# Electrochemistry of Phosphorus and Sulfur Compounds: A Unique Tool for Organic Synthesis

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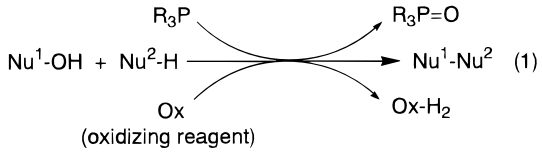
## Introduction

Organophosphorus compounds play an important role in synthetic organic chemistry. Their reactions may be divided into three categories: deoxygenation and desulfurization,[1,2] olefination,[1,3] and molecular transformation via the formation of phosphonium salts.[1,4] From the viewpoint of electrochemistry, the last reaction is the most intriguing. Molecular transformations, e.g., dehydroxy substitution reactions of alcohols and condensations of carboxylic acids with alcohols or amines, are induced by oxidation of phosphorus compounds from trivalent to pentavalent states via phosphonium salts in the presence of compounds such as halogens, carbon tetrachloride, disulfides, and azodicarboxylates. These additives behave as oxidizing reagents, which are reduced by trivalent phosphorus compounds. Thus, this process is occasionally referred to as "oxidation−reduction condensation" (cf. eq 1).[4b] On the basis of the reaction scheme, an anode serves

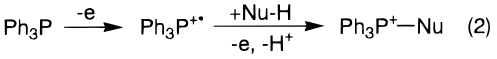



as an alternative to these reagents in the functional group conversions via phosphonium salts. The transformations under chemical conditions are always accompanied by conversion of oxidizing reagents into their reduction products, some of which behave as nucleophilic species to be incorporated into intermediates or final products; the others are regarded merely as byproducts. In contrast, oxidation of trivalent phosphorus compounds at an anode is believed to include only an electron-transfer reaction. Accordingly, oxidation−reduction condensation under electrochemical conditions appears to be simpler not only operationally but also chemically. In addition, the chemical simplicity might allow electrochemically generated phosphonium salts to enter reaction pathways totally different from those under common chemical conditions.

On the basis of these possibilities, since the late 1970s, we have been investigating the use of anodic oxidation of trivalent phosphorus compounds as a novel tool for molecular transformations. To date, only a limited number of studies have been performed by other groups on anodic oxidation of the phosphorus compounds from synthetic standpoints. This Account outlines and discusses our studies of the electrochemistry of phosphorus compounds as a synthetic tool. We also briefly describe some electrochemical reactions of sulfur compounds as synthetic tools developed by other groups, to provide a comparison of the results obtained for phosphorus and sulfur compounds. This will allow the readers to consider not only the synthetic but also mechanistic aspects of the electrochemistry of these compounds.

## Electrochemistry of Phosphorus Compounds

$Ph_3P$ exhibits an anodic peak at approximately 1 V against a saturated calomel electrode (SCE) in $CH_3CN$.[5,6] Cyclic voltammetry in $CH_3CN$ reveals an anodic wave due to oxidation of $Bu_3P$ at a similar potential.[7] Anodic oxidation of $(RO)_3P$ requires a more positive potential than that of $Ph_3P$ and $Bu_3P$,[8a,9] whereas $(R_2N)_3P$ undergoes an electrochemical reaction at an anodic potential similar to that of phosphines.[10] To the best of our knowledge, there has been only one reported example of electrochemical oxidation of pentavalent phosphorus compounds.[11] Anodic oxidation of $Ph_3P$ in the presence of primary amines[12] and aromatic compounds[5,8] yields alkylamino and aryl phosphonium salts, respectively. The formation of these salts is initiated by the attack of the nucleophiles (Nu-H) on $Ph_3P^{\bullet+}$ generated by one-electron oxidation of $Ph_3P$ (eq 2). These results suggest that the high activity of $Ph_3P^{\bullet+}$




enables a reaction with even a weak nucleophile such as benzene. Although good nucleophiles such as primary amines are usually susceptible to anodic oxidation, the less positive oxidation potential of $Ph_3P$ appears to allow the formation of phosphonium salts from amines via eq 2. Therefore, we reasoned that a wide range of compounds can be utilized as nucleophiles in electrochemical reactions initiated by selective anodic oxidation of $R_3P$. Thus, we investigated the electrochemical preparation and

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Hidenobu Ohmori was born near Kobe, Japan, in 1938. He spent almost all of his life at Osaka University after he began undergraduate study at the Faculty of Pharmaceutical Sciences: B.Sc., 1961; Ph.D., 1969. He was appointed Research Associate in 1966, spent a postdoctoral year at UCSC (Professor J. F. Bunnett) from 1972 to 1973, became Associate Professor in 1974, and was promoted to Full Professor in 1991. He is now working in cooperation with Dr. Maeda.



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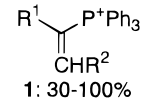
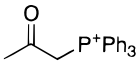
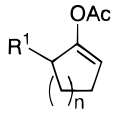
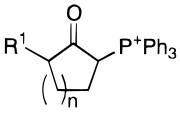
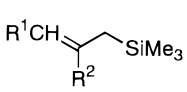
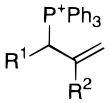
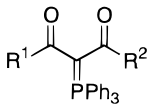
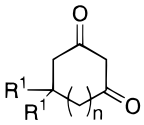
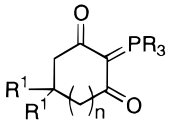
**Table 1. Preparation of Phosphonium Salts and Phosphoranes by Anodic Oxidation of $Ph_3P$ or $Bu_3P$ in the Presence of Nucleophiles (Nu-X) (cf. Eq 3)**

| Nu-X | products[a] | chemical method |
|---|---|---|
| $R^1CH{=}CHR^2$ |  **1**: 30-100% | ref. 13 |
|  |  **2**: 94% | ref. 14 |
|  |  **3**: 53-94% | ref. 15 |
|  |  **4**: 24-71% | ref. 16 |
| $R^1COCH_2COR^2$ |  **5**: 30-100% | ref. 17 |
|  |  **6**: R=Ph 35-94% **7**: R=Bu 58-70% | - |
| $R^1OH$ | $Ph_3P^+{-}OR^1$ **8**: 49-100% | ref. 18 |
| $R^1SSR^1$ | $R_3P^+{-}SR^1$ **9**: R=Ph 48-94% **10**: R=Bu 25-57% | ref. 19 |

