Studies on Organophosphorus Compounds. X.*
Phosphorylation of Enolates. Stereochemical Investigations of the Reaction between Salts of \( \beta \)-Dicarbonyl Compounds and \( O,O \)-Diethyl Phosphorochloridithioate**

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Sodium salts of \( \beta \)-dicarbonyl compounds are found to yield mainly Z-isomers and tetrabutylammonium (TBA) salts mainly E-isomers of vinyl phosphorothioates when reacted with \( O,O \)-diethyl phosphorochloridithioate. The structure of the products is ascribed to the geometry of the anion of the salts: the W-shape yields E-isomers and the U-shape Z-isomers. At elevated temperature decomposition and Z/E isomerization are observed. \( O,O \)-Diethyl \( O \)-(2-acetyl-1-phenylvinyl) phosphorothioate (6) undergoes a thermal rearrangement to \( O,O \)-diethyl \( O \)-(2-benzoxy-1-methylvinyl) phosphorothioate (5) and the reverse rearrangement is also observed.

Reactions of enolate ions of \( \beta \)-dicarbonyl compounds and similar species with phosphorylating agents such as \( O,O \)-dialkyl phosphoro-chloridithioate or \( O,O \)-dialkyl phosphorochloridate occur solely on oxygen to give stable vinyl phosphorothioates or phosphates \(^{1,4}\) while normal enolates in few cases give keto phosphonates as co-products.\(^9\) Even metal derivatives of malonic ester are postulated to give diethyl 2-ethoxycarbonyl-1-ethoxyvinyl phosphate by \( O \)-phosphorylation when reacted with diethyl phosphorochloridate.\(^{14,22}\) Also the reaction of \( \alpha \)-halo ketones with trialkyl phosphites (Perkow reaction) in most cases leads to the \( O \)-phosphorylated product.\(^8\) It is found that the ratio of geometrical isomers procuced changes remarkably as the polarity of the solvent is varied.\(^1\) This is accounted for by the shape of the enolate ion. When the enolate ion is U-shaped the phosphorylated product is the Z-isomer and when W-shaped,

Enol phosphates and related compounds are known as powerful insecticides\(^{4-8}\) and the physiological effect is dependent on the Z/E ratio.\(^5\) It is possible to separate the isomers by chromatography,\(^6\) and for Phosdrin the E-isomer is found to be the most active one.\(^5,6\) In recent years much effort has been made to design specific reactions, and this has been achieved through variations of solvent, concentration and counter ion of the enolates.

\[
\text{CH}_3\text{C}=\text{CH}-\text{COOCH}_3 \quad \text{(C}_3\text{H}_4\text{O})_2\text{P(S)Cl}
\]

\[
\text{O} \quad \text{P(O)(OCH}_3\text{)}_2 \quad \text{O,O-Diethyl phosphorochloridithioate}
\]

Phosdrin

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the product is the E-isomer. In aprotic, polar solvents (DMSO, HMPA) the nucleophilic species is the non-solvated dissociated anion in W-shape. Formation of products of Z-configuration in nonpolar, aprotic solvents is due to chelation of the anion in U-shape with the counterion, while formation of E-isomers in polar, aprotic solvents is due to reaction of the free, unchelated anions in W-shape. The same configuration is achieved if the size of the cation is enlarged to tetrabutylammonium (TBA+). Tetraethylammonium salts are postulated to exist largely as free ions even in relatively nonpolar solvents. This is concluded from the hypothesis that E-isomers exclusively are formed from free anions which should also explain why more dilute solutions give higher percentage of E-configuration. However, in relatively nonpolar solvents the presence of the free anions must be questioned and the E-isomer must be ascribed to the geometry of an ion pair. The smaller cations give much higher percentages of Z-isomers due to fixation of the anion in U-shape.

It is postulated that the protonic or nonprotonic nature of the solvent should have only little effect on the geometry of the products. That is rejected by Kurts et al., arguing that in polar aprotic solvents W-shape conformations are more stable while in protic solvents enolate ions of β-dicarbonyl compounds adopt the alternative U-shaped conformation. This should be ascribed to hydrogen bond stabilization by the protic solvent of the anionic ground state and it means that the O-phosphorylated product in a protic solvent should be the Z-isomer.

If the vinyl phosphates are prepared according to the Perkow reaction the products are mixtures of the Z- and E-isomers.

Previous investigations have supplied us with some helpful spectroscopic tools for the determination of the structure of vinyl phosphates and vinyl phosphorothioates. All compounds assigned to E-configuration have the vinyl proton resonance appearing downfield from those assigned to Z-configuration and if there is a methyl group attached to the double bond at carbon 1, e.g., in the products from alkyl acetooacetate, the methyl proton resonance also occurs at lower field in the E- than in the Z-isomers. In some previous investigations the coupling constant in the E-isomer between the vinylic proton and P is found to be greater than the corresponding constant in the Z-isomer and in the products from acetoacetates the coupling constant between the protons in the methyl group and P is found to be greater in the Z-isomer than in the E-isomer. From the above it is obvious that it should be possible to synthesize Z-isomers by reacting the sodium salts of β-dicarbonyl compounds in a suitable alcohol with a suitable electrophilic reagent and the corresponding E-isomer by reacting the TBA-salts in methylene chloride.

This paper concerns reactions between salts of β-dicarbonyl compounds and O,O-diethyl phosphorochloridithioate, (C\(_2\)H\(_5\)O)\(_2\)P(S)Cl.

