Tertiary phosphite – alkyl halide reactions in acetonitrile

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Olefin elimination does not occur during the interaction of ca. 0.2 M triisopropyl phosphite and isopropyl iodide (and of other simple tertiary phosphite – alkyl halide mixtures) in acetonitrile, contrary to a previous report. At and below 50°, the Arbuzov reaction does occur very slowly in these systems. The reaction of trimethyl phosphite and *n*-butyl iodide in acetonitrile gives a larger yield of dimethyl methylphosphonate than of dimethyl *n*-butylphosphonate.

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There have been several recent kinetic investigations of the Arbuzov reaction

$$(RO)_3P{:} + R'X \rightarrow R'(RO)_3PX \rightarrow R'P(O)(OR)_2 + RX$$

using dilute solutions in acetonitrile (1, 2). In an infrared (i.r.) spectral study of the triisopropyl phosphite reaction with isopropyl iodide, Aksnes and Aksnes (3) observed that diisopropyl hydrogen phosphonate was formed instead of the Arbuzov product. Propene elimination was postulated to account for this. Olefin elimination from tri-*t*-butyl phosphite to give isobutylene and di-*t*-butyl hydrogen phosphonate has been reported (4) to occur readily either on warming the neat reagent, or (as the major reaction path) in its low temperature Arbuzov reaction with methyl iodide *in the absence of solvent.*

In the present work, several reactions in acetonitrile of tertiary phosphites with alkyl iodides were reinvestigated, with emphasis placed on isolation of products, and especially the detection of any olefins formed. Another aspect of the work dealt with the question of possible competition of the alkyl halide produced in the Arbuzov reaction with a different alkyl halide starting material; the system trimethyl phosphite – *n*-butyl iodide in acetonitrile was chosen for this study.

Experimental

Materials and Equipment

Transfers of reagents to reaction vessels and spectral cells were conducted in a nitrogen-filled dry box. Additions to and separations from reaction mixtures of solvent and volatile reagents, the final purification stages of such reagents, and the reactions themselves were conducted in an all glass high vacuum line in which the residual gas pressure had been reduced to $< 10^{-5}$ Torr.

Acetonitrile was repeatedly shaken with phosphorus(V) oxide, distilled from fresh phosphorus(V) oxide onto calcium hydride, and then redistilled from calcium hydride into the vacuum line. The alkyl iodides were doubly distilled. Trimethyl phosphite (Hooker Chemical Co. and Monsanto Chemical Co. samples) was redistilled in dry nitrogen; nuclear magnetic resonance (n.m.r.) (neat): δ 3.15 (d, $J_{\mathrm{POCH}} = 11$ Hz, OCH_3). Triisopropyl phosphite (Mobil Chemical Co.) was purified as follows. Sodium wire was added to react with any dialkyl hydrogen phosphonate present. After evolution of hydrogen had ceased, the liquid phase was decanted and distilled under reduced pressure in nitrogen using a Nester–Faust Teflon spinning band column. A middle fraction was taken, and then similarly redistilled; n.m.r. (neat): δ 0.98 (d, $J = 6$ Hz, $CH(CH_3)_2$), 4.05 (m, $CH(CH_3)_2$). Tri-*n*-butyl phosphite (Eastman Kodak) was purified in an identical fashion; n.m.r. (neat): δ 3.59 (m, CH_2O—).