[a] Counteranion of phosphonium salts is $ClO_4^-$ or $BF_4^-$.

synthetic reactions of phosphonium salts derived not only from $Ph_3P$ but also from $Bu_3P$.

**Preparation of Phosphonium Ions.** Table 1 shows the results of reactions of $R_3P^{\bullet+}$ (R = Ph or Bu) with various nucleophiles (Nu-X), leading to the formation of phosphonium salts or phosphoranes. Nonelectrochemical preparation of most salts in Table 1 generally includes multistep sequences or methods using rather ill-behaving, expensive reagents. Thus, only the electrochemical technique, involving *umpolung*[20] of $R_3P$ into $R_3P^{\bullet+}$, provides an effective and simple route to phosphonium salt formation. In general, electrochemical preparation of the salts is a two-electron oxidation process (eq 3). The electrochemical reactions are theoretically completed by passing 2 faradays/mol of electricity through $R_3P$. Except for a few cases, $CH_2Cl_2$ is used as a solvent for the electrochemical formation of phosphonium salts. Electrolysis is performed at a constant current in an undivided cell, which is important from a practical point of view. The key to success in performing electrolysis in an undivided cell is employing 2,6- and 3,5-lutidinium salt ($Lut^+H{\cdot}Y^-$: Y = $ClO_4$ or $BF_4$) as supporting electrolytes. The electrolytes are predominantly reduced at the cathode during electrolysis (eq 4), which prevents phosphonium salts from entering an in situ cathodic process. The cathodic reduction of $Lut^+H{\cdot}Y^-$ generates lutidine. The base scavenges $X^+$ liberated from Nu-X in the formation of phosphonium salts (eq 3), hence accelerating the anodic process. In electrolysis with an undivided cell, 2 equiv of the base against $X^+$ is always produced (eq 5). Excess base should

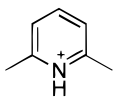
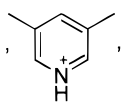
**Anodic process:**

$$R_3P \xrightarrow{-e} R_3P^{\bullet+} \xrightarrow[-e]{Nu\text{-}X} [\,R_3P{-}Nu\text{-}X\,]^{2+} \longrightarrow R_3P^+\text{-}Nu + X^+ \quad (3)$$

(X=leaving group: H, $SiMe_3$, Ac)

**Cathodic process:**

$$2\ B\text{-}H \xrightarrow{+2e} 2\ B + H_2 \quad (4)$$

(B-H:  ,  , $Ph_3P^+H$)

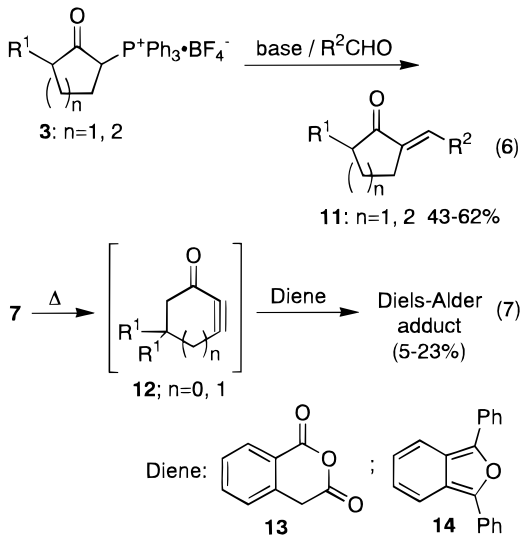
**Overall process:**

$$R_3P + Nu\text{-}X + 2\ B\text{-}H \longrightarrow R_3P^+\text{-}Nu + B + B\text{-}X + H_2 \quad (5)$$

be avoided when phosphonium salts are susceptible to base-catalyzed decomposition. For preparation of phosphonium salts unstable under basic conditions, electrolysis with $Ph_3P$ and $Ph_3P^+H{\cdot}Y^-$ (Y = $ClO_4$ or $BF_4$) is greatly advantageous. $Ph_3P^+H{\cdot}Y^-$ is reduced preferentially at the cathode, to prevent phosphonium salts from undergoing undesirable reactions, and this cathodic reduction generates $Ph_3P$. Hence, the electrolysis solution with a $Ph_3P{-}Ph_3P^+H{\cdot}Y^-$ system is maintained weakly acidic during electrolysis. We have established a methodology for electrochemical preparation of phosphonium salts as synthetic building blocks by examining and taking full advantage of the electrochemical behavior of supporting electrolytes as well as $R_3P$.