**FORMATION OF SALTS OF β-DICARBONYL COMPOUNDS**

The TBA-salts of the β-dicarbonyl compounds used in the present investigation (Table 1) were synthesized according to the method described by Brändström and Junggren. However, a more clean reaction was obtained by using methylene chloride instead of chloroform as solvent. The ammonium salts were isolated and, except for III and IV, purified before use. The sodium salts (Table 1) were not isolated before the subsequent reactions and they were generated by adding the β-dicarbonyl compound to a freshly prepared alcoholic solution of sodium alcoholate.

**PHOSPHORYLATION, STRUCTURE ELUCIDATION AND REARRANGEMENTS**

The phosphorylation reactions were performed by adding (C\(_2\)H\(_5\)O)\(_2\)P(S)Cl to solutions of the salts in the respective solvents. Some of the mixtures were heated to reflux temperature (see experimental). The reactions of the sodium salts in alcoholic solutions yielded the vinyl phosphorothioates in lower yields. Other products isolated were the parent β-dicarbonyl compound and trialkyl phosphorothioates. After workup the product distribution (Table 1) in the reaction mixture was determined by NMR spectroscopy. In Table 2 are shown the NMR chemical shifts and coupling constants of the vinylic and other protons of the vinylic part of the phosphorothioates. Also the products obtained by the Perkow reaction of triethyl phosphite with

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Table 1. The product distribution in the vinyl phosphorothioates from the reaction between TBA- and sodium salts of $\beta$-dicarbonyl compounds and $O,O$-diethyl phosphorochloridothioate and in the vinyl phosphates from the reaction between triethyl phosphite and 2-chloro-1-phenyl-1,3-butanedione.

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Salt No.</th>
<th>R</th>
<th>R'</th>
<th>M$^+$</th>
<th>Z (%)</th>
<th>E (%)</th>
<th>Prod. No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>CH$_3$</td>
<td>CH$_3$</td>
<td>TBA$^+$</td>
<td>30</td>
<td>70</td>
<td>1</td>
</tr>
<tr>
<td>II</td>
<td>CH$_3$</td>
<td>OCH$_3$</td>
<td>TBA$^+$</td>
<td>~0</td>
<td>100</td>
<td>2</td>
</tr>
<tr>
<td>III</td>
<td>CH$_3$</td>
<td>OC$_2$H$_5$</td>
<td>TBA$^+$</td>
<td>~0</td>
<td>100</td>
<td>3</td>
</tr>
<tr>
<td>IV</td>
<td>C$_2$H$_5$</td>
<td>OC$_2$H$_5$</td>
<td>TBA$^+$</td>
<td>25</td>
<td>75</td>
<td>4</td>
</tr>
<tr>
<td>V</td>
<td>CH$_3$</td>
<td>C$_2$H$_5$</td>
<td>TBA$^+$</td>
<td>0</td>
<td>100</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>C$_2$H$_5$</td>
<td>CH$_3$</td>
<td>TBA$^+$</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VI</td>
<td>CH$_3$</td>
<td>CH$_3$</td>
<td>Na$^+$(EtOH)</td>
<td>90</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>VII</td>
<td>CH$_3$</td>
<td>OCH$_3$</td>
<td>Na$^+$(EtOH)</td>
<td>90</td>
<td>10</td>
<td>2 + 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(MeOH)</td>
<td>75</td>
<td>25</td>
<td>2</td>
</tr>
<tr>
<td>VIII</td>
<td>CH$_3$</td>
<td>OC$_2$H$_5$</td>
<td>Na$^+$(EtOH)</td>
<td>100</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>IX</td>
<td>C$_2$H$_5$</td>
<td>OC$_2$H$_5$</td>
<td>Na$^+$(EtOH)</td>
<td>100</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>X</td>
<td>CH$_3$</td>
<td>C$_2$H$_5$</td>
<td>Na$^+$(EtOH)</td>
<td>72</td>
<td>21</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>C$_2$H$_5$</td>
<td>CH$_3$</td>
<td>Na$^+$(EtOH)</td>
<td>7</td>
<td></td>
<td>6</td>
</tr>
</tbody>
</table>

(Perkow reaction)

![Chemical structure](image)

chlorobenzoylaceton 
(2-chloro-1-phenyl-1,3-butanedione) are included in Tables 1 and 2.

One of the products from the reaction between the TBA-salts and (C$_2$H$_5$O)$_2$P(S)Cl is TBA$^+$Cl$^-$. For determination of the yields it is also of interest to isolate this product, but as the chloride is hygroscopic it is converted to the TBA$^+$I$^-$ by treating the reaction mixture with a water solution of an iodide. For TBA$^+$Cl$^-$ and TBA$^+$I$^-$, $E_{TBAX}$ from the equation

$$\frac{[TBA^+X^-]_{aq}}{[TBA^+]_{aq}[X^-]_{aq}} = E_{TBAX}$$

is 0.5 and 3.34, respectively, when the organic phase is CH$_3$Cl.$^{14}$ According to that, tria-

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Table 2. NMR chemical shifts and coupling constants of the protons from the vinylic part of the vinyl phosphorothioates and phosphates generated by the reactions depicted in Table 1 (CDCl₃).

