REACTION OF DIMETHYLPHOSPHOROUS ACID WITH 2,5-BIS(CARBOMETHOXY)-3,4-DIPHENYLCYCLOPENTADIENONE

B. A. Arbuzov, A. V. Fuzhenkova,
N. I. Galyautdinov, and R. F. Shaikhullina

As was shown by us previously [1-3], hydrophosphoryl compounds can, depending on the reaction conditions, react with tetraphenylcyclopentadienone (TC) either at the C=C group to give α-hydroxy phosphonates and enol phosphates, or by the scheme of 1,4- and 1,6-addition to the conjugated C=C—C=C—C=O system to give γ-phosphono ketones and unconjugated β-phosphono ketones. The latter under the reaction conditions can undergo prototropic isomerization. The direction of the reaction is also affected by the nature of the hydrophosphoryl compound [3, 4]. In the present paper we report the results of studying the reaction of dimethyl phosphite (DMP) with 2,5-bis(carbomethoxy)-3,4-diphenylcyclopentadienone (BCDC). According to the literature data, such nucleophiles as alcohols [5, 6] and primary amines [7] add to BCDC in the 1,4-position of the conjugated C=C—C=O system to give β-substituted cyclopentenones. Depending on the reaction conditions, diazomethane and hydroxylamine can react not only at the conjugated system, but also at the C=O group [7]. It seemed of interest to ascertain which position the DMP will attack in BCDC.

BCDC has stronger electron-acceptor properties than TC. Thus, based on the data given in [8], the electron affinity of BCDC is equal to 2.1 eV, and that of TC is 2.0 eV. Consequently, DMP reacts with BCDC much easier than with TC. Based on the DTA data, the temperature at which DMP reacts with BCDC in the absence of catalysts is 90°C lower than the reaction temperature of TC with DMP [1] (the starting temperature of the exo effect is 70°, and the maximum temperature is 110°).

In contrast to TC, the direction of the reaction is independent of the reaction conditions. Both in the presence of a basic catalyst like triethylamine, and in the absence of catalyst, the primary reaction product is the unconjugated β-phosphono ketone, namely the dimethyl ester of 2-oxo-4,5-diphenyl-1,3-dicarbomethoxy-4-cyclopentene-1-phosphonic acid (I) (Scheme 1).

Infrared spectrum of (I) (v, cm^{-1}): 1038, 1070 (POC), 1263 (P=O), 1735 (ester C=O), and 1770 (ketone C=O). PMR spectrum (δ, ppm): 4.91 s (1H, CH), 3.74 and 3.57 d. d (6H, POCH$_3$, $^3J_{PH}$ = 11 Hz), 3.87 s and 3.63 s (6H, COOCH$_3$).

In the presence of diethylamine or MeONa the reaction goes with the respective formation of the diethylammonium (II) or sodium salt (III) of the enol form of β-phosphono ketone (I). The salt structure of (II) and (III) is indicated by the presence of a band at 1535 or 1555 cm^{-1} in the IR spectra and also, when compared with (I), by a higher intensity of the 1580-1590 and 1600-1610 cm^{-1} bands, which is characteristic for the enolate anion fragment of salts. A low value of vC=O (1665 cm^{-1}) for the COOMe group, found on the unsaturated C atom, is related to the delocalization of the negative charge of the enolate anion fragment on the carboxyl oxygen. The shift of the COOMe group on the C_{sp^3} atom in salt (III) toward lower values of vC=O (1720 cm^{-1}) probably occurs due to the electrostatic interaction of Na$^+$ with the oxygen of the C=O group. In salt (II) the character of vN̅H̅ (2500, 2530, and a broad diffuse band in the 2700-3150 region with a maximum at 3000 cm^{-1}) indicates that an H bond primarily exists between the Et$_2$N̅H$_2$ cation and the unshared electron pairs of the negatively charged O atom of the enolate fragment. The studies reported in [9] testify to the possibility of such a bond. When compared with (I), the small decrease observed for (II) in the vC=O of the COOMe group on the C_{sp^3} atom (1725 cm^{-1}), and in vP=O (1255 cm^{-1}), can be explained the same as in the case of salt (III), i.e., by the electro-

