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Anodic Oxidation of Organophosphorus Compounds. III.[1] Anodic Alkoxylation and Thioalkoxylation of Triphenylphosphine

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Controlled potential electrolysis of triphenylphosphine in acetonitrile containing various primary alcohols and dialkyldisulfides resulted in the formation of the corresponding alkoxy and alkylthio triphenylphosphonium salts, $[Ph_3P^+\text{-}X][ClO_4^-]$. Compounds with $X=OMe$, OEt, OPr^n, SMe, SEt, and SPr^n were isolated. The alkoxy derivatives reacted with imidazole and thiophenol under mild conditions to give the corresponding *N*- and *S*-alkylated products quantitatively.

Keywords——alkoxytriphenylphosphonium perchlorates; alkylthiotriphenylphosphonium perchlorates; triphenylphosphine; anodic alkoxylation; anodic thioalkoxylation; controlled potential electrolysis

In the anodic oxidation of triphenylphosphine (TPP), nucleophilic attack of primary amines[3] and benzenes[4,5] on the anodically generated TPP cation radical to give the corresponding phosphonium ions has been observed. Since the nucleophilicities of primary amines and aromatic hydrocarbons differ considerably, these observations suggest the formation of various phosphonium ions by means of anodic substitution reactions.

Phosphonium ions having at least one alkoxy group are usually unstable, for instance in Arbuzov type reactions,[6] and cannot readily be isolated. With weakly nuclephilic counter anions, however, several examples of their isolation have been reported,[7,8] and the phosphonium ions were shown to be potential alkylating agents.[7,9] In electrochemical oxidations, the anions of supporting electrolytes should generally be weak nucleophiles, and hence it might be possible to isolate the phosphonium ions formed at the electrode. The formation of trialkoxy aryphosphonium ions has been noted in the anodic arylation of trialkylphosphites.[1]

This paper reports the results of anodic alkoxylation and thioalkoxylation of TPP. The corresponding phosphonium salts have been isolated and their applicabilities as alkylating agents tested. We know of no previous report on the direct reaction of alcohols with TPP to afford stable phosphonium salts.

Results and Discussion

Electrochemistry

Cyclic voltammetry of TPP in acetonitrile has been reported previously.[3,4] The peak current of TPP in acetonitrile increased when an alcohol was added, but the increase did not

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exceed 1.5 times the peak current observed in the absence of the alcohol. When 2,6-lutidine was added to a solution of TPP in acetonitrile containing an excess of the alcohol, the peak current increased further with the amount of the base and reached a limiting value, which was about twice that observed in the absence of the base. Typical voltammograms are shown in Fig. 1. Similar results were obtained with added ethanethiol or phenol in place of alcohol.

Table I summarizes the results of controlled potential electrolysis of TPP under various conditions. Details of the procedure and identification of the products are described in the Experimental section.

Electrolysis of TPP in acetonitrile containing an excess of methanol gave $Ph_3P^+\text{-}OMe$ and Ph_3P^+H as major products, with small amounts of $Ph_3P^+\text{-}Me$ and Ph_3PO (run No. 1 in Table I). Essentially the same results were obtained on electrolysis in methanol (run No. 4). Since the

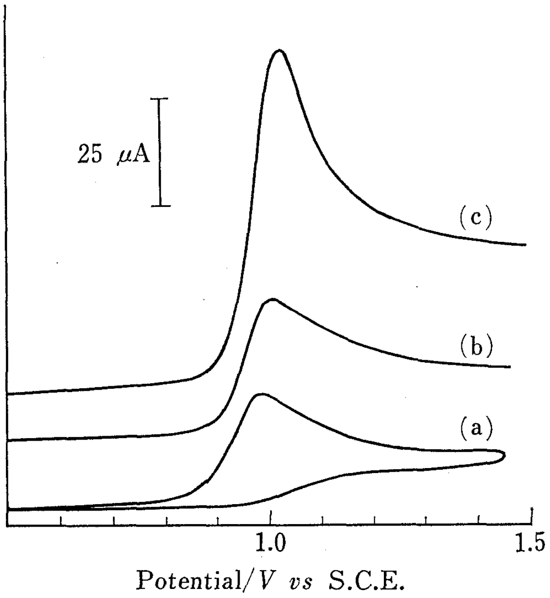

Fig. 1. Cyclic Voltammogram of TPP (5 mM)

(a) In acetonitrile, (b) in acetonitrile containing 1% methanol, and (c) in acetonitrile containing 1% methanol and 1% 2,6-lutidine; 0.1 M $NaClO_4$, at a glassy carbon electrode (area 0.071 cm^2), 0.05 V s^{-1}.

