

## On the Reactivity of Ethyl $\gamma$ -Bromoacetoacetate with Triethyl Phosphite

V. Jagodić

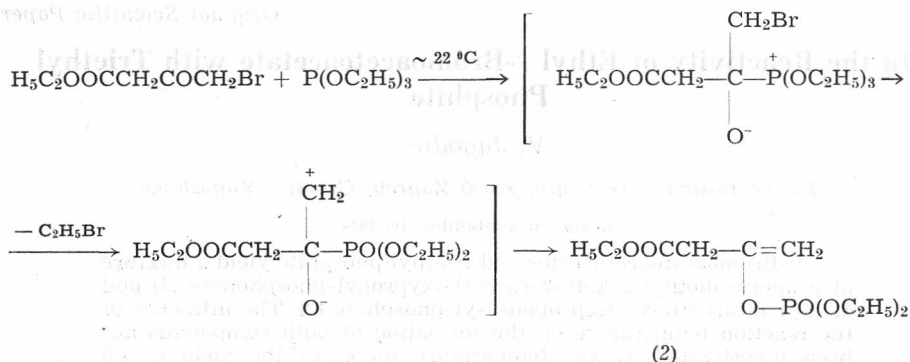
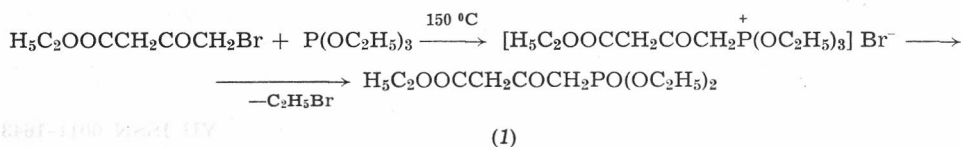
Ruder Bošković Institute, 41000 Zagreb, Croatia, Yugoslavia

Received September 10, 1976

$\gamma$ -Bromoacetoacetic ester and triethyl phosphite yield a mixture of isomeric diethyl 2-keto-3-carbethoxypropyl-phosphonate (1) and diethyl 1-carbethoxy-isopropen-2-yl-phosphate (2). The influence of the reaction temperature on the formation of both compounds has been investigated. Lower temperature increases the yield of (2) and higher of (1). The compounds were separated by vacuum distillation and were identified by elemental analysis, ir and  $^1\text{H}$  NMR spectra.

The reactivity of trialkyl phosphites with  $\alpha$ -halocarbonyl compounds has been extensively studied<sup>1</sup>. The reaction products, obtained with  $\alpha$ -halo- $\beta$ -keto-carboxylic acid e. g.  $\alpha$ -haloacetoacetic ester, and trialkyl phosphites have also been described<sup>2</sup>. These compounds were found to yield a mixture of  $\alpha$ -keto-alkylphosphonates and unsaturated alkylphosphate esters<sup>3</sup>. It was further demonstrated that the course of these competitive reactions depends on the reaction temperature, kind of the halogen atom and its site in the molecule<sup>1</sup>. However, the reactivity of  $\gamma$ -halogen-substituted acetoacetic ester with a trialkyl phosphite has not been investigated. This study was therefore undertaken in order to elucidate the course of the reaction and to prepare the anticipated new  $\beta$ -ketoalkylphosphonate (1) which was desired as an intermediate for further syntheses.

Triethyl phosphite and  $\gamma$ -bromoacetoacetic ester undergo two competitive reactions, the course of which depends on the reaction temperature. By slow addition of the bromo compound to triethyl phosphite, previously warmed up to over 140 °C, normal Arbuzov reaction takes place so that (1) is the major reaction product. Under this condition, a mixture consisting of 38% of (1) and 26% of (2) is obtained. If the reactants are allowed to react at room temperature, (2) is predominantly formed. Here, the reaction yields a mixture of 74% of (2) and only 19% of (1). High temperature favours normal Arbuzov reaction and suppresses the exothermic formation of (2) and vice versa. Consequently, any change in the reaction temperature within the quoted extremes, brings about the change in the ratio of the reaction products. Formation of (2) probably takes place through two intermediate steps in which the positively charged phosphorus and the negatively charged oxygen atoms are first formed. This is followed by the separation of ethyl bromide and migration of the phosphorus to the oxygen leading finally to the vinylphosphate ester (2).



A phenomenon of this kind was first observed and explained by W. Perkow in the reaction of chloral with triethyl phosphite<sup>3</sup>. Similarly, many halogenated carbonyl compounds give unsaturated phosphate esters instead of ketoalkylphosphonates<sup>1</sup>.

The total yield of (1) and (2) obtained by conducting the reaction at room temperature, is over 90%. At 150 °C the yield of both compounds together is about 70% as certain decomposition of the reactants occurs in the process of heating. However, both (1) and (2) are stable colourless oils that can be distilled without decomposition providing that sufficient vacuum is attained. The products were identified by the ir and <sup>1</sup>H NMR spectra and elemental analysis.