Scheme 1

$B = Et_3N$, $X = P(O)(OMe)_2$.
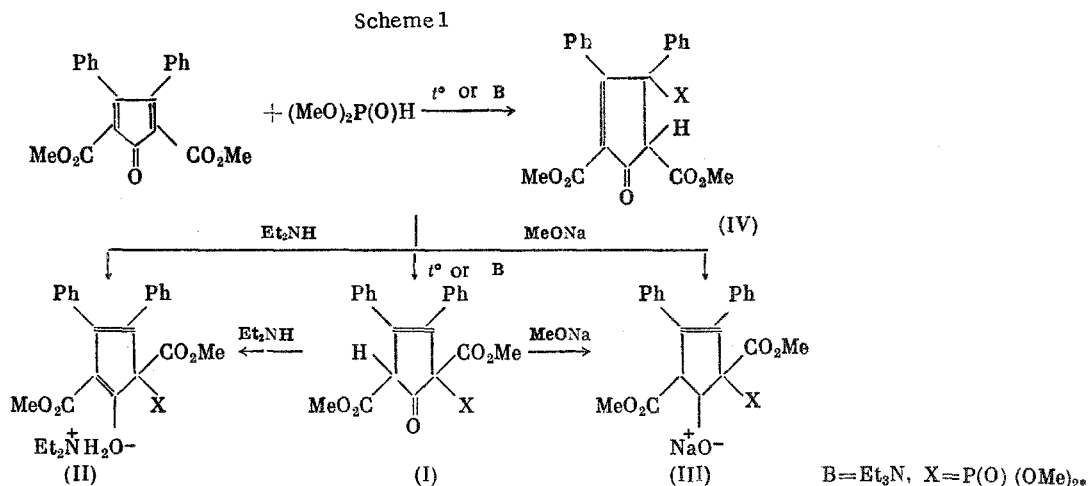
static interaction of the positively charged N atom with these groups. The formation of a large number of H bonds by the $Et_2NH_2^+$ cation assures a substantial stability of salt (II), which, based on the DTA data, does not decompose when heated to $100°$, in contrast to the triethylammonium salt, which is capable of existing only in solution in excess amine. The IR spectrum of such a solution has bands that are analogous to the bands of salt (II) (ν, cm^{-1}): 1560 with a sh., 1580, 1602, 1678, 1725. On dilution with solvents this salt decomposes and ketone (I) is liberated, while the diethylammonium salt (II) is converted to ketone (I) in high yield when treated with acetyl chloride.

The reaction of BCDC with DMP, whether run in the presence of triethylamine or without a solvent, gives, together with ketone (I), the conjugated β-phosphono ketone, the dimethyl ester of 2-oxo-4,5-diphenyl-1,4-dicarbomethoxy-3-cyclopentene-1-phosphonic acid (V) (Scheme 2). The IR spectrum of phosphono ketone (V) has the bands (ν, cm^{-1}): 1030, 1060 (POC), 1270 (P=O), 1630 (C=C), 1705 (ketone C=O), and 1740 (ester C=O). Ketone (V) is formed by the prototropic isomerization of ketone (I). When (I) is kept in solution in the presence of triethylamine it gradually changes to (V).

Scheme 2

$X = P(O)(OMe)_2$.
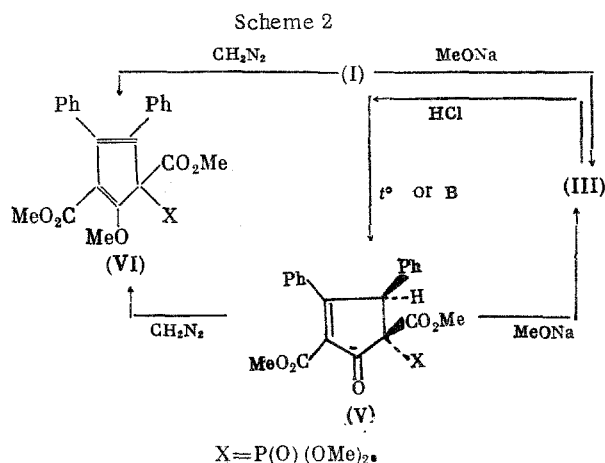
The position of the phosphono group in (V) was proved in the following manner. The reaction of (V) with diazomethane gives the methyl ester of the enol, which in its IR spectrum (ν, cm^{-1}): 1030, 1045, 1060 (POC), 1270 (P=O), 1620 (C=C), 1705 (conjugated C=O), 1735 (unconjugated C=O), and PMR spectrum (δ, ppm): 3.72 and 3.61 d.d (6H, POCH$_3$, $^3J_{PH}$ = 11 Hz), 4.04, 3.86 and 3.55 s (9H, OCH$_3$), is identical with the dimethyl ester of 2-methoxy-4,5-diphenyl-1,3-dicarbomethoxy-2,4-cyclopentadiene-1-phosphonic acid (VI), obtained from (I). The presence in the IR spectrum of two bands of the ester groups (1705 and 1735 cm^{-1}) indicates that one of them is found on the unsaturated, and the other on the saturated C atom. Ketones (I) and (V) react with MeONa to give the Na salt of (III), in which connection (I) was isolated when the Na salt, obtained from (V), is treated with dilute HCl

