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Reactions of Triphenylphosphine with 2,3-Dihalo-2-methylpropionic Acids and Their Methyl Esters

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Abstract — Triphenylphosphine reacts with 2,3-dichloro-2-methylpropionic acid and its ester along the dehydrochlorination pathway with the participation of the less labile hydrogen atom from the methyl group. The subsequent reaction of the unsaturated product with triphenylphosphine yields 2-carboxypropane- and 2-methoxycarbonylpropane-1,3-diylbis(triphenylphosphonium) dichlorides, respectively. The unusual course of dehydrochlorination may be due to easier electron density transfer from the C–H bond of the methyl group as compared to the chloromethyl group in the carbocationoid intermediate. With the bromine analogs, the reaction pathways are different. The ester reacts similarly to dibromopropionic acid and its derivatives, following the debromination scheme, whereas the free acid gives the product of double nucleophilic substitution.

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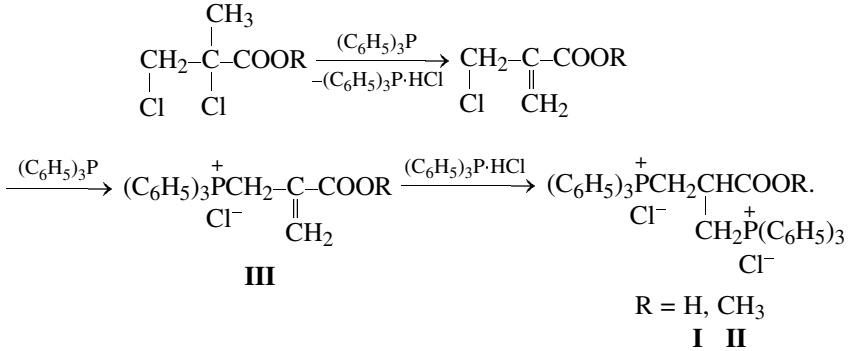
We have previously studied the reactions of 2,3-dihalopropionic acids with triphenylphosphine. The data obtained show that in the case of dichlorides the primary reaction step was dehydrochlorination, whereas in the case of dibromides the debromination took place. These results agree with the published data on high bromophilicity of phosphorus [1].

With the aim to reveal the effect of 2-methyl substituent on the reaction pathway, we studied the reaction of triphenylphosphine with 2,3-dihalo-2-methylpropionic acid and its esters.

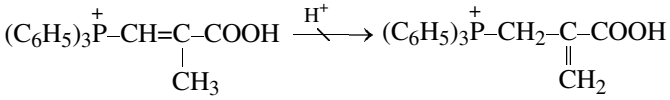
We found that 2,3-dichloro-2-methylpropionic acid and its methyl ester, when refluxed for 12 h in acetonitrile with triphenylphosphine in 1 : 2 molar ratio, form 2-carboxypropane- and 2-carbomethoxypropane-1,3-diylbis(triphenylphosphonium)dichlorides **I** and **II** in 43% and 11% yield, respectively. From the ester, a small amount (~5%) of 2-methoxycarbonyl-2-propenyl(triphenyl)phosphonium chloride **III** was detected by ^{1}H NMR spectroscopy. At the reaction time increased to 40 h, the yield of the bisphosphonium salt from the ester reached 33%. In all the cases the unchanged phosphine was recovered.

The data obtained show that dehydrochlorination involves the methyl hydrogen atom, in spite of its lower proton mobility. This first step is followed by quarternization and the addition of triphenylphosphine to the methylene group.



III **I** **II**

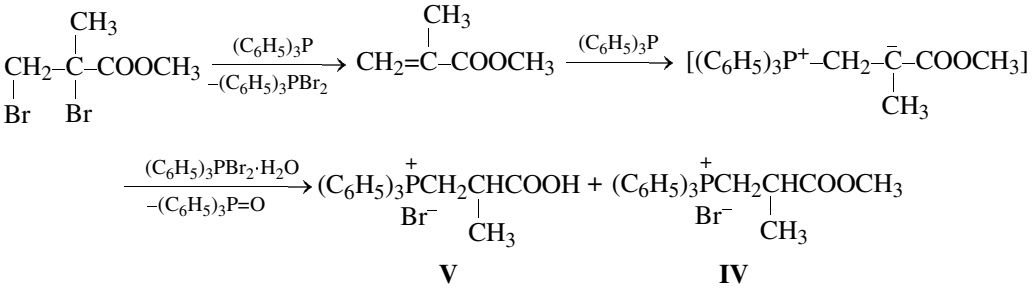
The alternative pathway involving the deprotonation of the chloromethyl group and subsequent isomerization can be ruled out, because it was found previously that 2-carboxy-1-propenyl(triphenyl)phosphonium bromide does not transform into the methylene isomer in the presence of protons [2].



