The analysis of the organotin compounds was carried out on a Tsvet-4 chromatograph with a katharometer in a stream of helium (60-80 ml/min). The column was $2 \text{ m} \times 4 \text{ mm}$ and contained 10% Apiezon on Chromosorb W (80-100 mesh). The quantitative determinations were carried out relative to an internal reference, viz., hexadecane. The analysis of the organogermanium compounds was carried out on an AG K-6 chromatograph with a katharometer in a stream of helium (80 ml/min). The column was $3 \text{ m} \times 4 \text{ mm}$ and contained 5% SE-30 on Chromaton N, which was treated with dimethyldichlorosilane. The analysis was carried out with programming of the temperature from 100 to 270° C and from 170 to 270° C at the rate of 20 deg/min. The internal reference was tetradecane.

CONCLUSIONS

1. The hydrostannation and hydrogermylation of olefins is efficiently initiated by 60 Co γ radiation.

2. The addition of Ge and Sn hydrides to olefins initiated by γ radiation is consistent with the main laws governing radical chain reactions in the liquid phase.

3. The radiation effects in the hydrometallation reaction decrease upon the transition from Sn hydrides to Ge hydrides and from hydrides of the aromatic series to the aliphatic series.

4. The rate of the radiation-chemical hydrometallation increases with increasing electron density in the double bond; the introduction of electron-acceptor substituents lowers the reaction rate.

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REACTIONS OF SEVERAL α -ENONES

WITH TRIMETHYL PHOSPHITE

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It is known [1-3] that the reaction of trialkyl phosphites with α,β -unsaturated ketones containing electron-acceptor groups proceeds with the formation in the first step of an adduct of bipolar structure and its subsequent stabilization in the form of a cyclic phosphorane or enol ester. We have previously [4-6] demonstrated the possibility of the formation of Δ^4 -oxaphospholenes in reactions of trialkyl phosphites with α -enones in which there are no electron-acceptor substituents, but which offer the possibility of the stabilization of the bipolar ion by means of a resonance interaction between the anionic center and the benzylidene group or an aromatic ring.

As a continuation of these investigations we studied the reaction of 2,5-dibenzylidenecyclopentanone (I) and 3,3-diphenyl-2-benzylidenehydrindone (II) with trimethyl phosphite (III). In analogy to 2,6-dibenzylidenecyclohexanone [4] and 2-benzylidenetetralone [6], in the case of I and II we postulated the formation of bipolar ions IV and V, which subsequently yield cyclic phosphoranes VI and VII:

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However, the addition products of III to I and II were not found even after prolonged heating. It is interesting that a small exothermic effect with an initial termperature of 74°C and a temperature at the maximum equal to 83°C was observed on the thermogram of a mixture of I and III. A compound not containing phosphorus was isolated with a small yield after the thermography. The data from the IR spectrum were as follows (ν , cm⁻¹): 1612, 1635 (C=C), 1720 (C=O). The determination of the molecular weight by Rast's method (the mol. wt. found was 571.5, and the mol. wt. calculated was 520.6) and the data from the elemental analysis allowed us to postulate the formation of a product of diene synthesis from two molecules of I:



The choice between possible structures VIIIa and VIIIb was not made. It should be noted that the formation of phosphoranes was not detected in any of the investigations in the literature on the reaction of five-membered cyclic and heterocyclic α -enones and diketones with trialkyl phosphites [7].