solution. All of these data definitely indicate the β-position of the carbonyl and phosphono groups in ketone (V).

Based on the data of the PMR spectra (δ, ppm): 5.36 d (1H, PhCH, $^3J_{CH}$ = 16 Hz), 3.88 d (6H, $POCH_3$, $^3J_{PH}$ = 11 Hz), 3.83 s (3H, $C=CCOOCH_3$) and 3.13 s (3H, $CCOOCH_3$), the methine proton in ketone (V) is found cis to the phosphono group, while the corresponding trans isomer was not detected. The substantial upfield shift of the signal of the protons of the $COOCH_3$ group on the C_{sp^3} atom can be explained by the shielding effect of the cis-phenyl group [10].

In contrast to TC [1, 2], in the absence of catalysts BCDC does not give with DMP the 1,4-addition product (IV) (see Scheme 1). The addition products at the carbonyl group, namely α-hydroxy phosphonate (VII) and enol phosphate (VIII), were not detected when the reaction is run in the presence of bases, as is observed for TC [2]. Reaction in the presence of triethylamine in refluxing benzene also does not lead to the formation of (VIII).


X = P(O)(OMe)₂
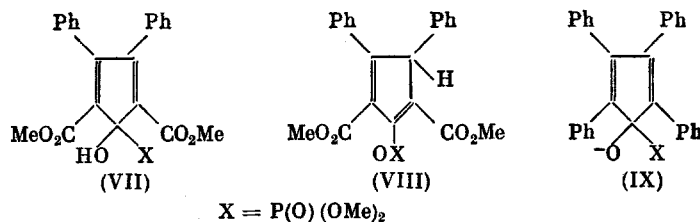
Based on the PMR spectral data, only ketone (V) is present in the reaction mixture under these conditions, which is formed by the complete isomerization of the initially obtained ketone (I).

In studying the reactions of DMP with α,β-unsaturated ketones it was shown by us that, besides the reaction conditions, the regioselectivity of addition to the two electrophilic centers (C=O and C=C) is affected by the distribution of the electron density in the starting ketones, steric factors, and also the conjugation effects in the intermediately formed anions [11, 12]. According to the existing calculation data given in the literature [13], in α,β-unsaturated ketones the effective positive charge on the C atom of the carbonyl group is greater than on the β-C atom.

Calculation data for the electron density on various atoms of the cyclopentadienone fragment in BCDC and TC are absent in the literature, and only calculations of the electronic structure of the unsubstituted cyclopentadienone by the HMO method exist [14]. According to these data, a carbonyl C is more electrophilic than a β-C atom, while the highest electron density is concentrated on the α-C atom. An analogous distribution of the electron density should also exist for TC. Consequently, under basic catalysis conditions the DMP preferentially attacks the carbonyl C, and not the β-C atom, to give the corresponding α-hydroxy phosphonate [2]. Such reagents as Grignard reagent, organo Li compounds [15], and diazo compounds [16] also add easily to the carbonyl group of TC.

It should be mentioned that, in contrast to dibenzylidene ketones (for example, dibenzalcyclopentanone), during attack of the nucleophile on the carbonyl C of the TC molecule the formed intermediate anion (IX) remains a quite highly conjugated system.