The unexpected dehydrochlorination pathway may be explained by the easier transfer of the electron density from the methyl C–H bond as compared to the chloromethyl C–H bond in the carbocationoid intermediate.

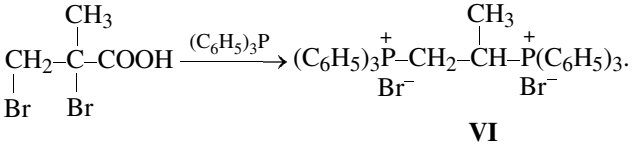
Interesting results were obtained with the bromine analogs.

The reaction of the dibromo ester with triphenylphosphine occurred similarly to the derivatives of 2,3-dibromopropionic acid and followed the debromination scheme. The subsequent hydrolysis at room temperature gave 2-methoxycarbonylprop-1-yl(triphenyl)phosphonium bromide and triphenylphosphine oxide in 35% and 86% yields, respectively. Refluxing in acetonitrile gave a mixture of 2-carboxyprop-1-yl-(triphenyl)phosphomium bromide **V** and compound **IV** in a total yield of 80% and the product ratio of 2.5 : 1. The yield of triphenylphosphine oxide in the latter case was 88%.



V **IV**

With dibromopropionic acid, the similar reaction unexpectedly yielded propan-1,2-diylbis(triphenylphosphonium) dibromide **VI** in 39% yield at room temperature and 46% yield with refluxing.



VI

The data obtained are difficult to explain. Introduction of the methyl substituent possibly increases the anionic mobility of the bromine α-atom, making possible the occurrence of the S_N2 reaction with the attack of the nucleophile on the carbon atom. With the ester, this is less possible, besause the attack on the α-carbon atom is hindered by electronic and steric factors.

EXPERIMENTAL

The ^1H and ^{31}P NMR spectra were taken on a Varian Mercury-300 spectrometer (300 MHz) against internal TMS.

Reaction of 2,3-dichloro-2-methylpropionic acid with triphenylphosphine. A mixture of 0.32 g of

2,3-dichloro-2-methylpropionic acid and 1 g of triphenylphosphine was refluxed for 12 h in acetonitrile. The reaction mixture was poured into ether, and the crystals obtained were filtered off, thoroughly washed with ether, and dried in a vacuum. Compound **I** was obtained in a yield of 0.56 g (43%), mp 185°C. ^{1}H NMR spectrum (DMSO-d_6 + CCl_4, 1 : 3), δ, ppm (*J*, Hz): 2.90 m (1H, CH), 4.25 br.d (2H, CH_2, *J* 14.8, 11.1), 5.30 br.t (2H, CH_2, *J* 14.8), 7.60–7.79 m (30H, $6C_6H_5$). Found, %: C 70.2; H 5.12; Cl 10.2. $C_{40}H_{36}\cdot Cl_2O_2P_2$. Calculated, %: C 70.5; H 5.29; Cl 10.4.

Triphenylphosphine was recovered in an amount of 0.55 g (50%).

Reaction of methyl 2,3-dichloro-2-methylpropionate with triphenylphosphine. A mixture of 0.86 g of methyl 2,3-dichloro-2-methylpropionate and 2.62 g of triphenylphosphine was refluxed for 12 h in acetonitrile. The reaction mixture was poured into ether. The crystals obtained were filtered off, thoroughly washed with ether, and dried in a vacuum. A mixture of compounds **II** and **III** in 4 : 1 ratio was obtained; yield 0.5 g. ^{1}H NMR spectrum of **II** (DMSO-d_6 + CCl_4, 1 : 3), δ, ppm: 2.75 m (1H, CH), 3.40 s (3H, OCH_3), 4.30 br.d (2H, CH_2), 5.50 br.t (2H, CH_2), 7.70–7.80 m (30H, $6C_6H_5$). ^{1}H NMR spectrum of **III** (DMSO-d_6 + CCl_4), δ, ppm: 2.70 s (3H, OCH_3), 5.0 d (2H, CH_2), 6.15 d.d (1H, $=CH_2$), 7.55–7.70 m (15H, $3C_6H_5$).