Authentic samples of dialkyl hydrogen phosphonates and dialkyl alkylphosphonates were needed for analytical standards. Commercial samples of the following were redistilled under reduced pressure, with a middle fraction taken: dimethyl hydrogen phosphonate (Mobil Chemical Co. and Monsanto Chemical Co.); n.m.r. (neat): δ 3.55 ($J_{\mathrm{POCH}} = 12$ Hz, OHC_3), 6.55 (d, $J_{\mathrm{PH}} = 694$ Hz, PH); di-*n*-butyl hydrogen phosphonate (Mobil); n.m.r. (neat): δ 3.85 (m, OCH_2), 12.30 (one component of PH doublet, other component obscured by CH_3); dimethyl methylphosphonate (Aldrich); n.m.r. (neat): δ 3.54 (d, $J_{\mathrm{POCH}} = 12$ Hz, OCH_3), 1.32 (d, $J_{\mathrm{PCH}} = 18$ Hz, PCH_3). Diisopropyl hydrogen phosphonate was prepared (3) by boiling triisopropyl phosphite with water in acetonitrile under nitrogen. The solvent and water were stripped off and the product (60%) distilled: b.p. 73–74° (9 mm); n.m.r. (neat): δ 1.07 (d, $J = 7$ Hz, $CH(CH_3)_2$), 4.50 (m, $CH(CH_3)_2$), 6.78 (d, $J_{\mathrm{PH}} = 704$ Hz, PH). The previously unreported dimethyl *n*-butylphosphonate was prepared by the Arbuzov reaction from neat trimethyl phosphite and *n*-butyl bromide at ca. 110°, with methyl bromide evolved. The product (25%) was distilled: b.p. 76–78° (19 mm); n.m.r. (neat): δ 3.55 (d, $J_{\mathrm{POCH}} = 11$ Hz, OCH_3). Di-*n*-butyl ethylphosphonate was synthesized by treating di-*n*-butyl hydrogen phosphonate in hexane first with sodium and then with ethyl bromide. The reaction mixture was washed with water to remove sodium bromide, the solvent was stripped off, and the product (60%) was distilled under reduced pressure using a spinning band column; n_{D}^{25} 1.4258 [lit. (5), n_{D}^{25} 1.4258]; n.m.r. (neat): δ 3.86 (m, OCH_2). An attempted synthesis of diisopropyl isopropylphosphonate by the Arbuzov reaction using neat triisopropyl phosphite and isopropyl bromide was unsuccessful. However, a sample was obtained in very low yield after heating a mixture of 50 ml of triisopropyl phosphite, 25 ml of isopropyl bromide,

TABLE I

Reaction conditions and results

Reaction conditions	% 3° Phosphite remaining	Products observed by g.l.c.	Comments
0.193 *M* $(nBuO)_3P$ + 0.213 *M* EtI 7 days, 31°	83*	$(nBuO)_2P(O)Et$, *n*BuI	Nuclear magnetic resonance accounted for by $(n\text{-}BuO)_3P$ + $(n\text{-}BuO)_2P(O)Et$
0.203 *M* $(MeO)_3P$ + 0.215 *M* *n*BuI 7 days, 50°	87†	$(MeO)_2P(O)Me$ (10%), $(MeO)_2P(O)nBu$ (2%), $HP(O)(OMe)_2$ (1%), MeI, MeOH	No P—H apparent in nuclear magnetic resonance or infrared spectroscopy
0.214 *M* $(isoPrO)_3P$ + 0.229 *M* isoPrI 13.5 days, 50°	100‡	$(isoPrO)_2P(O)(isoPr)$, X§	Essentially no reaction; gas–liquid chromatography shows products as traces only. Slight development of P═O (but no P—H) in infrared; only starting material apparent in nuclear magnetic resonance

*By quantitative infrared spectrophotometry at 870 cm^{-1}.
†By gas–liquid chromatography.
‡By quantitative infrared spectrophotometry at 862 cm^{-1}.
§Trace of unknown impurity.

and a trace of iodine in 200 ml of purified anhydrous acetonitrile at 78° for 10 days. The solvent and unreacted isopropyl bromide were stripped off and the residue was distilled. Most of the starting phosphite was recovered: b.p. 64–69° (11.5 mm), and then a small fraction (6%) of the desired product was collected: b.p. 92° (11.5 mm); infrared (i.r.): (CCl_4) 1202 and 1242 cm^{-1} (P═O); n.m.r. (neat): δ 4.46 (m, $CH(CH_3)_2$), 1.14 (d, J = 5 Hz, $OCH(CH_3)_2$), 0.82 (d, J = 6 Hz, $PCH(CH_3)_2$). The ratio of the (planimeter) integrated intensities of the latter two doublets was 1.8 ± 0.2, theory 2.0.