TABLE I. Results of Controlled Potential Electrolysis of TPP[a]

Run No.	Amount of TPP/mmol	Additives[b] (ml)	Applied potential[c]	n-Value	Products identified[d] (yield/%)[e]
1	2	MeOH(1)	1.00	1.26	YOMe(33), YMe(6), YH(32), PO(trace)
2	2	MeOH(1), Lut(0.4)	1.00	1.17	[f], YMe(26), PO(30)
3	2	MeOH(1), K_2CO_3(2 g)	1.15	1.18	YOMe(7), YMe(26), PO(37)
4	1.4[g]		1.05	1.00	YOMe(30), YMe(5), YH[h]
5	3.7[i]	EtOH(2)	1.05	1.30	YOEt(37), YH[h]
6	1.5	EtOH(1), Lut(0.4)	1.10	1.49	YOEt(46), PO[h]
7	1.5[j]		1.05	0.93	YOEt(38), YH[h]
8	1.5	Pr^nOH(1)	1.05	1.01	$YOPr^n$(31), YH[h]
9	1.6	Pr^nOH(1), Lut(0.4)	1.10	1.56	$YOPr^n$(49), PO[h]
10	4[i]	Bu^tOH(2)	1.10	0.71	[k], YBu^t(14), YH,[h] PO[h]
11	3.1[i]	Bu^tOH(2), Lut(0.8)	1.10	1.04	[f], YBu^t(29), PO(44)
12	3[i]	$PhCH_2OH$(1.2)	1.00	0.66	[f], YCH_2Ph(22), YH(28), PO(31)
13	2[i]	EtSH(1)	1.05	1.53	YSEt(34), YH[h]
14	1.5[i]	Me_2S_2(0.8)	0.92	1.22	YSMe(70)
15	1.5[i]	Et_2S_2(0.8)	0.87	0.88	YSEt(71)
16	1	$Pr^n_2S_2$(0.8)	0.95	0.82	$YSPr^n$(72)
17	3[i]	PhOH(2 g)	1.05	1.03	YOPh(28), YH[h]
18	1.5	2,6-Bu^t_2–C_6H_3OH(1 g)	0.95	0.94	YC_6H_2-3,5-Bu^t_2-4-OH(39), YH[h]

a) In acetonitrile (20 ml) containing 0.2 M $NaClO_4$ unless otherwise stated: an H-type electrolysis cell was used throughout, with a glassy carbon plate as the anode and a platinum foil as the cathode.
b) Lut=2,6-lutidine.
c) V *vs* S.C.E.
d) Y=Ph_3P^+-; PO=Ph_3PO.
e) Based on the isolated product after recrystallization: all phosphonium salts were isolated as perchlorates except for YH, which was isolated as TPP.
f) Formation of the corresponding alkoxyphosphonium ion was not detected.
g) In methanol (20 ml).
h) The yield was not determined.
i) In 40 ml of acetonitrile.
j) In ethanol (20 ml).
k) The presence of $YOBu^t$ was detected in the product mixture by PMR spectroscopy, but the amount was too small to be isolated.

voltammetric behavior of TPP in acetonitrile containing an excess of methanol (Fig. 1) is similar to that in acetonitrile containing an excess of benzene,[5] the following scheme can be suggested for Ph_3P^+-OMe formation by analogy with the anodic phenylation of TPP.[4]

$$\mathrm{Ph_3P} \xrightarrow{-e} \mathrm{Ph_3P^{+\cdot}} \xrightarrow[+\mathrm{MeOH},\ +\mathrm{Ph_3P}]{-e} \mathrm{Ph_3P^{+}\text{-}OMe} + \mathrm{Ph_3P^{+}H} \qquad (1)$$

It is not clear whether the proton transfer takes place before, after, or concurrently with the attack of methanol on the TPP cation radical. In any case, half of the starting TPP will be protonated, and the coulometric n-value amounts to unity.

