# 43. The Synthesis and Reactions of Dialkyl 1-Vinylvinyl-Phosphates

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*Summary*

3,4-Dichlorobutanone reacts with trialkyl phosphites to give dialkyl 1,3-butadien-2-yl phosphates. Their structures were determined by spectroscopic methods and various chemical reactions.

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Vicinal dihalides with electron-withdrawing groups adjacent to one or both halogen atoms are known to be dehalogenated on treatment with trialkyl phosphites [1-5]. For instance, reaction of 3,4-dibromobutanone with triethyl phosphite was reported [5] to give exclusively methyl vinyl ketone. In contrast we have found that 3,4-dichlorobutanone (**1**) does not react like its bromo analog, but rather like a normal $\alpha$-halo ketone giving a mixture of mainly a dialkyl vinyl phosphate (the product of a *Perkow* reaction [6]) and some phosphonate esters (products of a *Michaelis-Arbuzov* reaction [7]). Thus when equimolar amounts of **1** and trimethyl phosphite were mixed, a strongly exothermic reaction started at once and gaseous methyl chloride was given off. The resulting product, presumably **2**, proved to be unstable under the reaction conditions. On distillation, a second gas (HCl) evolved and dimethyl 1,3-butadien-2-yl phosphate (**3**) was isolated in 35-40% yield. Similarly with triethyl phosphite, the diethyl analog **4** was formed. In addition to compound **3**, small amounts of a mixture of ketones, likely **5** and **6**, could be detected by IR. spectroscopy. Although **3** and **4** did polymerize to some extend when heated, they were stored unchanged for several months at 0°. No trace of methyl vinyl ketone was found in the reaction mixture. The results are best accomodated in the following reaction scheme.

The structure of compounds **3** and **4** were determined from analytical and spectral data. Both exhibited bands in the IR. spectrum at 1650 $cm^{-1}$ and 1600 $cm^{-1}$ which indicated the presence of a C=C and a C=C–OR group [8]. Strong bands at 1280 and 1045 $cm^{-1}$ were indicative of covalent phosphate. The UV. spectrum of **3** (in methanol) exhibited a strong absorption at 220 nm ($\varepsilon$ 16420) characteristic of a conjugated diene [9] and the $^1$H-NMR. spectrum showed five olefinic protons in addition to two three-proton singlets for the methoxy groups.

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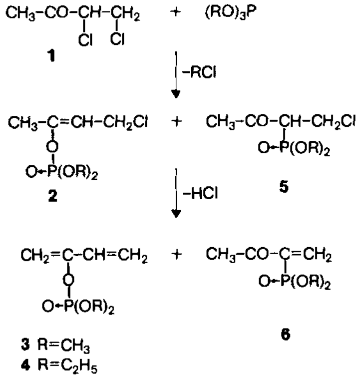
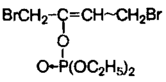
*Scheme 1*

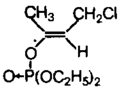


Further proof of structure of compounds **3** and **4** came from their chemical reactions. For instance 1,4-addition of bromine to **4** led to the dibromo compound **7**. Although this product gave a correct elemental analysis and seemed to be uniform by thin layer chromatography, NMR. spectroscopy showed it to be a 4:1 mixture of the *trans* and *cis* isomers. Compound **2** which could not be isolated from the reaction that led to **4**, was obtained in good yield by addition of hydrogen chloride to **4**. Theoretically two positional isomers might be expected in this 1,4-addition but only one, namely **2**, was formed; moreover, **2** turned out to be the pure *trans* isomer **2a**.

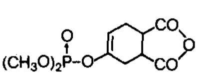
*Diels-Alder* addition of maleic anhydride, tetracyanoethylene, methyl vinyl ketone, and nitrosobenzene to **3** or **4** gave compounds **8**, **9**, **10**, **11** and **12**, respectively. The addition of methyl vinyl ketone to **3** led as expected to a mixture of the two possible adducts **10** and **11** as indicated by different signals for the $CH_3-CO-$ group in the $^1$H-NMR. spectrum. The two compounds which were present in a ratio of 2:1 could not be separated further and we were unable to make a definite assignment of the predominating isomer. Surprisingly the nitrosobenzene addition to **4** which would also be expected to give two isomers, furnished only one, namely **12**, in good yield.