<table>
<thead>
<tr>
<th></th>
<th>R</th>
<th>R'</th>
<th>X</th>
<th>R</th>
<th>R'</th>
<th>Hₑ</th>
<th>Hₓ</th>
</tr>
</thead>
<tbody>
<tr>
<td>1E</td>
<td>CH₃</td>
<td>CH₃</td>
<td>S</td>
<td>t, 2.35, (J = ~ 0.5 Hz)</td>
<td>s, 2.20</td>
<td>m, 6.19</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>CH₃</td>
<td>CH₃</td>
<td>S</td>
<td>dd, 2.18, (J₁ = ~ 2.0 Hz, J₂ = ~ 1.0 Hz)</td>
<td>s, 2.31</td>
<td>–</td>
<td>m, 5.56</td>
</tr>
<tr>
<td>2E</td>
<td>CH₃</td>
<td>OCH₃</td>
<td>S</td>
<td>t, 2.38, (J = ~ 0.5 Hz)</td>
<td>s, 3.71</td>
<td>m, 5.78</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>CH₃</td>
<td>OCH₃</td>
<td>S</td>
<td>dd, 2.14, (J₁ = ~ 2.0 Hz, J₂ = ~ 1.0 Hz)</td>
<td>s, 3.68</td>
<td>–</td>
<td>m, 5.40</td>
</tr>
<tr>
<td>3E</td>
<td>CH₃</td>
<td>OC₂H₅</td>
<td>S</td>
<td>t, 2.38, (J = ~ 0.5 Hz)</td>
<td>CH₃: q, 4.19 (J = 7.1 Hz), CH₃: t, 1.28 (J = 7.1 Hz)</td>
<td>m, 5.77</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>CH₃</td>
<td>OC₂H₅</td>
<td>S</td>
<td>dd, 2.14, (J₁ = ~ 2.0 Hz, J₂ = ~ 1.0 Hz)</td>
<td>CH₃: q, 4.17 (J = 7.2 Hz), CH₃: t, 1.26 (J = 7.2 Hz)</td>
<td>–</td>
<td>m, 5.39</td>
</tr>
<tr>
<td>4E</td>
<td>C₆H₅</td>
<td>OC₂H₅</td>
<td>S</td>
<td>m, 7.3 – 7.8</td>
<td>CH₃: q, 4.09 (J = 7.0 Hz), CH₃: t, 1.37 (J = 7.0 Hz)</td>
<td>d, 6.06, (J = ~ 2.2 Hz)</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>C₆H₅</td>
<td>OC₂H₅</td>
<td>S</td>
<td>m, 7.3 – 7.8</td>
<td>CH₃: q, 4.06 (J = 7.0 Hz), CH₃: t, 1.32 (J = 7.0 Hz)</td>
<td>–</td>
<td>d, 6.00 (J = ~ 2.2 Hz)</td>
</tr>
<tr>
<td>5E</td>
<td>CH₃</td>
<td>C₆H₅</td>
<td>S</td>
<td>t, 2.44 (J = ~ 0.7 Hz)</td>
<td>2H: m, 7.8 – 8.1, 3H: m, 7.4 – 7.7</td>
<td>m, 6.97</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>CH₃</td>
<td>C₆H₅</td>
<td>S</td>
<td>dd, 2.23, (J₁ = ~ 2.0 Hz, J₂ = ~ 1.0 Hz)</td>
<td>2H: m, 7.8 – 8.1, 3H: m, 7.3 – 7.6</td>
<td>–</td>
<td>m, ~ 6.2</td>
</tr>
<tr>
<td>6E</td>
<td>C₆H₅</td>
<td>CH₃</td>
<td>S</td>
<td>2H: m, 7.8 – 8.1, 3H: m, 7.3 – 7.6</td>
<td>s, 2.56</td>
<td>–</td>
<td>m, ~ 6.2</td>
</tr>
<tr>
<td>7E</td>
<td>CH₃</td>
<td>C₆H₅</td>
<td>O</td>
<td>d, 2.46, (J = ~ 0.8 Hz)</td>
<td>2H: m, 7.8 – 8.1, 3H: m, 7.3 – 7.7</td>
<td>m, 7.02</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>CH₃</td>
<td>C₆H₅</td>
<td>O</td>
<td>dd, 2.29, (J₁ = ~ 1.5 Hz, J₂ = ~ 1.0 Hz)</td>
<td>5H: m, 7.3 – 8.0</td>
<td>–</td>
<td>m, ~ 6.18</td>
</tr>
<tr>
<td>8E</td>
<td>C₆H₅</td>
<td>CH₃</td>
<td>O</td>
<td>5H: m, 7.3 – 8.0</td>
<td>s, 2.06</td>
<td>d, 6.40 (J = ~ 1.9 Hz)</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>C₆H₅</td>
<td>CH₃</td>
<td>O</td>
<td>5H: m, 7.3 – 8.0</td>
<td>s, 2.44</td>
<td>d, 6.18 (J = ~ 1.0 Hz)</td>
<td>–</td>
</tr>
</tbody>
</table>
butylammonium ion is found as TBA\(^+\)I\(^-\) in the organic phase when the mixture is treated with iodide. Evaporation of the organic phase followed by treatment with ether yields TBA\(^+\)I\(^-\) as clean, nonhygroscopic, and white crystals suitable for regeneration of TBA\(^+\)HSO\(_4\)\(^-\). The vinyl phosphorothioate is in the ether phase. That iodide is postulated to be a "catalyst poison" by some authors \(^{11,18}\) is due to the equilibrium constant above. For chloride and bromide (log \(E_{TBABr} = 1.23\) \(^{14}\)) some TBA\(^+\)X\(^-\) is found in the water phase and TBA\(^+\) can then serve as catalyst.