Electrolysis of TPP in the presence of ethanol or n-propanol gave similar results, but the formation of the corresponding alkyl triphenylphosphonium ion (Ph_3P^+-R) and Ph_3PO was hardly detected (run Nos. 5, 7, and 8). On the other hand, on electrolysis with t-butanol Ph_3P^+-Bu^t was the major product (No. 10), and with benzyl alcohol formation of Ph_3P^+-OCH_2Ph was not detected at all (No. 12). Since Ph_3PO was always formed together with Ph_3P^+-R, reaction (2) can be suggested for their formation. Similar reactions of alkyl[7]

$$\mathrm{Ph_3P^{+}\text{-}OR} + \mathrm{Ph_3P} \longrightarrow \mathrm{Ph_3P^{+}\text{-}R} + \mathrm{Ph_3PO} \qquad (2)$$

and aryl trialkoxyphosphonium ions[1] with trialkylphosphites have been reported. Based on the results shown in Table I, the order of reactivity of Ph_3P^+-OR in reaction (2) is $R = PhCH_2 > Bu^t > Me > Et \sim Pr^n$, indicating that the reaction for Ph_3P^+-OCH_2Ph and Ph_3P^+-OBu^t probably proceeds by an S_N-1 type mechanism[10,11] while that for the other Ph_3P^+-OR salts may proceed by an S_N2-type mechanism.[10,12]

As described above, half of the starting TPP is protonated in the electrolysis. The effect of 2,6-lutidine on the cyclic voltammetry of TPP suggested that the base served as a proton acceptor in place of TPP. In the anodic oxidation of anthracene, 2,6-lutidine has been reported to act as an effective base but as a weak nucleophile because of the steric hindrance by the two methyl groups.[13] On electrolysis of TPP in the presence of the base, the yields of Ph_3P^+-OEt and Ph_3P^+-OPr^n increased (Nos. 6 and 9), but those of Ph_3P^+-OMe and Ph_3P^+-OBu^t decreased and the corresponding Ph_3P^+-R increased (Nos. 2 and 11). In all cases the coulometric n-values were considerably smaller than expected ($n=2$). These results suggest that in the presence of 2,6-lutidine some reaction (or reactions) of the starting TPP, probably to yield Ph_3PO, takes place in addition to reaction (2). Similar results were obtained when suspended potassium carbonate was used as a base (No. 3).

The formation of Ph_3P^+-SEt in the electrolysis of TPP in the presence of ethanethiol (No. 13) can be explained by a process similar to Scheme (1). The larger coulometric n-value (1.53) is probably due to the oxidation of a part of the thiol at the anode potential applied. On electrolysis with dialkyldisulfides the yields of the corresponding alkylthiophosphonium ions were almost doubled, and the n-values were approximately one (Nos. 14—16). Scheme (3) can be suggested for this process from the results described so far.

$$\mathrm{Ph_3P} \xrightarrow{-e} \mathrm{Ph_3P^{+\cdot}} \xrightarrow{+\mathrm{RSSR}} [\mathrm{Ph_3P\text{-}S(R)\text{-}SR}]^{+\cdot} \xrightarrow[+\mathrm{Ph_3P}]{-e} 2\,\mathrm{Ph_3P^{+}\text{-}SR} \qquad (3)$$

When no voltage was applied to the reactions, no products were formed over a period of two days, although formation of arylthiophosphonium ions has been suggested in the reactions of TPP and diaryldisulfides.[14]

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TABLE II. Alkylation of Organic Compounds Containing a Heteroatom with [Ph$_3$P$^+$-OR][ClO$_4^-$] in Acetonitrile[a)]

Run No.	Compound (mmol)	Phosphonium salt (mmol)	K$_2$CO$_3$ (g)	Amount of solvent/ml	Reaction time/min	Products (yield/%)[b)]
1	PhSH(0.67)	R=Me(1.34)	1	10	30	PhSMe(~100)
2	PhSH(0.76)	R=Et(1.52)	1	10	30	PhSEt(~100)
3	PhSH(0.82)	R=Pr^n(1.37)	1	10	30	PhSPr^n(~100)
4	Imidazole(1.07)	R=Me(1.79)	0.5	5	30	1-Me-imidazole(~100)
5	Imidazole(0.83)	R=Et(1.62)	0.5	5	30	1-Et-imidazole(~100)
6	EtSH(0.47)	R=Et(0.70)	0.5	5	30	Et$_2$S(86)
7	Pr^{n}SH(0.36)	R=Pr^n(0.49)	0.5	5	30	Pr$_2^n$S(27)
8	PhOH(0.79)	R=Me(1.23)	1	10	210	PhOMe(11)
9	PhOH(0.47)	R=Et(0.82)	0.5	5	180	PhOEt(6)
10	PhNH$_2$(0.92)	R=Me(0.91)	1	10	15	PhNHMe(21), PhNMe$_2$(8)
					30	PhNHMe(16), PhNMe$_2$(17)
11	PhNH$_2$(0.52)	R=Me(1.58)	0.5	5	15	PhNHMe(19), PhNMe$_2$(20)
					30	PhNHMe(55), PhNMe$_2$(31)
					45	PhNHMe(60), PhNMe$_2$(31)
12	PhNHMe(0.52)	R=Me(0.87)	0.5	5	15	PhNMe$_2$(35)

a) Reactions were carried out at room temperature, and no attempt was made to determine optimum conditions.

b) Determined by GLC: PEG 20 M was used as packing for run Nos. 1—3, 6, and 8—12, and silicon DC 550 for the other runs.