Olefins such as ethylene, cycloalkenes, and styrene react smoothly with $Ph_3P^{\bullet+}$, yielding **1** (Table 1).[21] The salts are useful building blocks for the synthesis of carbocyclic and heterocyclic compounds.[1,22,23] A recent study reported that $(RO)_3P^{\bullet+}$ anodically generated from $(RO)_3P$ undergoes similar nucleophilic reactions with simple alkenes, affording alkenyl phosphonates.[24] Acyclic and cyclic enol acetates were also found to react with $Ph_3P^{\bullet+}$, affording **2** and **3**, respectively.[25] For the electrochemical preparation of **1**−**3**, 2,6-$Lut^+H{\cdot}Y^-$ (Y = $ClO_4$ or $BF_4$) is the supporting electrolyte of choice. When **3** with $BF_4^-$ as a counteranion was subjected to the Wittig reaction with aldehydes, **11** was obtained (eq 6),[25] indicating that $BF_4^-$ and $ClO_4^-$ as a counteranion for **1**−**3** do not cause problems in these synthetic applications.

Allyl silanes are relatively susceptible to electrochemical oxidation.[26] However, anodic oxidation of $Ph_3P$ has been shown to prevail over that of the silyl compounds in electrolysis, yielding **4** through the exclusive formation of

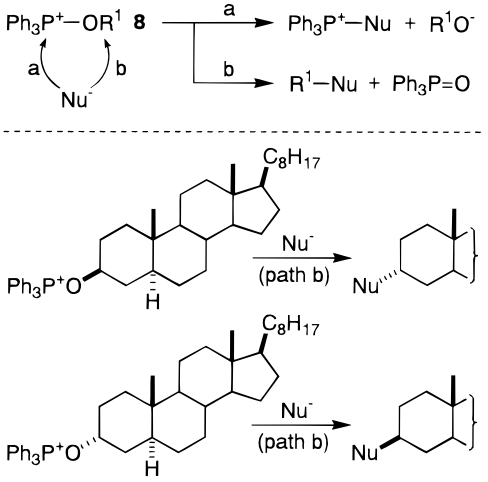



C−P bonds at the $\gamma$-position of the nucleophiles.[27] In the electrolysis, 3,5-Lut$^{+}$·$BF_4^-$ is the supporting electrolyte of choice over 2,6-Lut$^{\bullet+}BF_4^-$. Addition of allyl silanes to $Ph_3P^{\bullet+}$ appears to proceed more effectively in the presence of cathodically generated 3,5-lutidine rather than 2,6-lutidine. This is probably because 3,5-lutidine can scavenge the trimethylsilyl group more effectively than 2,6-lutidine (cf. eqs 3 and 4). 1,3-Dicarbonyl compounds were expected to work as not only carbon nucleophiles but also oxygen nucleophiles against $R_3P^{\bullet+}$. However, formation of **5**−**7** was observed exclusively, implying that $R_3P^{\bullet+}$ behaves as a soft electrophile which reacts with a double bond rather than a hydroxy group in the enol form of a 1,3-dicarbonyl compound.[28,29] The phosphoranes were afforded through deprotonation of the initially formed phosphonium salts by cathodically generated 2,6-lutidine. Contrary to the observation that thermal decomposition of $Ph_3P{=}C(R)COR'$ affords acyclic alkynes,[28,30] the thermolysis of **6** failed to generate cyclic alkynones. However, **7** with five- and six-membered rings could thermally decompose into **12**. The fleeting species was trapped by dienes such as **13** and **14** in the presence of trimethylsilyl chloride, giving Diels−Alder adduct albeit in low yield (eq 7).[29]

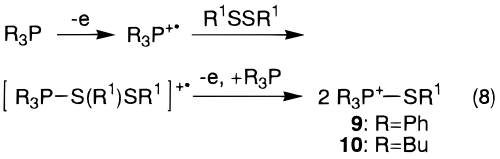
The electrochemical reaction of $R_3P$ in the presence of oxygen and sulfur nucleophiles such as alcohols and disulfides was found to afford the corresponding alkoxy and thioalkoxy phosphonium salts **8**−**10**. The formation of **8** is effectively achieved by electrolysis with $Ph_3P$ and $Ph_3P^+H{\cdot}Y^-$ (Y = $ClO_4$ or $BF_4$).[31] Electrolysis in $CH_3CN$ containing $Ph_3P$, a disulfide, and $HClO_4$ (70%) was useful for the synthesis of **9**.[7] The preparation of **10** was achieved by electrolysis of a $CH_3CN$ solution of $Bu_3P$, a disulfide, and anhydrous HY (Y = $ClO_4$ or $BF_4$).[7] The formation of **9** and **10** is an apparent one-electron oxidation process as depicted in eq 8. Thus, only 1 faraday/mol of electricity was passed in the electrochemical formation of **9** and **10**.

The reaction of **8** prepared from $\beta$- and α-cholestanol with various nucleophiles was examined. The results indicated that the reaction site of the phosphonium ions is dictated by the identity of the nucleophiles (Scheme

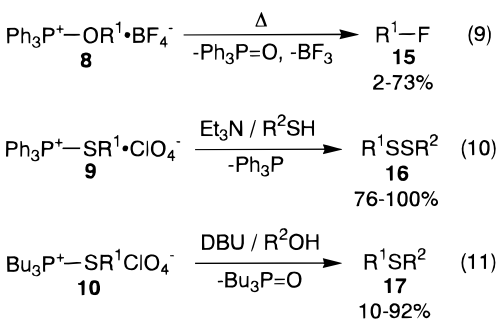
**Scheme 1**




1). Soft nucleophiles such as $Br^-$, $Cl^-$, $SCN^-$, and PhSH were apt to attack at the α-carbon, giving the correspond-