Replacing the two phenyl groups in the 2 and 5 positions of TC by electron-acceptor COOMe groups should increase the effective positive charge on the β-C atom of BCDC when compared with TC. Consequently, the possibility of nucleophilic attack on the β-C atom not only by alkoxy ion [5, 6], but also by such weak nucleophiles as primary amines and hydroxylamine [7], becomes clear.
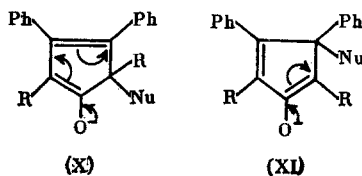
R=Ph, COOMe.

An analysis of the distribution of the electron density in the TC and BCDC molecules shows that nucleophilic attack is more probable on the β-C atom than on the α-C atom, although the anion (X) formed in the latter case is thermodynamically more favorable than anion (XI). However, in not a single case is the attack of nucleophiles on the α-C atom of TC or BCDC described in the literature.

As a result, charge control does not permit explaining the formation of unconjugated β-phosphono ketones when DMP and alkyl phenyl phosphonites are reacted with TC [1-4] and BCDC. Consequently, it may be assumed that β-phosphono ketones are not formed by the nucleophilic attack of DMP on the α-C atom of these acceptors (1,6-addition), but instead by initial addition to the more electrophilic C atom of the C=O group to give anion (XII), which via migration of the phosphono group is quickly rearranged to the more stable anion (XIV) (Scheme 3):

Scheme 3

(XII)   (XIII)   (XIV)
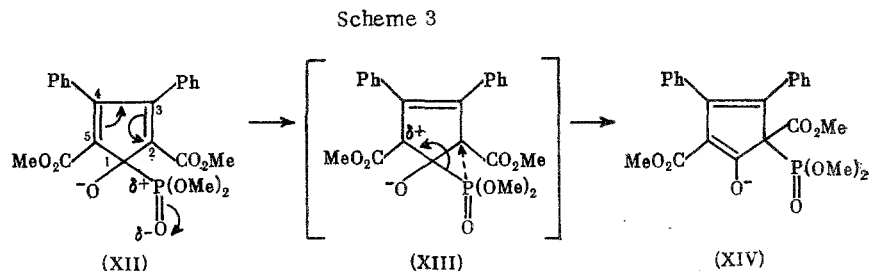
A similar rearrangement is observed for the α-hydroxy phosphonates, which were obtained by reacting TC with DMP [2] and ethyl phenyl phosphonite [4], and also for 1,2,3,4,5-penta-phenyl-2,4-cyclopentadien-1-ol [17] when they are heated or treated with bases.

In anion (XII) the P atom, which has a partial positive charge, will react with C^2 (or C^5), and as a result a redistribution of the electron density will occur in the diene system and an electron-deficient center arises on the C^5 atom. The C^1—P bond is broken, and probably a new C^2—P bond is formed at the same time, in which connection the obtained anion (XIV), due to delocalization of the negative charge, will be more stabilized than the starting (XII). From this scheme it can be seen that in anion (XII) the presence of COOMe groups increases the positive charge on the C^5 atom in (XIII), in this way facilitating cleavage of the C^1—P bond and assisting the rearrangement. It can be seen that the easy migration of the phosphono group in anion (XII) is the specific reason for the inability to observe the formation of α-hydroxy phosphonate (VII).

In the presence of bases the α-hydroxy phosphonate, formed from TC and DMP, rearranges simultaneously to both the β-keto phosphonate and the corresponding enol phosphate [2]. The absence of enol phosphate (VIII) among the reaction products of BCDC with DMP is probably related to the fact that in the initially formed anion (XII) the two COOMe groups, as was mentioned above, facilitate cleavage of the C^1—P bond to give anion (XIV). During the phosphonate-phosphate rearrangement of anion (XII) (Scheme 4) the COOMe groups, formed in transition state (XV), do not facilitate cleavage of the C^1—P bond, like in transition state (XIII), and consequently the formation of anion (XIV) is more preferred than the formation of anion (XVI).