The realization of the first step in the nonclassical Arbuzov rearrangement is indicated by the reaction of I and II with III in the presence of AcOH or Ac₂O. It was found that the reaction of I with III in the presence of AcOH produces γ -ketophosphonate IX with a small admixture of enol acetate X. We previously noted [4] the unexpected formation of enol acetates in the reactions of 2,6-dibenzylidenecyclohexanone with trialkyl phosphites in the presence of AcOH. It may be postulated that the formation of enol phosphonates occurs initially in these processes and that these intermediates are either irreversibly transformed into γ -ketophosphonates or acetylated:



The structure of products IX and X was demonstrated by the data from the elemental analysis and the IR spectra $(\nu, \text{ cm}^{-1})$: for IX, 1035, 1060 (P-O-C), 1255 (P=O), 1750 (C=O); for X, 1034, 1063 (P-O-C), 1197 (P-O-CH₃), 1255 (P=O), 1605, 1652 (C=C), 1775 (C=O). In addition, the constants of IX coincided with those of the γ -ketophosphonate we obtained in [8] by reacting I with (MeO)₂POH with catalysis by MeONa. Enol acetate X has also been isolated as a result of the reaction of I with III in the presence of Ac₂O.

3,3-Diphenyl-2-benzylidenehydrindone reacts with III in the presence of AcOH, yielding stable enol XI, which does not undergo a transition to a keto form:



The IR spectrum of XI contains characteristic absorption bands $(\nu, \text{ cm}^{-1})$ at 1030, 1055 (P-O-C), 1210 (P=O), and 1615 (C=C), and a diffuse band in the 2500-2700-cm⁻¹ region (ν OH). The realization of the reaction of II with III in the presence of Ac₂O made it possible to obtain enol acetate XII.

The monobenzylidene ketones benzylideneacetone (XIII), 2-benzylidenecyclohexanone (XIV), and 2-benzylidenecyclopentanone (XV), i.e., α -enones, in which there are no groups which stabilize the bipolar ion, do not react with III. However, the thermographic study of the reaction of ketones XIII-XV with III in the presence of AcOH demonstrated the presence of an exothermic effect with an initial temperature of 120°C and a temperature at the maximum equal to ~187°C. These reactions resulted in the production of γ -ketophosphonates XVI-XVIII:



The extended exothermic effect on the thermograms is not attributed to the reaction of the α -enols with the phosphite, but it is the result of two processes. At first III reacts with AcOH (exothermic effect, initial temperature 120°C, temperature at the maximum 155°C) to form (MeO)₂POH, which then reacts with α -enones XIII-XV at ~185-189°C, as was shown in [9], yielding γ -ketophosphonates XVI-XVIII.

Thus, the styryl and aryl fragments in cross-conjugated ketones I and II can bring about the stability of the bipolar ion and thereby provide for the occurrence of the first step in the nonclassical Arbuzov rearrangement. The absence of groups which stabilize the bipolar ion in α -enones XIII-XV makes it impossible to obtain products of the reaction with trimethyl phosphite, even in the presence of a third component. However, there are some examples [10, 11], in which systems (acrolein, methyl vinyl ketone) not containing groups which stabilize adducts with a bipolar structure yield phosphoranes. We suggest that the possibility of the formation of phosphoranes in these cases is determined by the smaller loss of conjugation energy [12] during the attack of the phosphite on the carbon atom of alkylidene ketones than in the case of benzylidene ketones. Additional support for this hypothesis is provided by the detection of oxaphospholene structure XIX in the reaction of ethylidene acetone with III ($\delta^{31}P+32$ ppm):

EXPERIMENTAL

The thermographic investigations were carried out on a Kurnakov PK-52 pyrometer with a Chromel-Alumel thermocouple in sealed Stepanov vessels. Calcined MgO served as a reference. The rate of heating of the furnace was 4-5 deg/min. The IR spectra were recorded on a UR-10 spectrophotometer. The melting point was determined on a Kofler apparatus.

<u>Reaction of 2,5-Dibenzylidenecyclopentanone (1) with Trimethyl Phosphite (III)</u>. A mixture of I and a twofold excess of III was held at ~20°C and heated at 40-60°C for 40 h, at 100°C for 20 h, and at 150°C for 7 h with thermographic monitoring. An adduct containing phosphorus was not found (by IR and ³¹P NMR spectral analysis) in any of the experiments. After passage of the exothermic effect (the temperature at the maximum was 83°C) the mixture was held in a Stepanov vessel at 20°C for 2 weeks. The white crystalline compound VIII was separated by washing with ether. The yield was 32.6%, and the mp was 263-264.5°C. Found: C, 87.45; H, 6.30%. Calculated for $C_{38}H_{32}O_2$: C, 87.65; H, 6.19%.