The TBA-salt of acetylacetone (I) was refluxed in methylene chloride with (C\(_5\)H\(_4\)O\(_2\))P(S)Cl yielding 75% of 1Z and 1E (3:7). Distillation enhanced the content of the \(E\)-isomer to 75% and the expected conversion \(^{15,18}\) to products of the type \(C_3H_4-S-P\) was also observed. The isomers were separated by column chromatography. Addition of (C\(_5\)H\(_4\)O\(_2\))P(S)Cl to a solution of the sodium salt of acetylacetone (VI) yielded after a few minutes reflux 90% of 1Z and 1E (9:1).

The reaction of the TBA-salt of methyl acetoacetate (II) with (C\(_5\)H\(_4\)O\(_2\))P(S)Cl was exothermic and the yields of 2Z and 2E were 93% (apparent ratio 0:100). However, by column chromatography a fraction of 2.13 g containing 2E and a fraction of 0.08 g containing 50% 2E and 50% 2Z was isolated from 2.40 g product. This corresponds to less than 2% of the Z-isomer in the crude product. Addition of (C\(_5\)H\(_4\)O\(_2\))P(S)Cl to the sodium salt generated from methyl acetoacetate in ethanol yielded after reflux for a few minutes 82% vinyl phosphorothioate (90% Z- and 10% E-isomer). A neat Z-fraction containing 43.5% methyl ester (2Z) and 56.5% ethyl ester (2Z) was isolated by column chromatography. Transesterification of the carboxylic ester group has occurred. Refluxing diethyl 2-methoxyacrylonitrile-1-methylvinyl phosphorothioate (2Z and E) in ethanol did not give diethyl 2-ethoxyacrylonitrile-1-methylvinyl phosphorothioate (3) as shown by gas chromatography. Even ethanolysis of the vinyl phosphorothioate \(^{18}\) was not observed to any remarkable extent as alkyl acetoacetate or triethyl phosphorothioate were only detected in an amount less than 1% in the refluxed mixture.

When methanol was used as solvent for the generation and subsequent phosphorylation of the sodium salt of methyl acetoacetate (VII) the product isolated was 2 (75% 2Z and 25% 2E). If the sodium salt of methyl acetoacetate (VII) was generated in benzene from sodium hydride the yield of the vinyl phosphorothioate after addition of (C\(_5\)H\(_4\)O\(_2\))P(S)Cl was only 9% even after reflux for several hours and the added (C\(_5\)H\(_4\)O\(_2\))P(S)Cl was recovered in 75% yield. The poor yield must be ascribed to the low solubility of the salt in benzene.\(^1\)

When the TBA-salt of ethyl acetoacetate (III) was reacted with (C\(_5\)H\(_4\)O\(_2\))P(S)Cl the reaction was exothermic and yielded 84% of 3E and 3Z (apparent ratio 100:0). However, a fraction of 1.23 g 3E and a fraction of 0.06 g 3Z was isolated from 1.7 g of product by column chromatography. Addition of (C\(_5\)H\(_4\)O\(_2\))P(S)Cl to the sodium salt of ethyl acetoacetate (VIII) in hot ethanol yielded 3Z.

When the TBA-salt of ethyl benzoylacetaet (IV) was reacted with (C\(_5\)H\(_4\)O\(_2\))P(S)Cl at room temperature the product was a mixture of 4Z (25%) and 4E (75%). The sodium salt of ethyl benzoylacetaet (IX) when refluxed with (C\(_5\)H\(_4\)O\(_2\))P(S)Cl in ethanol gave 4Z as the only product.

Phosphorylation of salts of benzoylacetaet (V,X) can yield two products due to the non-symmetry of the salts. In Table 1, V and X are depicted in two ways to explain the two products 5 and 6, each with the two possible isomers Z and E. However, 6E is not isolated. When the TBA-salt of benzoylacetaet (V) was reacted with (C\(_5\)H\(_4\)O\(_2\))P(S)Cl at room temperature a slight elevation of the temperature was observed. The only product observed was diethyl 2-benzoyl-1-methylvinyl phosphorothioate (5E). Distillation of 5E gave to a great extent new products as shown in Fig. 1. The NMR spectra of the distillation products also showed the expected conversion \(^{18,35}\) to products of the type \(C_3H_4-S-P\). In Fig. 1 the \( \beta\)-diketone and the monothio-\( \beta\)-diketone are depicted in a similar way rather than necessarily in the most likely form. (About the true structure see Refs. 20 and 23). Simple heating of 5E in bromobenzene (155 °C) yielded 5E and 5Z as well as the rearranged product 6Z (Fig. 1). The product 6 together with 5E and 5Z is only formed from the sodium salt X and only one of the isomers 6E and 6Z is found (Table 1). This can be

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accounted for if 6 is generated only from the U-shaped anion. The product must then be expected to be 6Z and the NMR data of 6 do also correspond better to 8Z than to 8E. Heating a benzene solution of 5Z, 5E, and 6Z shows that 5Z is transformed to 5E while 6Z seems to have reached an equilibrium concentration or to be stable towards rearrangements at that temperature. Heating a chlorobenzene solution of the same compounds gave almost the same product distribution as when neat 5E was heated in chlorobenzene (Fig. 1). It is thought to be an equilibrium mixture.