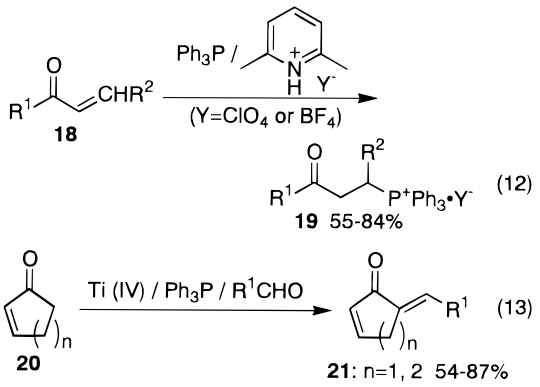



ing $S_N2$ reaction product (path b), while hard nucleophiles such as $F^-$, $N_3^-$, and PhOH tended to react at the phosphorus of **8**, leading to the regeneration of the cholestanol (path a).[31] In addition, the thermal decomposition of **8** with $BF_4^-$ as a counteranion by refluxing in THF or dioxane, affording alkyl fluoride **15**, was an interesting finding (eq 9).[32] In the thermal reactions, a fluorine atom arising from $BF_4^-$ attacks the carbon α to the oxygen atom in the salt from the side opposite to the oxy phosphonium moiety via an $S_N2$ mechanism. The transformation could be performed without the isolation of **8**. Thus, the dehydroxyfluorination of secondary and primary alcohols could be achieved by the electrochemical formation of **8** followed by thermal reaction of the residue obtained simply by evaporation of the solvent from the electrolyte. Fluorination with $BF_4^-$ as a fluoride source is interesting from the standpoint of synthetic organic chemistry, since such reactions do not involve the generation of dangerous HF, and hence the fluorination can be performed under mild conditions in normal laboratory glassware with few or no precautions.[33,34]



A unique characteristic of **9** was demonstrated by the formation of the unsymmetrical disulfides **16** in the reaction with a thiol in the presence of $Et_3N$ at room temperature (eq 10).[35] In general, the driving force in molecular transformations via phosphonium salts is the formation of a P═O or P═S bond due to the strong affinity of phosphorus atom for oxygen and sulfur atoms.[1,4] However, $Ph_3P$ was recovered in the synthesis of **16**, demonstrating the unusual reactivity of **9**. According to the observed chemistry of chemically prepared $Bu_3P^+$–SMe,[19b] various unsymmetrical sulfides **17** can be prepared by the reaction of **10** with alcohols in the presence of DBU (eq 11).[7] Accordingly, using the electrochemical technique has established novel routes for the formation of **16** and **17** from symmetrical disulfides with thiols and alcohols, respectively.

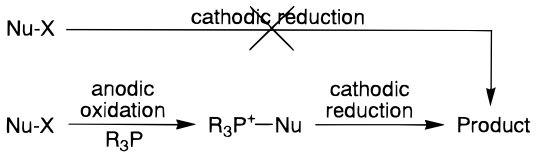
The addition of $Ph_3P^{\bullet+}$ to electron-poor olefins such as enones was unsuccessful. However, 2,6-$Lut^+H{\cdot}Y^-$ (Y = $ClO_4$ or $BF_4$) as a proton source induces nonelectrochemical 1,4-addition of $Ph_3P$ to enone **18**, affording adduct **19** (eq 12).[36] Lewis acids exhibit a similar effect. When cycloalkenone **20** was treated with an aldehyde in the presence of $Ph_3P$ and $TiCl_4$/Ti(OPr-*i*)$_4$, α-alkylidenecycloalkenone **21** was obtained (eq 13).[37] The highly




regioselective condensation can be explained as follows: α-enolate initially formed by 1,4-addition of $Ph_3P$ is in equilibrium with α′-enolate. Aldol condensation with an aldehyde takes place preferentially with the α′-enolate probably because the reaction of the α-enolate is sterically hindered by the phosphonium moiety at the *β*-carbon.

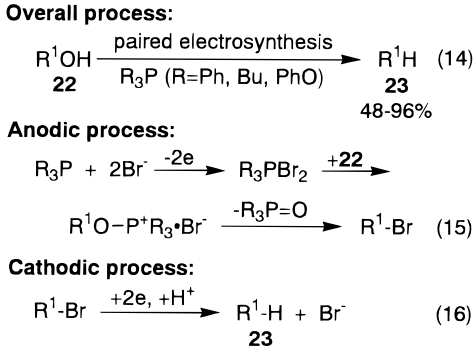
**Paired Electrosynthesis.** In most common electrolyses, the reaction at the counterelectrode is sacrificed. "Paired electrosynthesis" was coined by M. M. Baizer to refer to electrochemical reactions in which both cathodic and anodic reactions contribute usefully to the formation of the final products.[38] Paired electrosynthesis has drawn great attention because common organic reactions are unable to realize a process consisting simultaneously of oxidation and reduction; that is, the electrolysis takes full advantage of the advantages of electrochemistry in which the reaction vessel contains both a cathode (reducing) and an anode (oxidizing). In this section, we describe paired electrosynthesis on the basis of the strategy outlined in Scheme 2: a difficult to reduce compound such as a nucleophilic species is anodically transformed into a

**Scheme 2**



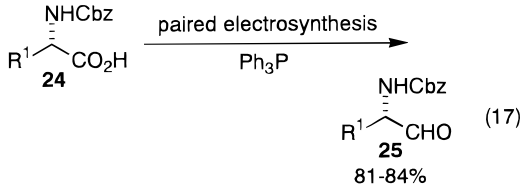

phosphonium salt, which is an activated form of the substrate for subsequent cathodic reaction. Hence, paired electrosynthesis with an undivided cell allows a nucleophile to be reduced in situ at a cathode through anodic *umpolung* to the corresponding electrophilic phosphonium salt (Scheme 2).