The ir spectrum of (1) shows a weak band at 3440 cm<sup>-1</sup> of the enolic OH group and the corresponding enolic C=C and C=O stretching frequencies at 1655 and 1630 cm<sup>-1</sup>. The latter two bands are weak and broad. A possible explanation for this is that the OH group can form hydrogen bonds with either the ester C=O or P=O group which leads eventually to a mixture of *cis*- and *trans*- form with respect to the double bond. As a result, the P=O stretching frequency is also very broad. One has to bear in mind, however, that the P=O band can be overlapping with the C—O—(Et) stretching which appears in the same region. Nevertheless, the P=O stretching in (1) is definitely broader than in (2) where hydrogen bonding of this kind is nonexistent. That (1) exists predominantly in the keto form is indicated by the two very strong and overlapping bands at 1748 and 1724 cm<sup>-1</sup>. These are assigned to the CO(OEt) and C=O group, respectively.

The ir spectrum of (2) gives a strong band at 1740 cm<sup>-1</sup> of the CO(OEt) group with a shoulder at 1775 cm<sup>-1</sup>. The latter absorption is an overtone frequency of the =CH<sub>2</sub> group. Indeed, a broad and medium band appears at 810 cm<sup>-1</sup> arising from the C—H deformation vibration in the 0—C=CH<sub>2</sub> group<sup>4</sup>. The other deformation vibration that should appear between 900—1000 cm<sup>-1</sup> is difficult to differentiate from the P—O—(R) frequencies. The existence of the vinyl group is further proved by the strong band at 1660 cm<sup>-1</sup> representing

the C=C vibrations. As anticipated from the above discussed, the P=O band in (2) is somewhat narrower than in (1) and is shifted toward higher frequency.

The  $^1\text{H}$  NMR spectrum of  $\beta$ -ketophosphonate (1) shows a singlet at  $\delta$  3.62 of the  $\gamma\text{-CH}_2$  group and a doublet at  $\delta$  3.24 resulting from the coupling of the  $\alpha\text{-CH}_2$  group to the phosphorus ( $J = 22.4$  Hz). The coupling constants of the same magnitude were also found with the benzylic Ph—CH—P group in anilino-benzylphosphonic acid derivatives<sup>5</sup>. The vinylphosphate ester (2) shows two sets of multiplets for the C=CH<sub>2</sub> protons centered at about  $\delta$  4.7 and 4.95 and a singlet at  $\delta$  3.22 of the CH<sub>2</sub>(CO) group. An interesting feature of (2) is that the two CH<sub>3</sub>—(CH<sub>2</sub>OP) groups are not quite equivalent since they show as two triplets separated by 1 Hz.

#### EXPERIMENTAL

$^1\text{H}$  NMR spectra were recorded on a Varian Model A-60A Spectrometer using a sweep width of 500 Hz and tetramethylsilane as internal standard. The ir spectra were obtained with a Perkin-Elmer Infrared Spectrometer Model 257. Only significant ir bands are quoted. Elemental analysis was performed in the Analytical Laboratory of the Rudjer Bošković Institute. Commercial grade triethyl phosphite and ethyl acetoacetate were distilled prior to use.  $\gamma$ -Bromoacetoacetic ester was prepared from equimolar amounts of bromine and ethyl acetoacetate dissolved in a double volume of CS<sub>2</sub> according to a known procedure<sup>6</sup>. It was obtained in a cca. 50 % yield as a colourless liquid, b. p. 59—61 °C/0.06 mm (Lit.<sup>7</sup> b. p. 78—80 °C/1—3 mm Hg)\*.

#### *Reaction of Ethyl $\gamma$ -Bromoacetoacetate with Triethyl Phosphite at Ambient Temperature*

Triethyl phosphite (34.3 g, 0.21 mol) was added dropwise to ethyl  $\gamma$ -bromoacetoacetate (41.2 g, 0.2 mol), placed in a round-bottomed flask submerged in an oil bath. The mixture was vigorously stirred throughout the experiment with a magnetic stirrer. The ethyl bromide formed was distilled off and collected in a flask cooled with ice and water. When all the phosphite was added, the mixture was warmed up to 90 °C and was kept at this temperature for 3 h. Finally, the temperature of the bath was gradually raised to 150 °C and maintained so for another 5 h. The resulting brown-coloured liquid was fractionated in vacuo. Since a continuous b. p. was observed, the identity of the fractions has to be established by the aid of the NMR spectra. The fractions distilling below 100 °C/0.15 mm Hg were discarded as they consisted of unreacted components and decomposition products. The fractions collected between 103—117 °C/0.15 mm Hg (39.3 g, 73.8%) consisted mainly of (2) and a small quantity of (1). The third fraction that distilled between 117—130 °C/0.15 mm (10 g, 18.8%) was (1) contaminated with traces of (2). Redistillation of both fractions afforded pure (1) and (2), respectively.