Reaction of 2-chloro-1-phenyl-1,3-butanedione with triethyl phosphite (Perkow reaction) yielded the products 7 and 8 (Table 1). By column chromatography 7E was isolated neat. Refluxing a mixture of 7Z, 8E, and 8Z in chlorobenzene yielded a mixture of benzoylaceton, 7Z, 7E, 8Z, and 8E, where the E-isomers were the most abundant of the vinyl phosphates.

So far only the vinyl phosphorothioates have been looked on as products, but also the parent \( \beta \)-dicarbonyl compounds were isolated together with trialkyl phosphorothioate from the reactions between salts of \( \beta \)-dicarbonyl compounds and \((\text{C}_2\text{H}_5\text{O})_3\text{P(S)}\text{Cl})\). In Table 3 is shown the distribution between those products. The trialkyl phosphorothioate is the \( \text{O,O,O-triethyl} \)

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**Table 3. The yields from the reactions between TBA- and sodium salts of \( \beta \)-dicarbonyl compounds and \( \text{O,O-diethyl phosphorothioate} \).**

<table>
<thead>
<tr>
<th>Salt</th>
<th>Solvent</th>
<th>Vinyl phosphorothioate %</th>
<th>( \beta )-Dicarbonyl compound %</th>
<th>( \text{O,O,O-Trialkyl phosphorothioate} ) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>( \text{CH}_3\text{Cl}_2 )</td>
<td>75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>( \text{CH}_3\text{Cl}_2 )</td>
<td>93</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>( \text{CH}_3\text{Cl}_2 )</td>
<td>84</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>( \text{CH}_3\text{Cl}_2 )</td>
<td>95</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>( \text{CH}_3\text{Cl}_2 )</td>
<td>85</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VI</td>
<td>( \text{EtOH} )</td>
<td>90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VII</td>
<td>( \text{EtOH} )</td>
<td>82</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>VII</td>
<td>( \text{MeOH} )</td>
<td>32</td>
<td>37</td>
<td>58</td>
</tr>
<tr>
<td>VIII</td>
<td>( \text{EtOH} )</td>
<td>70</td>
<td></td>
<td>30</td>
</tr>
<tr>
<td>IX</td>
<td>( \text{EtOH} )</td>
<td>32</td>
<td>64</td>
<td>64</td>
</tr>
<tr>
<td>X</td>
<td>( \text{EtOH} )</td>
<td>51</td>
<td>36</td>
<td>48</td>
</tr>
</tbody>
</table>

*2-methoxy carbonyl-1-methylvinyl phosphorothioate (2) 27 %, 2-ethoxy carbonyl-1-methylvinyl phosphorothioate (3) 55 %.*

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ester except when the solvent was methanol. In this case it was O,O-diethyl O-methyl phosphorothioate.

DISCUSSION

Polar aprotic solvents and bulky cations should give E-isomers when salts of β-dicarbonyl compounds are reacted with diethyl phosphorochloridithioate. In this investigation TBA-salts of β-dicarbonyl compounds produced mainly the E-isomers (Table 1), although methylene chloride is not a very polar solvent. If it is only the enolate anion in W-shape that gives the E-isomers the anion in the TBA-salts must adopt this W-shape when dissolved in methylene chloride although the ion pair is expected to be maintained. In the introduction it was also mentioned that Z-isomers were achieved through phosphorylation of enolate anions in U-shape. This U-shape should be found when the cation was small and nonpolar solvents were used. However, also protic solvents should generate an U-shaped anion. From these predictions the products shown in Table 1 were expected when sodium salts of β-dicarbonyl compounds were reacted with diethyl phosphorochloridithioate.

In an earlier work the structure of the products from the reaction between X and (C₆H₅)₂P(S)Cl, the reaction between X and (C₆H₅)₂P(O)Cl and the reaction between 2-chloro-1-phenyl-1,3-butanedione and triethyl phosphate are postulated to be 6 and 8, respectively. This assumption is made from isolating methyl glyoxal and benzoic acid when the products were ozonized. However, the products were purified by distillation before the ozonization and, as shown in the present investigation, this will increase the amounts of the compounds 6 and 8 in the respective mixtures, i.e. there is no evidence for the products to have been entirely 6 and 8.

The rearrangement from 5 to 6 or from 7 to 8 is expected to go via the Z-isomers as depicted in Fig. 2 (Direct displacement ¹¹). Two other mechanisms (elimination-addition and addition-elimination) suggested for nucleophilic substitution on phosphorus in phosphates ¹² are not considered as likely. The first is excluded because the rearrangements are performed under neutral conditions. The latter involves a charged intermediate probably with a trigonal bi-pyramidal structure.

The formation of the monothio-β-diketone when diethyl 2-benzoyl-1-methylvinyl phosphorothioate (5E) was distilled (Fig. 1) can be expected to go through the intermediate shown in Fig. 3. This is parallel to the finding of products of the type C₆H₅—S—P which are also found after distillation of 1.

The cleavage yielding a β-dicarbonyl compound was also observed when 7 and 8 were heated in chlorobenzene.