Paired electrosynthesis in $CH_3CN$ containing $R_3P$ (R = Ph, Bu, or PhO) and $Et_4NBr$ was found to achieve one-step deoxygenation of alcohols **22**, except aliphatic tertiary alcohols, into alkanes **23** without any tedious derivatization, simply by appropriate selection of R in $R_3P$ (eq 14).[39] The detailed mechanism of the transformation is not clear at present. However, it is likely that the reaction of anodically generated $R_3PBr_2$ with **22** forms an alkyl bromide, which is in turn reduced at the cathode to **23** (eqs 15 and 16).

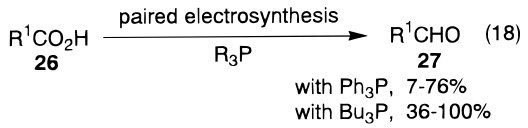



Carboxylic acids were also shown to undergo paired electrosynthesis in $CH_2Cl_2$ containing $Ph_3P$ and $Ph_3P^+H{\cdot}ClO_4^-$. Electrolysis at −30 °C is appropriate for partial reduction of *N*-Cbz-L-α-amino acids **24** to amino aldehydes **25** with little or no racemization (eq 17).[40] Over-reduction to amino alcohols did not occur during this transformation. Partial reduction of carboxylic acids **26** with $R^1$ = aryl and primary alkyl groups into aldehydes **27** proceeded smoothly under the same electrochemical conditions (eq 18).[41] In the case of **26** with $R^1$ = secondary alkyl groups, the transformation could be achieved by electrolysis under reflux, and with $R^1$ = *tert*-butyl, the aldehyde was obtained only in poor yield even under vigorous conditions. The mechanism depicted in eqs 19 and 21 is proposed on the basis of the voltammetric results of the anolyte in electrolysis of $Ph_3P$ and various forms of **26** in a divided cell. Anodic oxidation yields an acyloxy phosphonium ion **28**,[42] which reacts with another $Ph_3P$, leading to the formation of acyl phosphonium ion **29**; reduction to ylide **30** at the cathode followed by protonation provides phosphonium ion **31** as a final product in the electrolysis. Compound **31** decomposes into **27** through aqueous workup after electrolysis. A slow trans-

**Overall process:**

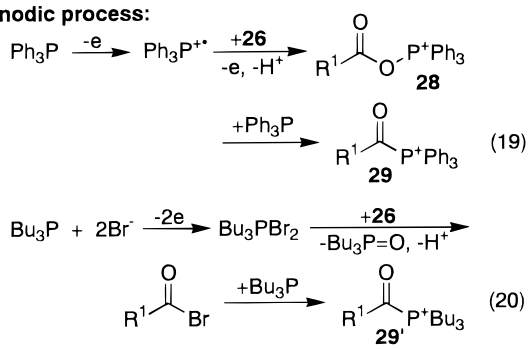



(17)




(18)

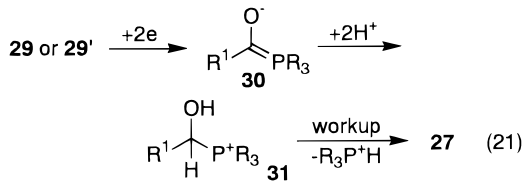
**Anodic process:**




(19)

(20)

**Cathodic process:**

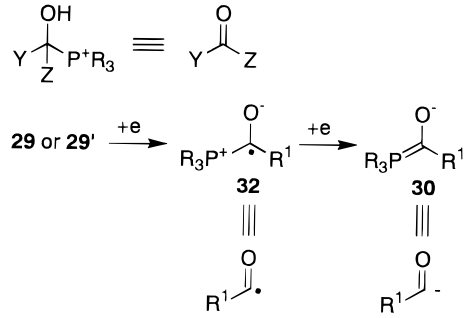



(21)

formation of **28** into **29** due to the weak nucleophilicity of $Ph_3P$ may be responsible for the unsatisfactory results in the cases of secondary aliphatic **26** and pivalic acid. This problem was solved by introducing a phosphine with a higher nucleophilicity than $Ph_3P$. As a result, effective electrochemical partial reduction of various forms of **26** into **27** was achieved even at room temperature when $Bu_3P$ was used instead of $Ph_3P$ (eq 18).[43] In the electrolysis, $Bu_4NBr$ and $CH_3SO_3H$ were used as a supporting electrolyte and a proton source, respectively. For electrolysis with $Bu_3P$ and $Bu_4NBr$, an anodic process appears to occur through oxidation of $Br^-$, leading to the generation of $Bu_3PBr_2$ (eq 20). Through the formation of an acid bromide by the bromination reagent, **29′** is generated, and the phosphonium ion enters a similar cathodic reaction, affording **31** (eq 21). Workup with aqueous $K_2CO_3$ is required to generate **27** from **31** with R = Bu.

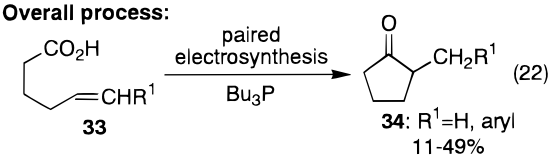
On the basis of the proposed mechanism in eqs 19−21 as well as the finding that the α-hydroxymethyl phosphonium moiety is equivalent to a carbonyl group, we expected the generation of novel acyl radical and acyl anion equivalents such as **32** and **30**, respectively, in Scheme 3 would proceed directly from a carboxyl group by paired electrosynthesis. When electrolysis with $Bu_3P$, $Bu_4NBr$, and $CH_3SO_3H$ was carried out for **33** ($R^1$ = H, aryl), **34** was obtained in a reasonable yield (eq 22).[44] Cyclization could be more effectively achieved when the internal olefin contained a phenyl group with an electron-withdrawing substituent. These results suggest that **32**

