J_{CP}$ 2.9, $P[OCHMe_2]_2$), 28.31 (d, $^2J_{CP}$ 188.3, C-3), 29.49 (d, $^2J_{CP}$ 2.9, C-2), 44.89 (d, $^2J_{CP}$ 2.9, C-1), 60.82/61.54 (2 × OCH_2CH_3), 72.48/72.63 (d, $^2J_{CP}$ 5.9, $P[OCHMe_2]_2$), 164.82 (d, $^3J_{CP}$ 7.5)/166.83 (d, $^3J_{CP}$ 4.4) (2 × C=O); δ_P($CDCl_3$) 17.22.

Methyl 1-(diethoxyphosphoryl)-*c*-3-(dimethoxyphosphoryl)-2,2-dimethyl-*r*-1-cyclopropanecarboxylate (*c*-3,*r*-1-15d)

Eluent AcOEt–EtOH = 9 : 1, R_f = 0.31 (819 mg, 44%) (Found: C, 41.8; H, 7.0; P, 16.6. $C_{13}H_{26}O_8P_2$ requires C, 41.9; H, 7.0; P, 16.6%); δ_H($CDCl_3$) 1.32 (3H, t, *J* 5.25, CH_2CH_3), 1.33 (3H, t, *J* 5.25, CH_2CH_3), 1.35 (3H, s, 2-Me), 1.43 (3H, s, 2-Me), 1.62 (1H, dd, $^3J_{PH}$ 14.8 and $^2J_{PH}$ 3.0, 3-H), 3.65 (3H, d, $^3J_{PH}$ 7.8, OMe), 3.71 (3H, s, COOMe), 3.81 (3H, d, $^3J_{PH}$ 7.8, OMe), 4.01–4.25 (4H, m, 2 × CH_2CH_3); δ_C($CDCl_3$) 15.73 (d, $^3J_{CP}$ 2.9)/15.99 (d, $^3J_{CP}$ 2.9) ($P[OCH_2CH_3]_2$), 19.89 (t, $^3J_{CP}$ = $^3J_{CP}$ 4.4)/23.08 (t, $^3J_{CP}$ = $^3J_{CP}$ 4.1) (CMe_2), 27.33 (dd, $^1J_{CP}$ 192.7, $^2J_{CP}$ 2.9, C-3), 28.54 (t, $^2J_{CP}$ = $^2J_{CP}$ 2.9, C-2), 37.77 (dd, $^1J_{CP}$ 170.6, $^2J_{CP}$ 5.9, C-1), 51.42 (d, $^2J_{CP}$ 5.9)/52.59 (d, $^2J_{CP}$ 5.9) ($P[OMe]_2$), 52.07 (COO*Me*), 62.50 (d, $^2J_{CP}$ 7.0)/62.83 (d, $^2J_{CP}$ 5.9) ($P[OCH_2CH_3]_2$), 165.76 (dd, $^2J_{CP}$ 7.35, $^3J_{CP}$ 4.4, *C*OOMe); δ_P($CDCl_3$) 20.48 (1P, d, $^3J_{PP}$ 9.8), 25.73 (1P, d, J_{PP} 9.8).

Column chromatography afforded also a mixture of *c*-3,*r*-1-**23d** and *t*-3,*r*-1-**23d** in an 83 : 17 ratio (112 mg, 6%). NMR data for *t*-3,*r*-1-**23d** taken from the mixture of *c*-3,*r*-1-**23d** and *t*-3,*r*-1-**23d** are as follows: δ_H($CDCl_3$) 1.29 (3H, t, *J* 5.2, CH_2CH_3), 1.31 (3H, t, *J* 5.2, CH_2CH_3), 1.34 (3H, s, 2-Me), 1.40 (3H, s, 2-Me), 1.58 (1H, dd, $^3J_{PH}$ 5.3 and $^2J_{PH}$ 3.0, 3-H), 3.63 (3H, d, $^3J_{PH}$ 7.8, OMe), 3.69 (3H, s, COOMe), 3.79 (3H, d, $^3J_{PH}$ 7.8, OMe), 3.92–4.25 (4H, m, 2 × CH_2CH_3); δ_P($CDCl_3$) 18.61 (1P, d, $^3J_{PP}$ 12.2), 23.55 (1P, d, $^3J_{PP}$ 12.2).

Dimethyl 2,5-dimethylfuran-3-ylphosphonate (16)

Eluent AcOEt–benzene = 6 : 4, R_f = 0.21 (143 mg, 14%) (Found: C, 47.2; H, 6.45; P, 15.3. $C_8H_{13}O_4P$ requires C, 47.1; H, 6.4; P, 15.2%); δ_H($CDCl_3$) 2.25 (3H, s, 5-Me), 2.48 (3H, d, $^4J_{PH}$ 2.5, 2-Me), 3.72 (6H, d, *J* 11.0, 2 × OMe), 5.99 (1H, d, $^3J_{PH}$ 2.3, 4-H); δ_C($CDCl_3$) 15.34 (C-5*Me*), 16.08 (d, $^3J_{CP}$ 7.8, C-2*Me*), 51.89 (d, $^2J_{CP}$ 5.8, 2 × OMe), 100.38 (d, $^1J_{CP}$ 199.8, C-3), 115.21 (d, $^2J_{CP}$ 9.9, C-4), 151.44 (d, $^3J_{PC}$ 12.5, C-5), 163.65 (d, $^2J_{CP}$ 24.2, C-2); δ_P($CDCl_3$) 17.35.