As shown in Table 3 phosphorylation of the sodium salts in alcoholic solutions yielded some

Fig. 2. A mechanism for the rearrangements of diethyl 2-benzoyl-1-methylvinyl phosphorothioate (δ) to diethyl 2-acetyl-1-phenylvinyl phosphorothioate (δ) (or vice versa) and of diethyl 2-benzoyl-1-methylvinyl phosphate (7) to diethyl 2-acetyl-1-phenylvinyl phosphate (8) (or vice versa).

Fig. 3. A reaction sequence for the formation of the monothio-β-diketone from diethyl 2-benzoyl-1-methylvinyl phosphorothioate (δE).
Fig. 4. Reaction sequences for the formation of the products shown in Table 3 from the reaction between \((\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{S})\text{Cl}\) and sodium salts of \(\beta\)-dicarbonyl compounds.

trialkyl phosphorothioate and the parent \(\beta\)-dicarbonyl compound. The products can be accounted for by the equilibrium existing between the sodium salt of the \(\beta\)-dicarbonyl compound and sodium alcocate as shown in Fig. 4. The amounts of \(\beta\)-dicarbonyl compound and \(O,O,O\)-trialkyl phosphorothioate can also be ascribed to base-catalyzed alcoholysis\(^{18}\) (Fig. 4), and for the reaction between IX and \((\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{S})\text{Cl}\) where the mixture was refluxed for several hours in ethanol, this might account for the poor yields of vinyl phosphorothioate. However, refluxing of 2 in ethanol as mentioned previously only yielded small amounts of the ethanolyis product. The isolation of \(\beta\)-dicarbonyl compound from III and V (Table 3) may be accounted for by hydrolysis of the respective vinyl phosphorothioates (3 and 5) during the work-up procedure.

The present investigation shows methods for preparing vinyl phosphorothioates, enriched either in the \(Z\)- or the \(E\)-isomer. For the vinyl phosphate phosdrin it is found that the \(E\)-isomer was 10 to 100 times more toxic to insects and mammals than the \(Z\)-isomer\(^{4,6}\) and our procedures should thus prove to be the methods of choice for selective synthesis. Preliminary experiments have been made on the reaction between \((\text{Me}_2\text{N})_2\text{P}(\text{O})\text{Cl}\) and salts of \(\beta\)-dicarbonyl compounds\(^{24}\) and the results were the same as in the present work.

EXPERIMENTAL

The IR spectra were recorded on a Perkin-Elmer model Infracord Spectrophotometer and the NMR spectra at 60 MHz on a Varian A-60 spectrometer using TMS as internal standard. The chemical shifts are expressed in \(\delta\)-values. The UV spectra were recorded on a PerkinElmer 402 Ultraviolet-Visible Spectrophotometer. Microanalyses were carried out by Micro Analytical Laboratory, Novo A/S, Novo Allé, DK-2880 Bagsvaerd, Denmark, and by Micro Analytical Laboratory, Løven's Kemiske Fabrik, DK-2750 Ballerup, Denmark. Column chromatography was made on silica gel (Kieselgel 60; 0.063 - 0.200 mm; 70 - 230 mesh ASTM; Merck)). B.p.'s and m.p.'s are uncorrected.

\(\text{TBA-salt of 2,4-pentanediene (acetylactone)}, (I)\). Compound I was synthesized\(^{15}\) in 95 % yield. However, methylene chloride was used instead of chloroform. M.p. 161 - 164 °C (acetone).\(^{17}\)

\(\text{TBA-salt of methyl acetacetate, (II)}\). Compound II was synthesized as I in 98 % yield, as yellow crystals, m.p. 87 - 90 °C (AcOEt). (Found: C 69.43; H 12.16; N 3.91. \(\text{C}_4\text{H}_8\text{N}_2\text{O}_4\) requires: C 70.54; H 12.12; N 3.92). IR: \(\nu_{\text{max}}\) (CHCl\(_3\)) 3000, 1655, 1515, 1380, 1150, 1125, 1057, 1000 and 885 cm\(^{-1}\). UV-Visible (EtOH) \(\lambda_{\text{max}}\) (log \(e\)): 245 nm (3.031). NMR (CDCl\(_3\)): \(\delta\) 0.7 - 1.3 (12 H, m), 1.2 - 2.0 (16 H, m), 2.24 (3 H, broad s), 3.1 - 3.7 (8 H, m), 3.53 (3 H, s), 7.55 (1 H, broad s).

\(\text{TBA-salt of ethyl acetacetate, (III)}\). Compound III was synthesized as I in 100 % yield. The compound did crystallize in a deep-freezer and in vacuum, but as it was too soluble in all attempted solvents it could not be recrystallized before use. IR: \(\nu_{\text{max}}\) (CHCl\(_3\)) 2960, 1630, 1505, 1375, 1160, 1065, 1012, 914 and 882 cm\(^{-1}\).
UV (EtOH) $\lambda_{\text{max}}$ (log e): 210 nm (2.929) and 283 nm (3.441). NMR (CDCl$_3$): $\delta$ 0.7 to 1.2 (12 H, m), 1.2 to 1.9 (16 H, m), 1.25 (3 H, t, $J$ 7.1 Hz), 2.34 (3 H, s), 3.0 to 3.5 (8 H, m), 4.10 (2 H, q, $J$ 6.6 Hz) 3.18 cm$^{-1}$. 