An F and M model 700 chromatograph was used for gas–liquid chromatography (g.l.c.) analyses, with dual 6 ft stainless steel columns and helium as the carrier gas. Two sets of columns were used: (*A*) 1/8 in., 10% silicone oil W98 on 80–100 mesh Chromosorb W; (*B*) 1/4 in., 20% Reoplex 400 on 30–60 mesh Chromosorb W. Spectra were obtained with a Varian A-60 proton n.m.r. spectrometer and a Beckman Microspec double beam recording i.r. spectrophotometer.

Reaction Studies

For each tertiary phosphite – alkyl iodide combination studied, the reaction flask was connected through the vacuum system to a manometer and gas storage bulb. The reaction conditions, degrees of conversion, and analytical observations are indicated in Table I. For each system, the vapor pressure of the reaction mixture remained constant during the entire period, and the equilibrium pressure dropped to < 1 mm when the reaction was terminated by quenching to −63.5°. The i.r. and g.l.c. analyses involved comparison of the acetonitrile reaction solutions with acetonitrile solutions of the reference standards. Where quantitative i.r. spectrophotometric analysis is indicated, the validity of Beer's Law and the lack of interference by other components had been established. Nuclear magnetic resonance spectra were obtained on the neat residues remaining after distillation of the volatile solvent and alkyl halides in the vacuum line.

Results and Discussion

The Arbuzov reactions of aliphatic tertiary phosphites and iodides in dilute solution in acetonitrile at and below 50° are very slow. In each of the systems studied, the major portions of the starting materials were recovered unchanged after a week or more. A previous report (1) of more rapid reaction in such systems has been attributed (2) to possible contamination of the solvent by traces of water. The present experimental results definitely prove that no olefin was formed in any of the systems studied, including the triisopropyl phosphite – isopropyl iodide system in which propene elimination had been postulated (3). The report of the formation of diisopropyl hydrogen phosphonate in that study (3) presumably may also be attributed to impurities in the solvent.[1]

That polar solvents may be of practical synthetic value as Arbuzov reaction media is suggested by the present work. Under typical synthetic conditions (neat reagents at reflux), triisopropyl phosphite and isopropyl bromide gave no reaction. When the reaction was conducted in acetonitrile at reflux, diisopropyl isopropylphosphonate slowly formed. The use of a higher boiling solvent should provide a more practical synthetic method for sterically hindered phosphonates. Alternatively, photolysis has been

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[1] G. Aksnes. Personal communication.

used (6) to generate diisopropyl isopropylphosphonate from the tertiary phosphite.

An explanation for this effect of a polar solvent may be suggested. Aksnes and Aksnes have reported (2) that the first step of the reaction is rate-determining in acetonitrile. That the second step is normally rate-determining is indicated by the isolation of the intermediate in aliphatic (7) as well as aromatic systems. The presence of a polar solvent would markedly increase (7) the ionic dissociation of a phosphorane or ion-paired phosphonium halide intermediate. The change in kinetics and the reduction in steric hindrance may both be attributed to this change in the structure of the intermediate.

Additional evidence is the formation of five times as much dimethyl methylphosphonate as dimethyl *n*-butylphosphonate, in the reaction of trimethyl phosphite with *n*-butyl iodide in acetonitrile. In the absence of a solvent, such competition of an alkyl halide product with a different alkyl halide starting material is not a practical problem. To the extent that formation of the intermediate is the fast step (and irreversible), the tertiary phosphite would no longer be available. Even in acetonitrile, the effect is not seen unless the alkyl halide formed is significantly more reactive; thus no mixed products were observed in the tri-*n*-butyl phosphite–ethyl iodide system.

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