Methyl (2*E*)-2-[2′,2′-dichloro-1′-(dimethoxyphosphoryl)vinyl]-3-hydroxybut-2-enoate (17a)

Mp 53–54 °C (from benzene–hexane) (1.18 g, 74%) (Found: C, 33.8; H, 4.1; Cl, 22.2; P, 9.8. $C_9H_{13}Cl_2O_6P$ requires C, 33.9; H, 4.1; Cl, 22.2; P, 9.7%); δ_H 2.00 (3H, d, $^5J_{PH}$ 1.7, 4-H), 3.79 (6H, d, J_{PH} 11.5, 2 × POMe), 3.80 (3H, s, OMe), 12.82 (1H, s, OH); δ_C($CDCl_3$) 19.24 (C-4), 51.81 (COO*Me*), 53.11 (d, $^2J_{CP}$ 5.8, $P[OMe]_2$), 99.29 (d, $^2J_{CP}$ 4.4, C-2), 125.69 (d, $^1J_{CP}$ 192.7, C-1′), 137.49 (d, $^2J_{CP}$ 20.6, C-2′), 170.77 (C-3), 175.35 (d, $^3J_{CP}$ 4.4, C-1); δ_P ($CDCl_3$) 13.42.

Methyl (2*E*)-3-(dimethoxyphosphoryl)-2-(1′-hydroxyethylidene)-4-methylpent-3-enoate (17b)

Eluent AcOEt, R_f = 0.38 (1.06 g, 76%) (Found: C, 47.5; H, 6.75; P, 11.0. $C_{11}H_{19}O_6P$ requires C, 47.5; H, 6.9; P, 11.1%); δ_H($CDCl_3$) 1.72 (3H, d, $^4J_{PH}$ 2.5, CMe*Me*), 1.88 (3H, d, $^5J_{PH}$ 1.7, 2′-H), 2.15 (3H, d, $^4J_{PH}$ 3.25, C*Me*Me), 3.65 (6H, d, $^3J_{PH}$ 10.8, 2 × POMe), 3.76 (3H, s, OMe), 13.13 (1H, s, OH); δ_C ($CDCl_3$) 18.92 (C-2′), 22.59 (d, $^3J_{CP}$ 7.3)/23.17 (d, $^3J_{CP}$ 19.1) (CMe_2), 51.22 (COO*Me*), 51.87 (d, $^2J_{CP}$ 5.9 $P[OMe]_2$), 99.29 (d, $^2J_{CP}$ 10.3, C-2), 118.83 (d, $^1J_{CP}$ 191.19, C-3), 156.34 (d, $^2J_{CP}$ 14.7, C-4), 172.20 (C-1′), 173.95 (d, $^3J_{CP}$ 5.88, C-1); δ_P($CDCl_3$) 19.37.

3,5,5-Trichloro-4-penten-2-one (18)

This compound was prepared according to the literature[6] procedure by heating 5,5,5-trichloro-3-penten-2-one **11c** (8.1 g, 43 mmol) with silica gel 50–100 mesh (14 g) at 180 °C for 1 h. The reaction mixture was then distilled 125–127 °C/16 mmHg (lit.[6] 40–42 °C/0.2 mmHg) to give **18** (4.1 g, 51%).

(*E*)- and (*Z*)-Dimethyl-4,4-dichloro-1-methylbuta-1,3-dienyl phosphate (*E*)- and (*Z*)-(14c)

The solution of **18** (3.5 g, 18.8 mmol) and trimethyl phosphite (2.6 g, 20.9 mmol) in benzene (2 mL) was heated under reflux for 2 h. The reaction mixture was then distilled under reduced pressure to give a mixture of (*E*)- and (*Z*)-**22c** in ~ 1 : 1 ratio. (2.7 g, 50%) bp 103–104 °C/0.4 mmHg; (*E*)-**14c**: δ_H($CDCl_3$)[21] 2.62 (3H, d, *J* 1.0, 1-Me), 4.11 (6H, d, *J* 11.0, 2 × OMe), 6.40 (1H, dd, *J* 11.0 and 1.0, 2-H), 6.85 (1H, d, *J* 11.0, 3-H); δ_P($CDCl_3$)[21] −5.03; (*Z*)- **14c** δ_H($CDCl_3$)[21] 2.55 (3H, d, *J* 1.0, 1-Me), 4.18 (6H, d, *J* 11.0, 2 × OMe), 6.02 (1H, dd, *J* 11.0 and 1.0, 2-H), 7.00 (1H, d, *J* 11.0, 3-H); δ_P($CDCl_3$)[21] −4.83

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