The attack of the TPP cation radical on phenol occurred at the oxygen atom (No. 17), whereas with 2,6-di-*t*-butylphenol the attack occurred at the ring *para* to the hydroxy group (No. 18). The latter result may be due to the steric hindrance of the *t*-butyl groups, and supports the possible formation of various phosphonium ions from the TPP cation radical.

Alkylation with Alkoxy Triphenylphosphonium Ions

Table II summarizes the preliminary results on the reaction of Ph$_3$P$^+$-OR salts with various nucleophiles. Alkylation of thiophenol and of imidazole proceeded quantitatively under mild conditions. The phosphonium salts can also be used for the alkylation of thiols. The reactions with phenol were less effective. With aniline, mono- and di-alkylated products were formed. In contrast to Ph$_3$P$^+$-OR salts, the reactivity of Ph$_3$P$^+$-SR salts was very low: a mixture of Ph$_3$P$^+$-SEt and PhSH did not give PhSEt after being kept at 100° in a sealed tube for 5 hr.

The present investigation suggests that the alkoxy phosphonium salts which decompose by an S_N2-type mechanism can be isolated, and that they represent potentially useful alkylating agents. *N*-Alkylation of imidazole with trialkylphosphates[15)] or dialkylphosphites,[16)] and *S*-alkylation of thiophenol with tris(dimethylamino)alkoxyphosphonium salts[17)] have been reported. Alkylation with Ph$_3$P$^+$-OR salts can be compared to these procedures. For the preparation of the phosphonium salts, however, rather troublesome controlled potential electrolysis is required at present, and half of the starting TPP is protonated. Studies on the modification of the electrochemical method to overcome these defects together with studies on the further application of the phosphonium salts are in progress.

Experimental

Materials——TPP was recrystallized from *n*-hexane and stored under reduced pressure. Sodium perchlorate and acetonitrile were purified as described previously.[3)] Primary alcohols and aniline were

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purified by conventional methods. Phenylethylsulfide and phenylpropylsulfide, used for comparison in identifying the alkylation products, were prepared by a known method.[18] All other chemicals were of reagent grade and were used without further purification.

Apparatus——Cyclic voltammetry and controlled potential electrolysis were carried out as described previously.[19] For the latter electrolysis a glassy carbon plate was used for the anode and a platinum foil for the cathode. IR and PMR spectra were obtained using Hitachi EPI-2 and R-20A spectrometers, respectively. GLC was carried out using a Nihondenshi JGC-20K gas chromatograph connected with a Takeda Riken TR-2215A digital integrator.

Controlled Potential Electrolysis and Isolation of Products——Typical examples of the procedures are described below.

(a) Electrolysis in Acetonitrile containing an Excess of Methanol: TPP (524.6 mg) was subjected to electrolysis in acetonitrile (20 ml) containing methanol (1 ml) and 0.2 M $NaClO_4$ at 1.0 V until the current became $<2\%$ of the initial value (*ca.* 380 min). From the current-time curve 243.9C, which corresponded to $n=1.26$, was found to have been consumed. The electrolysis solution showed no voltammetric peak due to TPP, but on work-up (see below) 32% of the starting TPP was recovered, indicating that protonated TPP had been formed on electrolysis. The solution from electrolysis was evapolated to dryness under reduced pressure and the residue was extracted with chloroform (3×20 ml). The chloroform was removed under reduced pressure. PMR spectra of the residue suggested that Ph_3P^+–OMe and Ph_3P^+–Me were present in a ratio of *ca.* 11 : 2, as estimated from the signals due to the P^+–OMe and P^+–Me protons. The crude product mixture was separated by column chromatography on silica gel with chloroform–methanol, first in a ratio of 50 : 1 and then 20 : 1. The following compounds were obtained and were identified by elemental analysis and/or IR and PMR spectroscopy: $[Ph_3P^+\text{–OMe}][ClO_4^-]$, 256 mg after recrystallization from methanol–