Scheme 4

(XV)   (XVI)
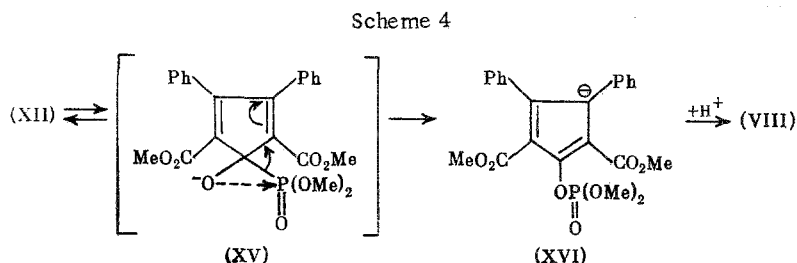
The absence of 1,4-adducts when DMP reacts with BCDC is probably explained by the fact that the process for the formation of anion (XII) and its conversion to anion (XIV) proceeds much more easily than does attack of the nucleophile on the β-C atom of BCDC.

The IR spectra were taken on a UR-10 spectrophotometer. The PMR spectra were recorded on a Varian T-60 spectrometer, using CHCl$_3$ as the solvent and TMS as the internal standard. The thermographing was run on an HTP-70 instrument, equipped with a Chromel—Alumel thermocouple, in sealed Stepanov vessels. The melting point of the products was determined on a Kofler block. The chromatographing was run on silica gel KSK, 0.25 mesh. Successive elution was done with benzene, benzene—ether mixture, ether, and ether—acetone mixture. The starting BCDC was synthesized as described in [5].

Dimethyl Esters of 2-Oxo-4,5-diphenyl-1,3-dicarbomethoxy-4-cyclopentene-1-phosphonic Acid (I) and 2-Oxo-4,5-diphenyl-1,3-dicarbomethoxy-3-cyclopentene-1-phosphonic Acid. a) A mixture of 1 g of BCDC and 0.4 g of DMF was thermographed until the exo effect was recorded completely (up to 130°). Treatment of the reaction mixture with ether gave 0.44 g (33% yield) of white crystals of ketone (I), mp 148-150° (from ethyl acetate—hexane). Found: C 60.04; H 5.21; P 6.91%. C$_{23}$H$_{23}$O$_8$P. Calculated: C 60.26; H 5.02; P 6.77%. The filtrate from the removal of (I) was chromatographed on a silica gel column. We isolated 0.54 g (41%) of ketone (V) with mp 125-126° (from ethyl acetate—hexane). Found: C 60.33; H 5.25; P 6.78%. C$_{23}$H$_{23}$O$_8$P. Calculated: C 60.26; H 5.02; P 6.77%.

b) A mixture of 2 g of BCDC and 0.9 g of DMF in 30 ml of xylene was refluxed for 1 h. After evaporating the solvent in vacuo the addition of ether to the residue gave 0.68 g (26%) of crystalline ketone (I). Based on the PMR spectral data, the solution contains mainly keto phosphonate (V), which was isolated by chromatographing on silica gel in 50% yield (1.32 g).

c) To a mixture of 1 g of BCDC and 0.5 g of DMF were added 0.32 g of Et$_3$N and 10 ml of ether. After 30 min the obtained white crystalline product was filtered and washed with ether to give 0.62 g (47%) of keto phosphonate (I).

d) A solution of 1 g of BCDC, 0.36 g of DMF, and 0.05 g of Et$_3$N in 20 ml of benzene was refluxed for 40 min. The obtained mass was characterized by a chemical shift of δ ^{31}P —19 ppm and, based on the PMR spectral data, contained only β-keto phosphonate (V). After evaporating the benzene in vacuo a part of (V) was isolated by treating the residue with ethyl acetate—hexane mixture. The yield was 0.50 g (38%).

Isomerization of β-Keto Phosphonate (I) in Presence of Et$_3$N. A mixture of 0.5 g of ketone (I), 0.2 g of DMF, and 0.04 g of Et$_3$N in 10 ml of benzene was refluxed for 20 min. Based on the IR and PMR spectral data, the reaction mass contained exclusively the conjugated β-keto phosphonate (V).