$BrCH_2-C(-O-P(OC_2H_5)_2)=CH-CH_2Br$

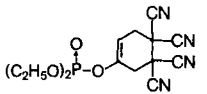
**7**



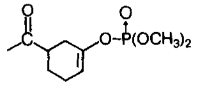
**2a**



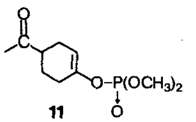
**8**



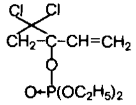
**9**



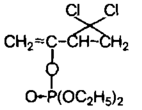
**10**



**11**

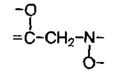


**17**



**18**

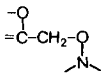
The structure of **12** could not be unequivocally assigned from $^1$H-NMR. data alone since the chemical shift for the signal of the methylene singlet would be predicted to be rather similar for both structural features *i.e.* **a** and **b**.



$=\overset{-O}{\overset{|}{C}}-CH_2-\underset{\underset{O-}{|}}{N}-$

**a**

and



$=\overset{-O}{\overset{|}{C}}-CH_2-\underset{\underset{N}{|}}{O}$

**b**

Therefore the following chemical transformations were carried out: Reduction with zinc in acetic acid gave the alcohol **13** which with phenyl isocyanate in carbon tetrachloride was converted to the urea derivative **14** ($\tilde{\nu}$CO 1680 cm$^{-1}$); on the other hand, the same reaction in DMSO solution yielded the carbamate **15** ($\tilde{\nu}$CO 1740 cm$^{-1}$). Such an interesting solvent-dependent orientation of the isocyanate attack has also been observed in other cases [10] [11]. Reaction of **13** with two equivalents of phenyl isocyanate furnished the ureido-carbamate **16** ($\tilde{\nu}$CO 1740 and 1690 cm$^{-1}$) *(Scheme 2)*. Since none of these compounds were known, proof of structure had to come from spectral data. For the same reason outlined for compound **12**, the $^1$H-NMR. data of each compound would have been insufficient for an unequivocal structure determination. However, observing the up or downfield shift of individual resonance signals on introduction of neighboring substituents (see *Table*) lead to the final assignment. For instance, the conversion of **13** to the urea derivative **14** caused the downfield shift of a methylene singlet from $\delta$ 3.85 to $\delta$ 4.47. A methylene doublet remained practically unchanged. On the other hand conversion of **13** to carbamate **15** brought the downfield shift of a methylene doublet from $\delta$ 4.07 to $\delta$ 4.77; the methylene singlet at $\delta$ 3.85 moved only slightly. For the ureido-carbamate derivative **16** the methylene singlet as well as the methylene doublet were shifted to lower field. Thus clear indication was given that the methylene group attached to an N-atom had no adjacent proton-bearing carbon atom, a fact consistent with the structures **12**-**16**.

Heating of **4** in refluxing benzene in the presence of phenyl (bromodichloromethyl) mercury resulted in a smooth addition of dichlorocarbene. The product was

*Scheme 2*

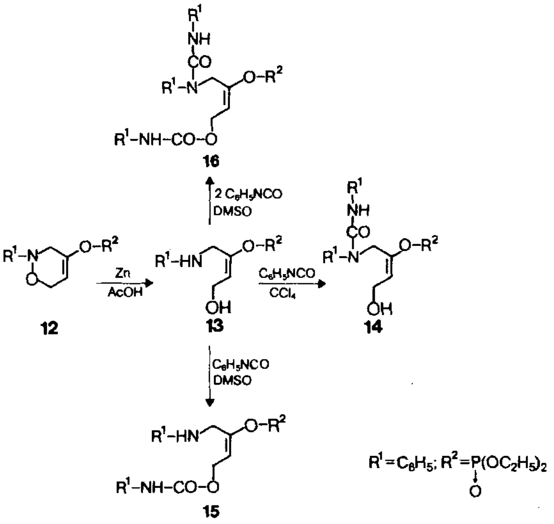


Table. *$^1$H-NMR. data of compounds* **12–16**

| Compound | Solvent | $-N-CH_2-$ | Signals[a] | | |
|---|---|---|---|---|---|
| | | | $-O-CH_2-$ | $-CH=C$ | $PO-CH_2-CH_3$ |
| **12** | $CDCl_3$ | 3.85*s* | 4.50*m* | 5.75*m* | |
| **13** | $CDCl_3$ | 3.91*s* | 4.18*d* | 5.69*t* | 4.07*m* 1.23 |
| | DMSO-$d_6$ | 3.85*s* | 4.07*d* | 5.52*t* | 4.02*m* 1.20*t* |
| **14** | $CDCl_3$ | 4.45*s* | 4.07*d* | | 3.93*m* 1.17*t* |
| | DMSO-$d_6$ | 4.47*s* | 3.76[b] | 5.46*t* | 4.00*m* 1.19*t* |
| **15** | DMSO-$d_6$ | 3.95*s* | 4.77*d* | 5.52*t* | 3.99*m* 1.17*t* |
| **16** | $CDCl_3$ | 4.65*s* | 4.46*d* | 5.74*t* | |
| | DMSO-$d_6$ | 4.61*s* | 4.55*s* | 5.65*t* | |

[a] In δ values. *s* = singlet; *m* = multiplet; *d* = doublet; *t* = triplet. Most signals showed some additional fine-splitting.