**TBA-salt of ethyl 3-0xo-3-phenylpropionate** (ethyl benzoylacetate), (IV). Compound IV was synthesized as I in almost 100% yield. As the compound was too soluble in all attempted solvents to be recrystallized it was not further purified before use. NMR (CDCl$_3$): $\delta$ 0.8 to 1.6 (31 H, m), 2.9 to 3.3 (8 H, m), 4.02 (2 H, q, $J$ 7.0 Hz), 7.1 to 7.5 (3 H, m), 7.46 (1 H, s), 7.7 to 8.0 (2 H, m).

**TBA-salt of 1-phenyl-1,3-butanedione (benzoylacetone),** (V). Compound V was synthesized as I in almost 100% yield. Red-orange crystals, m.p. 100 to 101°C. (AcOEt). (Found: C 77.26; H 11.31; N 3.48. C$_{12}$H$_8$NO$_3$ requires: C 77.36; H 11.24; N 3.47). IR: $\nu_{\text{max}}$(CHCl$_3$) 2950, 1605, 1565, 1495, 1460, 1415, 1370, 1275, 987 and 867 cm$^{-1}$. $\nu_{\text{max}}$(KBr) 2950, 1580, 1555, 1495, 1430, 1380 (sh), 1340, 1235, 1190, 1172, 1143, 1057, 1021, 987, 880, 865, 795, 758 and 707 cm$^{-1}$. UV (EtOH) $\lambda_{\text{max}}$ (log e): 298 nm (3.916), 246 nm (3.803) and 313 nm (4.189). NMR (CDCl$_3$): $\delta$ 0.7 to 1.1 (12 H, m), 1.1 to 1.6 (16 H, m), 2.46 (3 H, s), 2.8 to 3.2 (8 H, m), 7.1 to 7.4 (3 H, m), 7.49 (1 H, s), 7.6 to 8.0 (2 H, m).

Phosphorylation of the TBA-salts I-V. Equivalent amounts of TBA-salt and diethyl phosphorochloridothioate were mixed in methylene chloride (25 ml to about 0.01 mol of salt). The product mixture from I was refluxed for about 7 h. The other reactions were observed to be more or less exothermic and therefore only stirred for a couple of hours at room temperature.

**I→II**. The reaction mixture of 0.0146 mol of I and C$_6$H$_5$O$_2$P(S)Cl was treated with a solution of 0.02 mol NaI in water. The methylene chloride phase was separated, dried (Na$_2$SO$_4$) and the solvent evaporated. TBA$^+$ (0.0134 mol, 92%) was then precipitated by adding ether. Evaporation of the ether phase yielded 2.77 g of I (75%) with 30% 1Z and 70% 1E as confirmed by NMR spectroscopy (Table 2). Distillation enhanced the content of 1E to 75% and also small amounts of a product containing the structure element $-\underset{\text{P-S}}{\text{C}_6\text{H}_5}$. 

**II→III**. $\delta$ 2.88 (2 H, broad q, $J$ 7.3 Hz). (Found: C 42.69; H 6.86; P 12.28. C$_{12}$H$_8$O$_2$PS requires: C 42.85; H 6.79; P 12.28). The isomers were isolated by column chromatography and the NMR spectra shown in Table 2 were recorded. The groups C$_6$H$_5$O$_2$P(S) showed the known NMR-patterns.$^{16}$ IR(IE): $\nu_{\text{max}}$(CCl$_3$) 2985, 1705, 1625, 1410, 1380, 1350, 1210, 1153, 1023, 948 and 862 cm$^{-1}$. $\nu_{\text{max}}$(CS$_2$) 2980, 1695, 1615, 1375, 1350, 1210, 1153, 1021, 948 and 818 cm$^{-1}$.

**III→IV**. The reaction mixture was treated as above yielding 93% of almost neat 2E and 99% of TBA$^+$-I. A fraction of 2.40 g of the product was separated by silica gel column chromatography (CH$_2$Cl$_2$) to yield 2.13 g of neat 2E and 0.08 g of a mixture of 2E and 2Z (1:1).

Data of 2E: (Found: C 38.65; H 6.30; P 11.63. C$_8$H$_5$O$_2$PS requires: C 38.50; H 6.30; P 11.53). For NMR data see Table 2. UV(EtOH) $\lambda_{\text{max}}$ (log e): 227 nm (3.984). IR: $\nu_{\text{max}}$(CCl$_3$) 3010, 1740, 1665, 1435, 1385, 1335, 1230, 1127, 1025, 965, 944, 891, 853 and 822 cm$^{-1}$. $\nu_{\text{max}}$(CS$_2$) 3020, 1740, 1665, 1385, 1335, 1230, 1127, 1025, 968, 946, 893, 855 and 822 cm$^{-1}$.

**IV→V**. The reaction mixture was treated as above and yielded 84% of almost neat 3E and 16% of ethyl acetoxacetic acid, which is likely generated by hydrolysis of 3E. TBA$^+$-I was isolated in 92% yield. However, as silica gel column chromatography (CH$_2$Cl$_2$) 0.06 g of 3Z and 1.23 g of 3E was isolated from 1.7 g of 3. (Found C 42.52; H 6.77; P 11.08. C$_8$H$_5$O$_2$PS requires: C 42.55; H 6.78; P 10.97). For NMR data see Table 2. UV(EtOH) $\lambda_{\text{max}}$ (log e): 225 nm (3.924). IR: $\nu_{\text{max}}$(CCl$_3$) 2970, 1720, 1650, 1430, 1375, 1355, 1235, 1157, 1120, 1060, 1020, 968, 897, 855 and 822 cm$^{-1}$. $\nu_{\text{max}}$(CS$_2$) 2975, 1725, 1655, 1380, 1360, 1330, 1225, 1160, 1123, 1093, 1025, 970, 896, 857, 822 and 730 cm$^{-1}$.