Reaction of 2,5-Dibenzylidenecyclopentanone (I) with Trimethyl Phosphite (III) in the Presence of Acetic Acid. A mixture of equimolar amounts of I, III, and AcOH was thermographed until the first exothermic effect had been passed (the initial temperature was 74°C, and the temperature at the maximum was 120°C). Upon cooling the mixture crystallized. The white crystals were washed with ether. γ -Ketophosphonate IX and enol acetate X were separated mechanically (according to the shape of the crystals). The yield of IX was 42% and the mp was 126-127.5°C (from cyclohexane). The yield of X was 9.3% and the mp was 156-157°C (from cyclohexane). IR spectrum of IX (ν , cm⁻¹): 1035, 1045, 1059 (P-O-C), 1225 (P=O), 1636 (C=C), 1720 (C=O). Found: C, 57.63; H, 6.34; P, 8.29%. Calculated for C₂₁H₂₃O₄P: C, 57.91; H, 6.29; P, 8.36%. IR spectrum of X (ν , cm⁻¹): 1034, 1063 (P-O-C), 1197 (P-O-CH₃), 1255 (P=O), 1605, 1652 (C=C), 1775 (C=O). Found: C, 67.08; H, 6.10; P, 7.08%. Calculated for C₂₃H₂₅O₅P: C, 66.97; H, 6.11; P, 7.05%.

Reaction of 2,5-Dibenzylidenecyclopentanone (I) with Trimethyl Phosphite (III) in the Presence of Acetic Anhydride. An equimolar mixture of I, III, and Ac_2O was heated with thermographic monitoring until an exothermic effect had been passed (the initial temperature was 122°C, and the temperature at the maximum was 147°C). The contents of the vessel crystallized upon cooling to ~20°C. The crystals were filtered off and washed with ether, and compound X was obtained in an 87% yield, mp 156-157°C.

Reaction of 3.3-Diphenyl-2-benzylidenehydrindone (II) with Trimethyl Phosphite (III) in the Presence of Acetic Acid. Equimolar amounts of II in AcOH with an excess of III were thermographed to the first exothermic effect (the temperature at the maximum was 112°C). The contents of the vessel crystallized upon standing in a refrigerator. The precipitate was filtered off and washed with petroleum ether. This yielded enol phosphonate XI, mp 201-202°C (from a benzene-petroleum ether mixture). The yield was 85%. Found: C, 74.63; H, 5.67; P, 6.43%. Calculated for $C_{30}H_{27}O_4P$: C, 74.6; H, 5.64; P, 6.42%.

<u>Reaction of 3,3-Diphenyl-2-benzylidenehydrindone (II) with Trimethyl Phosphite (III) in the Presence of $(CH_3CO_{2}O)$. A mixture of 0.1023 g of II, 0.1371 g of III, and 0.0236 g of Ac₂O was thermographed to the first exothermic effect (the temperature at the maximum was 140°C). White crystals precipitated in the cold over the course of 24 h. Product XII was filtered off and washed with ether. The yield was 70%, and the mp was 167-168°C (from cyclohexane). IR spectrum (ν , cm⁻¹): 1030, 1068 (P-O-C), 1218 (P=O), 1250 (OCOCH₃), 1612, 1652 (C=C), 1770 (C=O). Found: C, 73.28; H, 5.99; P, 5.85%. Calculated for $C_{32}H_{29}O_5P$: C, 73.26; H, 5.57; P, 5.90%.</u>