[b] On $D_2O$ exchange the triplet collapses to a doublet as the triplet due to the OH-proton (at 4.39 δ) disappears.

shown by $^1$H-NMR. spectroscopy to consist of a 10:1 mixture of the two possible adducts **17** and **18**.

## Experimental Part

Unless otherwise indicated, evaporations were done *in vacuo* at 35-40° (bath temperature). Melting points (m.p.) were determined with a *Thomas-Hoover* apparatus and are uncorrected. IR. spectra were taken on a *Perkin Elmer* Model 237B grating infrared spectrometer (maxima of absorption band in $cm^{-1}$, intensity of absorption: *s* = strong, *m* = medium, and *w* = weak). $^1$H-NMR. data were obtained on a *Varian* A-60A instrument (δ-values in ppm). The term petroleum ether refers to the fraction of b.p. 30-60°. Abbreviations: TLC. = thinlayer chromatography, RT. = room temperature.

*3,4-Dichlorobutanone* (**1**). Chlorine was introduced into a solution of 140 g (2 mol) of methyl vinyl ketone in 600 ml of chloroform with ice-cooling. When 142 g of chlorine (2 mol) had been absorbed, the chloroform was evaporated (bath temperature < 35°) leaving 290 g of slightly impure **1**, which was used without further purification.

*Dimethyl 1,3-butadien-2-yl phosphate* (**3**). Trimethyl phosphite (28.6 g) was treated with 3,4-dichlorobutanone (32 g) as described for the synthesis of **4**. Distillation gave three fractions: a) 2.2 g (mainly trimethyl phosphite), b.p. 30-80°; b) 10.1 g (crude **3**), b.p. 80-90°/0.75 Torr; c) mainly ketonic material, b.p. 95-105°/0.4 Torr. On redistillation of fraction b) pure **3**, b.p. 79-83°/1.5 Torr, was obtained. Compound **3** is hygroscopic. – UV.: 220 nm (ε 16520) in methanol. –

$C_6H_{11}PO_4$ (178.13) Calc. C 40.46 H 6.23% Found C 39.83 H 6.25%

*Diethyl 1,3-butadien-2-yl phosphate hemihydrate* (**4**). Triethyl phosphite (166 g, 1 mol) was cooled in an ice bath and 3,4-dichlorobutanone (140 g, 1 mol) was added. The mixture was stirred under $N_2$ for 2 h at 0°, then for 20 h at room temperature. After 0.5 g of hydroquinone and 0.5 g of aluminium

| Fraction | Distillation[a] | | Product |
|---|---|---|---|
| | B.p./Torr | Amount (g) | |
| a | 30-89°/> 5 | 10.8 | Mixture of triethyl phosphite and **4** |
| b | 89-114°/> 5 | 34.5 | Crude **4** |
| c | to 108°/1-1.5 | 27.5 | Crude **4** |
| d | Temperature dropped | 5.8 | Mixture of **4** and some ketonic material[b] |

[a] Since HCl is evolved during the distillation, pressure and therefore the b.p. vary erratically.

[b] As determined by IR. spectroscopy.

chloride had been added, the mixture was distilled *in vacuo*. A dark brown polymeric residue remained. Fractions b and c were combined and redistilled to give 34.4 g of pure **4**, b.p. 91-92°, 1.5 Torr.

$C_8H_8PO_4 \cdot \frac{1}{2} H_2O$ (215.19) Calc. C 44.75 H 7.49% Found C 45.14 H 7.40%.

*Diethyl 1,4-dibromo-2-buten-2-yl phosphate* (**7**). To a solution of 1 g of **4** in 30 ml of carbon tetrachloride was added 1 equivalent (745 mg) of bromine. The solution was kept at 0° for 1 h before it was evaporated leaving 1.70 g (100%) of crude **7**. Prep. TLC. (ethyl acetate/petroleum ether 1:1) on a small amount produced a colorless oil with practically the same IR. spectrum as that of the crude product. The compound decomposed on distillation. - IR. (neat): 1665 (C=C); 1265 and 1240 (covalent phosphate).