**Scheme 3**



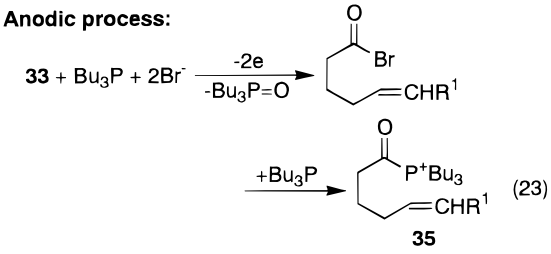

with R = Bu (Scheme 3) is nucleophilic in nature. The formation of a six-membered ring system by the electrolysis for 6-heptenoic acids failed. As in the partial reduction of carboxyl groups, anodic process generates acyl phosphonium ion **35** (eq 23). The key intermediate is cathodically reduced to a neutral radical **36**, which undergoes intramolecular cyclization, leading to the formation of **37** (eq 24). Workup with aqueous $K_2CO_3$ is required to obtain **34** after electrolysis, which will rule out the possibility that an acyl radical itself is generated from **36** and then cyclizes to the double bond to give **34**.

**Overall process:**



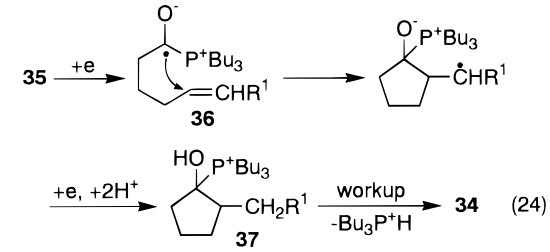

(22)

**Anodic process:**




(23)

**Cathodic process:**



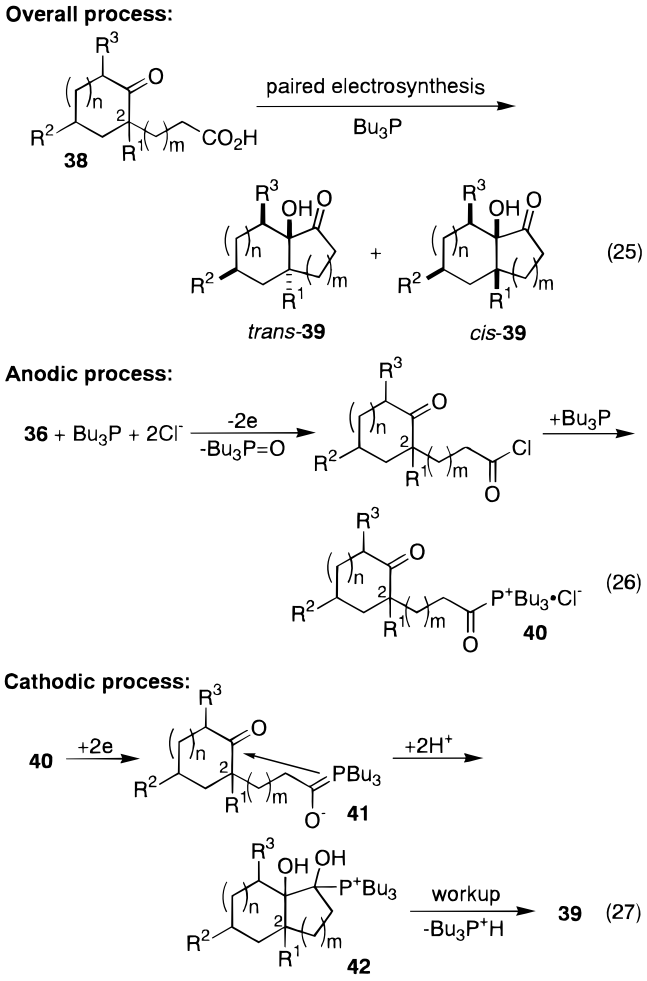

(24)

The paired electrosynthesis with $Bu_3P$ has also proven to be useful for the generation of novel acyl anion equivalents from free carboxyl groups.[45,46] Electrolysis with $Bu_3P$, $PhCH_2(Et)_3NCl$, and $CH_3SO_3H$ induced the formation of bicyclo[*n*.*m*.0] skeletons with $m = 1$ or 2 from cyclic $\delta$- or $\epsilon$-keto acids **38** (eq 25). Although the chloride salt was used as a supporting electrolyte in the transformation, the anodic process generates acyl phosphonium ion **40** through a reaction scheme similar to the case of the above-mentioned partial reduction and radical cyclization (eq 26). Two-electron reduction of **40** will give ylide **41**, which cyclizes to internal carbonyl group, giving

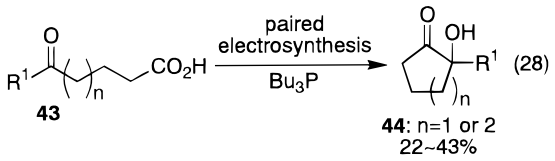
**Table 2. Transformation of Cyclic Keto Acids (38) to Bicyclo α-Ketols (39) by Paired Electrosynthesis in the Presence of $Bu_3P$**

| | 38 | | | | | yield of **39** (%) |
|---|---|---|---|---|---|---|
| entry | $R^1$ | $R^2$ | $R^3$ | *n* | *m* | (*trans*/*cis*) |
| 1 | H | H | H | >0 | 1 or 2 | 44−73 (1.4−6.7) |
| 2 | H | H | H | 0 | 1 | 29 (only *cis*) |
| 3 | Me | H | H | 0 | 1 | 50 (only *cis*) |
| 4 | Me | H | H | 1 | 1 | 44 (only *cis*) |
| 5 | H | *t*-Bu | H | 1 | 1 | 54 (10) |
| 6 | H | H | Me | 1 | 1 | 58 (9) |