Triphenylphosphine was recovered in an amount of 2 g (78%).

When a mixture of 0.215 g of methyl 2,3-dichloro-2-methylpropionate and 0.66 g of triphenylphosphine was refluxed for 40 h, 0.3 g (33%) of **II** was obtained, mp 143°C. The ^{1}H NMR data agree with those presented above. Found, %: C 70.5; H 5.2; Cl 9.9. $C_{41}H_{38}\cdot Cl_2O_2P_2$. Calculated, %: C 70.8; H 5.47; Cl 10.2.

Triphenylphosphine was recovered in an amount of 0.38 g (56%).

Reaction of methyl 2,3-dibromo-2-methylpropionate with triphenylphosphine. A solution of 1.3 g of methyl 2,3-dibromo-2-methylpropionate and 2.62 g of triphenylphosphine in acetonitrile was left at room temperature for 15 min. Heat evolution was observed. The reaction mixture was poured into water. The crystals obtained were filtered off and thoroughly washed with water. Triphenylphosphine oxide, 1.2 g (86%), was obtained, mp 154°C. The aqueous filtrate was extracted with chloroform, and the organic solution was treated with ether to precipitate crystals of **IV**. Yield 0.7 g (32%), mp 144–145°C.

^{1}H NMR spectrum (DMSO-d_6 + CCl_4, 1 : 3), δ, ppm: 1.4 d (3H, CH_3), 2.9 m (1H, CH), 3.30 s (3H, OCH_3), 3.85 m (1H, CH_2), 4.20 t (1H, CH_2), 7.65–7.75 m (15H, $3C_6H_5$). ^{31}P NMR spectrum, δ_P, ppm: 28.24. Found, %: C 61.9, H 5.1, Br 17.8, $C_{23}H_{24}Br\cdot O_2P$. Calculated, %: C 62.3, H 5.4, Br 18.0.

When a solution of 0.65 g of methyl 2,3-dibromo-2-methylpropionate and 1.31 g of triphenylphosphine in acetonitrile was refluxed for 12 h and treated as described above, 0.53 g (88%) of triphenylphosphine oxide and a 2.5 : 1 mixture of salts **V** and **IV** (^{1}H and ^{31}P NMR data) in 80% yield were obtained. Yield of **V** 0.57 g (53.3%). ^{1}H NMR spectrum (DMSO-d_6 + CCl_4, 1 : 3), δ, ppm: 1.3 d (3H, CH_3), 2.95 m (1H, CH), 3.90 m (1H, CH_2), 4.23 t (1H, CH_2), 7.70–8.0 m (15H, $3C_6H_5$). ^{31}P NMR spectrum: δ_P 28.80 ppm. Yield of **IV** 0.22 g (20%). The ^{1}H and ^{31}P NMR data agree with those presented above.

Reaction of 2,3-dibromo-2-methylpropionic acid with triphenylphosphine. A solution of 0.9 g of 2,3-dibromo-2-methylpropionic acid and 1.9 g of triphenylphosphine in acetonitrile was left for 15 min at room temperature. The mixture spontaneously warmed up, and a precipitate formed. The precipitate was filtered off, thoroughly washed with acetonitrile, and dried in a vacuum. Compound **VI**, 1 g (38.5%) was obtained, mp 166–168°C. ^{1}H NMR spectrum (DMSO-d_6 + CCl_4 1 : 3), δ, ppm: 1.30 d (3H, CH_3), 2.80 m (1H, CH), 3.85 d (2H, CH_2), 7.40–7.79 m (30H, $6C_6H_5$). Found, %: C 64.1; H 4.5; Br 21.6. $C_{39}H_{36}Br_2P_2$. Calculated, %: C 64.5; H 4.96; Br 22.0.

Triphenylphosphine was recovered in an amount of 0.9 g (47%).

When a solution of 0.9 g of 2,3-dibromo-2-methylpropionic acid and 1.9 g of triphenylphosphine was refluxed in acetonitrile, 1.2 g (46%) of **VI** was obtained.

Triphenylphosphine was recovered in an amount of 0.8 g (42%).

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