#### *Reaction of Ethyl $\gamma$ -Bromoacetoacetate with Triethyl Phosphite at 150 °C*

Using the apparatus described above, the temperature of the oil bath was adjusted to 150 °C and then triethyl phosphite (180 g, 1.1 mol) was introduced immediately. After allowing it for a few min to attain the temperature of the bath, ethyl  $\gamma$ -bromoacetoacetate (206 g, 1 mol) was added dropwise over a period of 4 h. Following the addition, the mixture was heated at 150—160 °C for another 2 h during which period the evolution of the ethyl bromide practically ceased. By distillation in vacuo, two fractions were collected, one passing between 100—117 °C/0.15 mm (69.8 g, 26.2%) consisting mainly of (2) and the second one between 117—128 °C/0.15 mm (102 g, 38.5%) containing (1) and traces of (2). Both fractions were further purified by distillation.

Pure (1) distills at 118—120 °C/0.15 mm Hg. Ir spectrum: 3440 (enolic OH); 1748 (ester C=O); 1724 (C=O); 1655, 1630 (enolic C=C, C=O); 1260 (P=O); 1170 (Et—O—P); 1030, 975 (P—O—Et) cm<sup>-1</sup>.  $^1\text{H}$  NMR spectrum:  $\delta$  (CCl<sub>4</sub>) 3.86—4.34 (6 H, m,

\* 1 Torr = 1 mm Hg = 133.322 Pa

OCH<sub>2</sub>(CH<sub>3</sub>); 3.62 (2 H, s,  $\gamma$ -CH<sub>2</sub>); 3.24 (2 H, d,  $J = 22.5$  Hz,  $\alpha$ -CH<sub>2</sub>); 1.28 (6 H, t,  $J = 7$  Hz, (POCH<sub>2</sub>)CH<sub>3</sub>); 1.23 (3 H, t,  $J = 7$  Hz, (COCH<sub>2</sub>)CH<sub>3</sub>).

Anal. C<sub>10</sub>H<sub>19</sub>O<sub>6</sub>P (266,23) calc'd: C 45.11; H 7.19; P 11.63%.  
found: C 44.95; H 7.13; P 11.88%.

Pure (2) distills at 103–105 °C/0.06 mm Hg. Ir spectrum: 1775 (=CH<sub>2</sub>); 1740 (ester C=O); 1660 (vinyl C=C); 1280 (P=O); 1170 (Et—O—P); 1030, 990, 960 (P—O—Et) cm<sup>-1</sup>. <sup>1</sup>H NMR spectrum:  $\delta$  (CCl<sub>4</sub>) 4.53–4.98 (2 H, m, vinyl CH<sub>2</sub>); 3.88–4.38 (6 H, m, OCH<sub>2</sub>(CH<sub>3</sub>)); 3.22 (2 H, s, CH<sub>2</sub>CO); 1.29, 1.28 (6 H, two t,  $J = 7$  Hz, (POCH<sub>2</sub>)CH<sub>3</sub>); 1.22 (3 H, t,  $J = 7$  Hz, (CH<sub>2</sub>)CH<sub>3</sub>).

Anal. C<sub>10</sub>H<sub>19</sub>O<sub>6</sub>P (266.23) calc'd: C 45.11; H 7.19; P 11.63%.  
found: C 45.17; H 7.30; P 11.67%.

## REFERENCES

1. Houben-Weyl, *Methoden der organischen Chemie*, Georg Thieme Verlag, Stuttgart, 1963, Vol **XII**/1, pp. 490–493.
2. N. Kreutzkamp and H. Kayser, *Ann.* **609** (1957) 39.
3. W. Perkow, *Chem. Ber.* **87** (1954) 755.
4. L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, Chapman and Hall, London, 1975, p. 57.
5. V. Jagodić, *Croat. Chem. Acta* **48** (1976) 325.
6. M. Conrad and L. Schmidt, *Ber.* **29** (1896) 1043.
7. J. Botters and P. Chiffert, *Fr. patent*; *C. A.* **71** (1969) 38369.

## SAŽETAK

O reaktivnosti etil- $\gamma$ -bromacetoacetata s trietilfosfitom

V. Jagodić

$\gamma$ -Bromacetocteni ester i trietilfosfit daju smjesu izomernih dietil-2-keto-3-karbetoksipropilfosfonata (1) i dietil-1-karbetoksi-izopropen-2-il-fosfata (2). Ispitan je utjecaj temperature na nastajanje ovih spojeva. Pri nižoj temperaturi veće je iskorištenje spoja (2) a pri višoj spoja (1). Ti spojevi odijeljeni su vakuum-distilacijom i identificirani elementarnom analizom, ir i <sup>1</sup>H-NMR-spektrima.

INSTITUT »RUĐER BOŠKOVIĆ«  
41000 ZAGREB

Prispjelo 10. rujna 1976.