**V→VI** (and 5Z + 6Z). The reaction mixture was treated as above and yielded quantitatively a mixture of 85% 5E and 15% benzoylacetone. The yield of TBA$^+$-I was 98%. 5E was isolated by silica gel column chromatography (CH$_2$Cl$_2$). (Found: C 53.53; H 6.05; P 9.85. C$_8$H$_5$O$_2$PS requires: C 53.50; H 6.09; P 9.85). For NMR data, see Table 2. IR: $\nu_{\text{max}}$(CCl$_3$) 2970, 1675, 1615, 1440, 1385, 1245, 1150, 1022, 965, 908 and 697 cm$^{-1}$. $\nu_{\text{max}}$(CS$_2$) 2970, 1670, 1615, 1430, 1235, 1150, 1090, 1020, 965, 905, 818 and 698 cm$^{-1}$. The products obtained when 5E was heated in bromobenzene (155°C) for 2 h. (5E, 5Z, and 6Z, Fig. 1) were determined by NMR spectroscopy. Distillation of 5E onto a cold finger (130°C/0.15 mmHg) yielded the products shown in Fig. 1 and traces of a product containing the structural element C$_6$H$_5$—S—P. They were determined by NMR spectroscopy, also the monothio-$\beta$-diketone $^{*}$ for which the

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were removed by vacuum at room temperature leaving a fraction containing 85 % of $2Z + 2E$ (3:1) and 15 % of O-methyl-O,O-diethyl phosphoroioate.

The reaction of VII (prepared from sodium hydride and methyl acetocetate) in benzene with $(C_2H_5)_3POCl$ yielded 9 % of Z, a poor yield corresponding to previous statements.1

**VIII→3Z.** By a procedure as above from 0.046 mol VII in ethanol was isolated 11.82 g of a mixture of 0.032 mol of 2-ethoxycarbonyl-1-methylmethyl phosphoroioate (3Z) (70 % yield) and 0.014 mole of triethylphosphoroioate (30 % yield). For NMR data of 3Z, see Table 2.

**IX→4Z.** The refluxed reaction mixture of 0.054 mol of IX and 0.064 mol of $(C_2H_5)_3POCl$ in ethanol yielded by the procedure described above 19.32 g of a mixture containing 4Z (32 % yield), ethyl benzoyleacetae (64 % yield) and triethyl phosphoroioate (64 % yield). Distillation of 8 g of this mixture yielded three fractions: 1.59 g (37 °C/0.05 mmHg; triethylphosphoroioate (confirmed by NMR spectroscopy)), 2.54 g (82–83 °C/0.05 mmHg; 39 % triethylphosphoroioate and 61 % ethyl benzoyleacetae) and 2.10 g (115–138 °C/0.08 mmHg; 36 % ethyl benzoyleacetae and 64 % 4Z). By silica gel column chromatography $(CH_2Cl_2) 4.15 g of the above mentioned mixture was separated yielding 1.27 g of 4Z. (Found: C 52.22; H 6.12; P 8.82. $C_{11}H_{13}O_5$PS requires: C 52.32; H 6.15; P 8.99.).

By silica gel column chromatography $(CH_2Cl_2)$ it was possible to get fractions enriched in either of the components of the reaction mixture. A rapid treatment of the mixture with 5 M $NaOH + CH_2Cl_2$ removed 1-phenyl-1,3-butanedione and triethyl phosphoroioate. Heating a benzene solution of a mixture of 5Z, 5E, and 6Z (77, 6, and 17 %) ($80 ^\circC$) for 5 1/4 h yielded a mixture of the components with the distribution 47, 37, and 16 %. Heating a chlorobenzene solution of a mixture of 5Z, 5E, and 6Z (10, 71, and 19 %) ($132 ^\circC$) for 1 h yielded a mixture of the components with the distribution 8, 76, and 16 %. **Preparation of 7 and 8.** A mixture of 7 and 8 was synthesized from 1-phenyl-2-chloro-1,3-butanedione and triethyl phosphites in 77 % yield without distillation of the products. The mixture recovering 25 % of 1-phenyl-2-chloro-1,3-butanedione and 15 % of triethyl phosphite. Based on the NMR spectrum 7Z, 7E, 8Z, and 8E showed 50 %, 10 %, 10 %, and 30 %

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appearance. Treatment of the reaction mixture with 5 M NaOH + CH₃Cl, removed the β-dicarbonyl compound and triethyl phosphate yielding 7Z, 7E, 8Z, and 8E with the distribution 11, 45, 35, and 11 % By silica gel column chromatography (ether) it was possible to isolate neat 7E from the just mentioned mixture. Refluxing 7 and 8 in chlorobenzene yields 1-phenyl-1,3-butanediene (benzoylaceton): Refluxing a mixture of 7Z, 7E, and 8E (13, 65, and 22 %) in chlorobenzene (132 °C) for 1 1/4 h yielded benzoylaceton, 7Z, 7E, 8Z, and 8E (50, 15, 19, 7, and 9 %).

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