TABLE III. Physical and PMR Data for $[Ph_3P^+\text{–X}][ClO_4^-]$

X	mp (°C)	Analysis (%) Found (Calcd)				PMR δ ($CDCl_3$)[a]
		C	H	P	Cl	
OMe	118	58.22 (58.10	4.41 4.62	7.83 7.89	8.76 9.03)	4.11 (3H, d, $J=12$ Hz), 7.59—8.02 (15H, m)
Me	163	60.03 (60.57	4.53 4.81	8.11 8.22	9.07 9.41)	2.90 (3H, d, $J=13.2$ Hz), 7.48—8.01 (15H, m)
OEt	149—150	58.95 (59.05	4.78 4.96	7.83 7.61	8.92 8.71)	1.51 (3H, t, $J=7.5$ Hz), 4.41 (2H, quint, $J_{HH}=J_{PH}=7$ Hz), 7.52—8.07 (15H, m)
OPr^n	153—154	59.70 (59.94	5.23 5.27	7.58 7.36	8.68 8.42)	0.99 (3H, t, $J=7$ Hz), 1.52—2.22 (2H, m), 4.27 (2H, quart, $J_{HH}=J_{PH}=7$ Hz), 7.35—7.97 (15H, m)
OBu^t	—	—	—	—	—	2.35 (9H, s), 7.25—7.88 (15H, m)
Bu^t	192—194	61.82 (63.09	5.18 5.78	7.54 7.39	8.00 8.46)	1.33 (9H, d, $J=8$ Hz), 7.25—7.88 (15H, m)
CH_2Ph	239	65.35 (66.30	4.90 4.90	6.88 6.84	7.94 7.83)	4.65 (2H, d, $J=15$ Hz), 7.30—7.88 (20H, m)
OPh	>290	62.95 (63.38	4.45 4.43	7.01 6.81	7.79 7.79)	7.50—7.98 (20H, m)
3,5-Bu^t_2-4-OH-C_6H_2	275—276	68.01 (67.78	6.48 6.40	5.65 5.46	6.42 6.25)	1.38 (18H, s), 6.13 (1H, s), 7.35—7.95 (17H, m)
SMe	139	55.01 (55.82	4.28 4.44)			2.47 (3H, d, $J=15.2$ Hz), 7.48—7.98 (15H, m)
SEt	192	56.43 (56.81	4.77 4.77)			1.32 (3H, t, $J=7.5$ Hz), 2.65—3.27 (2H, qualt × d, $J_{HH}=7.5$ Hz, $J_{PH}=11$ Hz), 7.45—7.98 (15H, m)
SPr^n	169	56.97 (57.73	5.11 5.08)			0.97 (3H, t, $J=7$ Hz), 1.35—1.92 (2H, m), 2.62—3.15 (2H, m), 7.52—7.89 (15H, m)

[a] The PMR spectra (60 MHz) were recorded with Me_4Si as an internal standard.

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ether, as colorless crystals; $[Ph_3P^+–Me][ClO_4^-]$, 45 mg after recrystallization from methanol–ether, as colorless crystals; TPP, 167 mg after recrystallization from *n*-hexane; a small amount of Ph_3PO.

The other alkoxy and alkyl triphenylphosphonium perchlorates listed in Table I were obtained by similar work-up. Their physical and spectroscopic data are summarized in Table III.

(b) Electrolysis in the Presence of Dimethyl Disulfide: TPP (393.4 mg) was subjected to electrolysis in acetonitrile (40 ml) containing dimethyl disulfide (0.8 ml) and 0.2 M $NaClO_4$ at 0.92 V as described in (a). The electrolysis solution was evaporated to dryness under reduced pressure and the residue was extracted with chloroform (3 × 20 ml). The chloroform was removed under reduced pressure and the residue was recrystallized twice from methanol–ether to give $[Ph_3P^+–SMe][ClO_4^-]$ as colorless crystals (428 mg). The physical and spectroscopic data are listed in Table III.

General Procedure for Alkylation with Alkoxy Triphenylphosphonium Salts——A mixture of the phosphonium salt, the organic compound to be alkylated, and potassium carbonate in 10 ml of acetonitrile (the amounts of the components are listed in Table II) was stirred at room temperature in a 30-ml round-bottomed flask with a glass stopper. After the time cited in Table II, the mixture was analyzed by GLC. Authentic compounds were used to identify the alkylation products by comparison.

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