**42** (eq 27). Deprotection of **42** to **39** is also achieved by



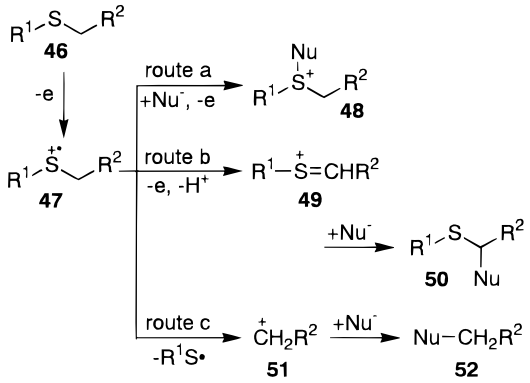

aqueous basic workup, indicating that generation of an acyl anion itself from **41** will not be involved in the transformation. The electrochemical formation of the bicyclic products showed a strong preference for *trans*-**39** over *cis*-**39** except for the cyclization on a cyclopentanone moiety (Table 2, entries 1 and 2). Electrolysis is also applicable to acyclic keto acids. The δ- and ϵ-keto alkanoic acids **43** were transformed into α-hydroxy cyclopentanones and cyclohexanones **44** in a reasonable yield (eq 28). Attempts to prepare four- and seven-membered ring carbocycles were unsuccessful. The effects of substituents in **38** upon the transformation were also investigated (Table 2).[46] Putting a methyl group at the C2 position in **38** induced the selective formation of the *cis*-fused bicyclo[4.3.0] skeleton (entry 4), and improved the



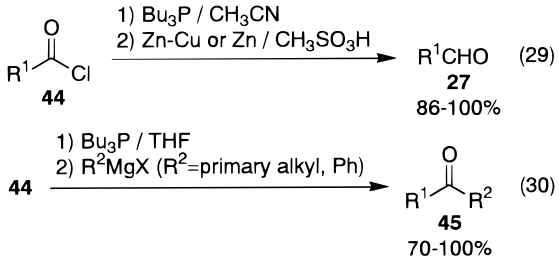

yield of *cis*-**39** with a bicyclo[3.3.0] skeleton (entry 3). In the case of **38** with an alkyl substituent at the C4 or C6 position, the corresponding products were afforded as a mixture of only two isomers, although the products were expected to consist of four isomers. Furthermore, high selectivity toward *trans*-**39** was retained in the formation of a bicyclo[4.3.0] system (entries 5 and 6). On the basis of these results, the setereochemical outcome of the present transformation of **38** into bicyclo[4.3.0]nonanones appears to be dictated primarily by the conformational bias in the starting acids. In particular, the conformational preference appears to be reflected in the stereochemistry of the product, where *trans*-**39** is formed from intermediates having the ylide moiety equatorial, whereas the nucleophilic site in the axial position results in the formation of *cis*-**39**. The process leading to the formation of *trans*-**39** is only disturbed by putting a methyl group at C2. Such a substituent will sterically hinder the approach of the nucleophilic ylide in the equatorial position to the carbonyl group, inducing the predominant formation of *cis*-**39**. Although various acyl anion equivalents have been developed and are well recognized as useful synthons for the direct introduction of a carbonyl moiety,[47] application of these equivalents to C−C bond formation is limited to intermolecular reactions. This is due to the difficulty in generating an acyl anion equivalent when an electrophilic site such as a carbonyl group exists in the same molecule. Thus, our methodology offers a novel approach to acyl anion equivalents applicable to intramolecular reactions. However, attempts to apply **30** with R = Bu (Scheme 3) to intermolecular C−C bond formation have been unsuccessful to date. Electrochemical formation of **34** and **39** cannot be achieved when $Ph_3P$ is utilized instead of $Bu_3P$ for paired electrosynthesis.

Acyl phosphonium ion **29′** with R = Bu also exhibits an interesting facility for nonelectrochemical synthetic reactions. Voltammetric examination demonstrated that **29′** with R = Bu is much more susceptible to cathodic reduction than acid chloride.[43] These results imply that **29′** should be regarded as an activated form of an acid chloride, not only as an electron acceptor but also as an electrophile, since the electrophilicity of a compound will increase as its reduction potential becomes more positive. In addition, **29′** with R = Bu is known to be accessible alternatively through chemical reaction of $Bu_3P$ with acid chloride **44**.[48] Thus, we examined the possibility of employing in situ formed **29′** as a simple solution to address problems encountered in some reactions with **44** itself. In fact, transformation of **44** into the corresponding aldehyde **27** without overreduction to alcohol was achieved by reduction using Zn−Cu couple or Zn in the presence of $CH_3SO_3H$, after admixing **44** and $Bu_3P$ in $CH_3CN$ (eq 29).[49] Reaction of Grignard reagents with **44** fails to provide synthetically useful access to ketones **45** due to

**Scheme 4**



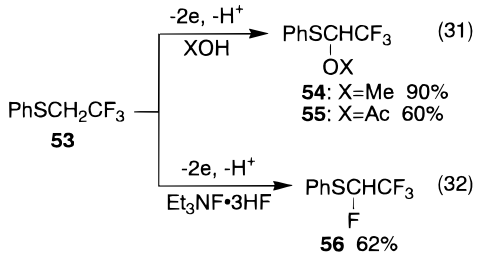

the inevitable formation of tertiary alcohols,[50] unless the reaction is carried out not only at very low temperature in THF but also with high excess of acid chlorides in many cases.[51] The problem is easily solved simply by using the preformed **29′** (R = Bu) instead of **44**. Thus, reaction of **29′** in situ generated from **44** and $Bu_3P$ in THF at −22 °C with primary alkyl- and phenylmagnesium halides provides a convenient and simple procedure to prepare **45** from **44** in one pot (eq 30).[52]