Reaction of Benzylideneacetone (XIII), 2-Benzylidenecyclohexanone (XIV), and 2-Benzylidenecyclopentanone (XV) with Trimethyl Phosphite in the Presence of CH_3COOH . A mixture of equimolar amounts of the α enone (XIII, XIV, and XV) and AcOH and of a twofold excess of III was heated with thermographic monitoring until an exothermic effect had been passed (the initial temperature was 120°C, and the temperature at the maximum was ~186°C). The excess of III was removed from the reaction mixture in a vacuum, and the residue was treated in analogy to the experiments involving the reaction of α -enones XIII, XIV, and XV with dimethylphosphorous acid [9]. γ -Ketophosphonates XVI-XVIII were obtained.

CONCLUSIONS

1. The reaction of 2,5-dibenzylidenecyclopentanone and 3,3-diphenyl-2-benzylidenehydrindone with trimethyl phosphite does not produce phosphoranes. The formation of phosphonates occurs in the presence of acetic acid and acetic anhydride.

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PHENYLALANINE DERIVATIVES CONTAINING ACYL GROUPS OF STEREOISOMERIC N-[TETRAMETHYLDIAMIDO(THIO)PHOSPHORYL]-AND N-[DIMORPHOLIDO(THIO)PHOSPHORYL]-4-AMINOCYCLOHEXANE-CARBOXYLIC ACIDS

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Guided by the interest attaching to the antitumor activity of the nonalkylating tetraalkyldiamidophosphoryl derivatives of cyclohexylamine, morpholine, and 4-aminocyclohexanecarboyxlic acid (ACHCA) [2], we have continued our earlier work on the biological properties of the stereoisomeric N-[diethyleneimido(thio)phosphoryl]aminocyclohexylcarbonyl amino-acids [1] by synthesizing certain compounds containing tetramethyldiamido(thio)phosphoryl and dimorpholido(thio)phosphoryl groups.

Synthesis was carried out by using dicyclohexylcarbodiimide (DCHC) to condense N-phthaloyl-cis- and N-phthaloyl-trans-4-ACHCA with the ethyl ester of DL-phenylalanine. Each of these isomers reacted equally well under the conditions in question here. The protective N-phthaloyl groups in the N-phthaloyl-cis- and N-phthaloyl-trans-4-ACHC*-DL-phenylalanine ethyl esters were eliminated by treatment with hydrazine hydrate in CH_2Cl_2 -alcohol solution at 40°C. PMR studies showed that complete elimination, without byproduct formation, could be attained in 15 h. The final reaction products, the stable salts of the ethyl esters of trans- and cis-4-ACHC-DL-phenylalanine with phthaloyl hydrazide, were broken down in alcoholic HCl solution. These procedures gave good yields of the chlorohydrates and free bases of the ethyl esters of trans- and cis-4-ACHC-DL-phenylalanine by the method described in [1].

The ethyl esters of N-tetramethyldiamido(thio)phosphoryl-trans- and cis-4-ACHC-DL-phenylalanine (I), (II), (IX), and (X) were obtained by reacting the dichlorohydrides with excess dimethylamine in solution in inert solvents. The ethyl esters of N-dimorpholido(thio)phosphoryl-trans- and cis-4-ACHC-DL-phenylalanine, (III), (IV), (XI), and (XII), were obtained by condensing the ethyl esters of N-dichloro(thio)phosphoryl-transand cis-4-ACHC-DL-phenylalanine with morpholine in the presence of triethylamine.

Hydrolysis of the ethyl esters (1)-(IV) and (X)-(XII) by the theoretical amount of MeONa in aqueous solution gave good yields of the sodium salts of N-tetramethyldiamido(thio)phosphoryl-trans-, N-dimorpholido-(thio)trans-, and cis-4-ACHC-DL-phenylalanine, (V)-(VIII) and (XIII)-(XV), as stable, water-soluble compounds. The characteristics of these compounds are summarized in Tables 1 and 2.

*ACHC designates aminocyclohexylcarbonyl.

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