Diethylammonium Salt of Dimethyl Ester of 2-Hydroxy-4,5-diphenyl-1,3-dicarbomethoxy-2,4-cyclopentadiene-1-phosphonic Acid (II). a) To 1.2 g of BCDC and 0.65 g of DMF in 10 ml of ether was added 0.30 g of Et$_2$NH in drops. After stirring for 15 min we obtained 1.80 g (98.5% yield) of salt (II) as a yellow precipitate. Found: C 60.87; H 6.51; N 2.91; P 5.72%. C$_{27}$H$_{34}$NO$_8$P. Calculated: C 61.01; H 6.40; N 2.63; P 5.83%.

b) To 0.5 g of ketone (I) as an ether suspension was added 0.11 g of Et$_2$NH. A yellow precipitate of diethylammonium salt (II) was formed immediately. Yield 0.58 g (100%).

Na Salt of Dimethyl Ester of 2-Hydroxy-4,5-diphenyl-1,3-dicarbomethoxy-2,4-cyclopentadiene-1-phosphonic Acid (III). a) To a mixture of 0.5 g of BCDC and 0.4 g of DMF was added 0.3 g of saturated MeONa solution in MeOH. After dissolving the obtained oily mass in a little CH$_2$Cl$_2$ and subsequent addition of hexane we obtained yellowish crystals of salt (III). Yield 0.66 g (98%), mp 138° (decompn.). Found: C 57.23; H 4.69; P 6.22%. C$_{23}$H$_{22}$NaO$_8$P. Calculated: C 57.50; H 4.58; P 6.45%.

b) To a suspension of 0.5 g of ketone (I) in 10 ml of pentane was added 0.12 g of saturated MeONa solution in MeOH. The obtained precipitate was filtered to give 0.52 g (100%) of salt (III).

c) In a similar manner, from 0.4 g of conjugated phosphono ketone (V) and 0.05 g of dry MeONa we obtained 0.39 g (93%) of salt (III).

Unconjugated β-Phosphono Ketone (I) from Ammonium Salt (II) and Na Salt (III). a) With stirring, to a suspension of 1 g of salt (II) in ether was added 0.15 g of AcCl in ether solution. The obtained white precipitate of phosphono ketone (I) was washed with hot water

to remove the hydrochloride and then dried. The yield of (I) was 0.76 g (88%) mp 148–150°.

b) An acetone solution of 0.5 g of salt (III) was treated with 1:5 HCl solution. The NaCl precipitate was filtered, the filtrate was evaporated in vacuo, and the residue was dissolved in benzene and washed several times with water. After evaporation of the benzene and subsequent treatment with ether we isolated 0.30 g (61%) of keto phosphonate (I).

Dimethyl Ester of 2-Methoxy-4,5-diphenyl-1,3-dicarbomethoxy-2,4-cyclopentadiene-1-phosphonic Acid (VI). a) With stirring, to a suspension of 0.5 g of ketone (I) in 25 ml of MeOH was added 30 ml of an ether solution of diazomethane. Here, together with N_2 evolution, was observed solution of the suspension. After 2 h the solution was evaporated in vacuo and the white crystals of (VI) were separated. Yield 0.45 g (87%), mp 147–148° (from ethyl acetate–hexane). Found: C 60.75; H 5.30; P 6.41%. $C_{24}H_{25}O_8P$. Calculated: C 61.01; H 5.29; P 6.56%.

b) With stirring, to 0.4 g of ketone (V) in 15 ml of MeOH was added 100 ml of an ether solution of diazomethane. At the end of N_2 evolution the solution was kept for another 4 h and then the solvent was evaporated in vacuo. We isolated 0.40 g (79%) of (VI), mp 147–148°, which, based on the IR and PMR spectra, is identical with the above described product.

c) To 0.5 g of diethylammonium salt (II) in 25 ml of MeOH or benzene was added 30 ml of ethereal diazomethane solution. After 3 h the mixture was worked up as described above to give 0.37 g (83%) of (VI).

CONCLUSIONS

The reaction of 2,5-bis(carbomethoxy)-3,4-diphenylcyclopentadienone with dimethyl phosphite, both in the presence of Et_3N and in the absence of catalysts, goes with the formation of the dimethyl esters of 2-oxo-4,5-diphenyl-1,3-dicarbomethoxy-4-cyclopentene- and 2-oxo-4,5-diphenyl-1,3-dicarbomethoxy-3-cyclopentene-1-phosphonic acids. In contrast to alcohols and primary amines, dimethyl phosphite does not form the 1,4-addition products with this acceptor.

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