$C_8H_{15}Br_2O_4P$ (366.00) Calc. C 26.25 H 4.13 Br 43.60% Found C 26.48 H 4.28 Br 43.80%

*Diethyl 4,4,5,5(tetracyano)-cyclohexen-1-yl phosphate* (**9**). To a solution of 2.15 g (0.01 mol) of **4** in 10 ml of tetrahydrofuran was added under $N_2$ 1.28 g (0.01 mol) of tetracyanoethylene. The yellow solution was left at RT. for 2 days before it was evaporated. The residual syrup was taken up in ethyl acetate. Petroleum ether was added to incipient turbidity and the mixture was stored at 0° for 5 days. Filtration gave 2.10 g (63%) of **9**, m.p. 97-98°. Recrystallization from ethyl acetate/petroleum ether afforded long prisms and short plates of pure **9** both with the same m.p. (98°). - IR. (Nujol mull): no absorption for CN; 1665 (C=C), 1260 and 1045 $cm^{-1}$ (covalent phosphate). - $^1$H-NMR. ($CDCl_3$): 1.39 (*t*, 6 H); 3.31 (*m*, 4 H); 4.25 (*q*, 4 H); 5.88 (*m*, 1 H).

$C_{14}H_{14}N_4O_4P$ (333.27) Calc. C 50.46 H 4.23 N 16.81% Found C 50.61 H 4.54 N 16.98%

*4-(O,O-Dimethylphosphoryloxy)-cyclohex-4-ene-*cis*-1,2-carboxylic anhydride* (**8**). A mixture of 0.98 g (0.01 mol) of maleic anhydride and 1.78 g (0.01 mol) of **3** in 50 ml of benzene was stirred at RT. for 20 h. Evaporation gave a syrup which crystallized from ethyl acetate/petroleum ether to give 0.810 g (29.5%) of **8**, m.p. 71-72°. Recrystallization from the same solvent system gave prisms, m.p. 73-74°. - IR. (Nujol mull): 1850 and 1785 (anhydride), 1670 (C=C); 1275 and 1045 (covalent phosphate). Other peaks: 1165*s*, 992*m*, 955*m*, 925*s*, 868*s*, 815*m*, 770*m*.

$C_{10}H_{13}O_7P$ (276.18) Calc. C 43.49 H 4.74% Found C 43.44 H 4.71%

*2-Phenyl-4(O,O-diethylphosphoryloxy)-3,6-dihydro-2*H*-1,2-oxazine* (**12**). To a solution of 3.24 g (0.03 mol) of nitrosobenzene in 150 ml of methylene chloride was added 6.25 g (0.029 mol) of **4**. The mixture was left at RT. for 20 h before it was evaporated. The remaining crude **12** was purified on a silica gel column [250 g $SiO_2$-grade 62 (Grace), 5 cm diameter, eluant ethyl acetate/petroleum ether 1:2] to give 7.1 g (78.5%) of slightly colored **12**. - Compound **12** could not be distilled without decomposition. - UV. (in ethanol): 240 nm ($\varepsilon$ 7880), 282 ($\varepsilon$ 850). - $^1$H-NMR.: (see discussion).

$C_{14}H_{20}NO_5P$ (313.30) Calc. C 53.67 H 6.43 N 4.47% Found C 53.52 H 6.57 N 4.26%

*Diethyl (2,2-dichloro-1-vinyl)cyclopropyl phosphate* (**17** and **18**). A solution of 2.42 g of **4** in 50 ml of dry benzene to which had been added 5.10 g of phenyl(bromodichlormethyl)mercury was refluxed under $N_2$ for 3 h. The mixture was cooled, filtered, and the filtrate evaporated. The residue was taken up in a little ether, filtered once more and the filtrate evaporated. Distillation of the residue gave 2.20 g, b.p. 112-123°/1 Torr of slightly impure phosphates. Redistillation gave a 10:1 mixture of pure **17** and **18**, b.p. 111-116°/0.6 Torr.

$C_9H_{15}Cl_2PO_4$ (289.10) C 37.39 H 5.23% Found C 37.02 H 5.21%

*Diethyl 4-chloro-2-buten-2-yl phosphate* (**2a**). To a solution of 0.33 g (0.009 mol) of dry HCl in 30 ml of dry benzene was added a solution of 1.94 g (0.009 mol) of **4** in 10 ml of dry benzene. The mixture was left at RT. protected from light for 18 h. Evaporation of the excess benzene (bath temperature < 30°) left crude **2a** (2.2 g). Column chromatography (silica gel grade 62; eluant: ethyl acetate/petroleum ether 1:2) gave 1.3 g of pure, liquid **2a**.