## Electrochemistry of Sulfur Compounds

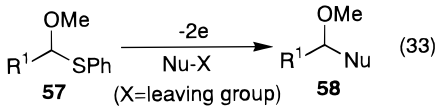
In contrast to the case of $R_3P$, one-electron oxidation of sulfides **46**, generating cation radicals **47**, is followed by three types of reactions, as shown in Scheme 4.[53,54] Therefore, selective regulation of the fate of **47** plays an important role in the application of anodic oxidation of **46** as a synthetic tool. From a synthetic standpoint, molecular transformations via routes b and c are more intriguing than those via route a, because such reactions can provide versatile tools for introducing various nucleophilic species on carbon atoms. Thus, to develop a methodology that allows **47** to enter either route b or route c in a controllable manner has been of interest. In electrochemical conversion and functionalization of $\beta$-lactam antibiotics such as cephalosporins, such methodologies have already been established and reviewed extensively.[55] Accordingly, this Account emphasizes only the recent approaches, which provide the general background for molecular transformations initiated by anodic oxidation of divalent sulfur compounds.

Placement of a perfluoroalkyl group on carbons α to sulfur atoms effectively induced molecular transformations via route b.[56] For example, anodic oxidation of **53** in MeOH and AcOH afforded **54** and **55**, respectively (eq 31). Similarly, a fluorine atom can be introduced by electrolysis of **53** in $CH_3CN$ containing $Et_3NF{\cdot}3HF$ (eq 32).

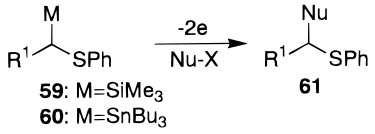



Anodic transformation was unsuccessful or much less effective in electrolysis of a nonfluorinated sulfide under essentially the same conditions. Thus, strong electron-withdrawing perfluoroalkyl groups may promote deprotonation of **47**, to form **50** via route b (Scheme 4). On the basis of the mechanism, Fuchigami et al. expected other electron-withdrawing groups to exhibit useful effects similar to the trifluoromethyl group, allowing carbons α to sulfur atoms to be anodically fluorinated, which is what they observed.[57] α-Monofluorination of sulfides bearing ketones, esters, amides, nitriles, etc. at α-carbons was also successful.[57] Electrochemical monofluorination has also been applied successfully to the preparation of monofluorinated heterocycles.[58]

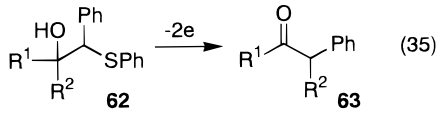
The introduction of heteroatoms such as O, Si, and Sn at α-carbons of sulfides is a useful method to control the fate of cation radicals generated anodically from sulfides. In this case, a methoxy group facilitated the generation of carbocations **51** via route c, resulting in the formation of α-substituted ethers **58** (eq 33).[59] Electrochemical transformation was also applicable to intramolecular C−C bond formation, resulting in the formation of tetrahydropyrans from α-organo thioethers with internal olefins.[59] Anodic oxidation of sulfides with a trimethylsilyl or a tributylstannyl group was shown to favor reactions via route b, giving α-substituted sulfides **61** with cleavage of the C−Si or C−Sn bond (eq 34).[60] Compounds **57** and **59** are oxidized at a potential similar to that of the corresponding unsubstituted sulfides, while a tributylstannyl group appears to activate electron transfer from the sulfur atoms, allowing anodic oxidation of **60** to proceed at much more negative potentials. Molecular transformation via route c is also preferred in the anodic oxidation of $\beta$-hydroxy sulfides **62**.[61] Anodically generated carbocations undergo pinacol-type rearrangements during electrolysis to yield ketones **63** (eq 35). A ring expansion reaction occurred during anodic oxidation of cyclic **62**. Electrochemical reactions were performed in $CH_2Cl_2$−MeOH containing $Et_4NCl$. Since the chloride ion is subjected to anodic oxidation at a less positive potential than **62**, the initial anodic process is the oxidation of the chloride ion to a chloronium ion. Sawaki et al. proposed that carbocations are generated through C−S bond cleavage in the adduct (cf. **48** with Nu = Cl) of **62** to chloronium ion, rather than via route c.[61] For detailed electrode processes of the transformations described in this section, original reports should be referred to.




(33)




(34)




(35)

## Conclusion

Molecular transformations initiated by anodic oxidation of phosphorus and sulfur compounds are controlled by the selection of reaction conditions such as the supporting electrolyte and solvent as well as by the molecular design of the starting phosphines and sulfides. This offers exquisite control of organic synthesis. In particular, the anionic components of supporting electrolytes exhibit great influence on the chemical reaction course which follows the first one-electron oxidation process from the heteroatoms. In addition, nonelectrochemical methodologies for organic synthesis have been established on the basis of the results of electrochemical studies of phosphorus compounds (eqs 29 and 30). All the electrolyses described in this Account are performed under practical conditions consisting of a constant current in an undivided cell. Although electrolysis can be achieved under such conditions without any specialized equipment even in conventional synthetic organic laboratories,[62] the application of electrochemical methods in everyday practice is unlikely at present. However, the results presented herein should provide some background of not only how electron-transfer reactions take place in organophosphorus and sulfur compounds, but also how the electrochemical and nonelectrochemical behaviors of the compounds are related. This should lead to the development of improved methodologies in the field of organic chemistry.

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