$C_8H_{16}ClPO_4$ (242.64) Calc. C 39.60 H 6.65 Cl 14.61% Found C 39.58 H 6.54 Cl 14.70%

*Diethyl* cis*(1-anilino-4-hydroxy)-2-buten-2-yl phosphate* (**13**). The oxazine **12** (6 g) was dissolved in 50 ml of glacial acetic acid and 10 g of zinc dust was added. The mixture was stirred at RT. for 3 days before it was filtered. The filtrate was neutralized with 75 ml of 10N NaOH (ice-cooling) and the precipitate of zinc hydroxide was filtered off. The filtrate was extracted several times with ether;

evaporation of the dried ($MgSO_4$) ether extracts left 3.46 g of crude **13**. Purification over a silica gel column (ethyl acetate/petroleum ether 3:1) gave 2.3 g of **13** as a brown oil.

$C_{14}H_{22}NPO_5$ (315.33) Calc. C 53.55 H 7.03 N 4.44% Found C 53.17 H 6.68 N 4.10%

*Diethyl* cis-*4-hydroxy-1-[*N*-(phenylcarbamoyl)anilino]-2-buten-2-yl phosphate* (**14**). Compound **13** (315 mg) was dissolved in 30 ml of chloroform, and 200 mg of phenyl isocyanate was added. After 60 min at RT., the solvent was evaporated and the residue purified on a silica gel layer plate to give 225 mg of colorless, syrupy **14**. - IR. ($CHCl_3$ solution): 2430*w*, 1680*s*, 1600*m*, 1535*s*, 1500*m*, 1280*s*, 1040*s*, and 975*m*.

$C_{21}H_{27}N_2PO_6$ (434.43) Calc. C 58.06 H 6.27 N 6.45% Found C 57.05 H 6.43 N 6.24%

cis-*[4-Anilino-3-(*O,O*-diethylphosphoryloxy)-2-buten-1-yl]-*N*-phenylcarbamoate* (**15**). The reaction was carried out as described for the synthesis of compound **14** but in DMSO as solvent instead of chloroform. After prep. TLC. there was obtained 242 mg of compound **15**, m.p. 79-80° (recrystallized from ethyl acetate/petroleum ether). - IR. (in $CHCl_3$): 3450*s*, 1740*s*, 1605*s*, 1535*s*, 1280*s*, and 1040*s*.

$C_{21}H_{27}N_2PO_6$ (434.43) Calc. C 58.06 H 6.27 N 6.45% Found C 58.35 H 6.11 N 6.40%

cis-*3-(*O,O*-Diethylphosphoryloxy)-4-(*N,N'*-diphenylureido)-2-buten-1-yl-*N*-phenylcarbamoate* (**16**). Compound **13** (5 g) was dissolved in 25 ml of DMSO, and 25 ml of pyridine and 3.8 g of phenyl isocyanate were added and the mixture evaporated after 2 days at RT. Water (30 ml) was added and the mixture extracted with 5 portions of ether. The ether extract was dried and evaporated. The residue was taken up in methanol/petroleum ether 5:3. A solid (1 g, m.p. 235° (dec.)) was filtered off and identified as 1,3-diphenylurea (lit. m.p. 238°). Its formation may be explained by the presence of water in the reaction mixture.

The filtrate crystallized when left at 0° to give 1.6 g of **16**, m.p. 125-127°. Recrystallization from ethyl acetate/petroleum ether, m.p. 127°. - IR. (in $CHCl_3$): 3450*w*, 1740, 1690, 1600, 1535, and 1040 (all *s*).

$C_{28}H_{32}N_3PO_7$ (539.54) Calc. C 60.11 H 5.60 N 7.79% Found C 60.40 H 5.90 N 7.64%

*Addition of methyl vinyl ketone to compound* **3**. Compound **3** (1.78 g) was dissolved in 30 ml of methyl vinyl ketone and stirred for 20 h at 65° under $N_2$. The excess methyl vinyl ketone was evaporated off to give 3.60 g of the crude adducts. Column chromatography gave then 1.21 g of an oily but pure 2:1 mixture of **10** and **11**.

$C_{10}H_{17}PO_5$ (248.22) Calc. C 48.39 H 6.91% Found C 48.58 H 7.00%

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