Heteroatom Chemistry
Volume 12, Number 4, 2001

Kinetic Study on Debromination of *vic*-Dibromides with Trivalent Phosphorus Compounds

Shinro Yasui,[1] Kenji Itoh,[2] and Atsuyoshi Ohno[2]

[1]*Tezukayama College, Gakuen-Minami, Nara, 631-8585 Japan*

[2]*Institute for Chemical Research, Kyoto University, Uji, Kyoto, 611-0011 Japan*

Received 18 September 2000; revised 16 November 2000

ABSTRACT: *Various types of trivalent phosphorus compounds (***1***) brought about reductive debromination of vic-dibromides (***2***) to afford olefins. The reaction was accelerated by either electron-releasing substituents on the phosphorus of* **1** *or electron-withdrawing substituents on the α-carbon of* **2***. The substituent effects, along with the stereochemistry of the reaction, are consistent with an E1CB-like mechanism for the elimination of the two bromine atoms. That is,* **1** *initially undergoes nucleophilic attack upon a bromine of* **2***. At the transition state, a fractional positive charge is developed on the phosphorus of* **1** *and a fractional negative charge on the carbon of* **2***. This mechanism suggests the importance of an electronic character of the vic-dibromide in determining the relative ease of bromophilicity, carbophilicity, and basicity of the phosphorus of a trivalent phosphorus compound in a reaction with the dibromide.* © 2001 John Wiley & Sons, Inc. Heteroatom Chem 12:217–222, 2001

INTRODUCTION

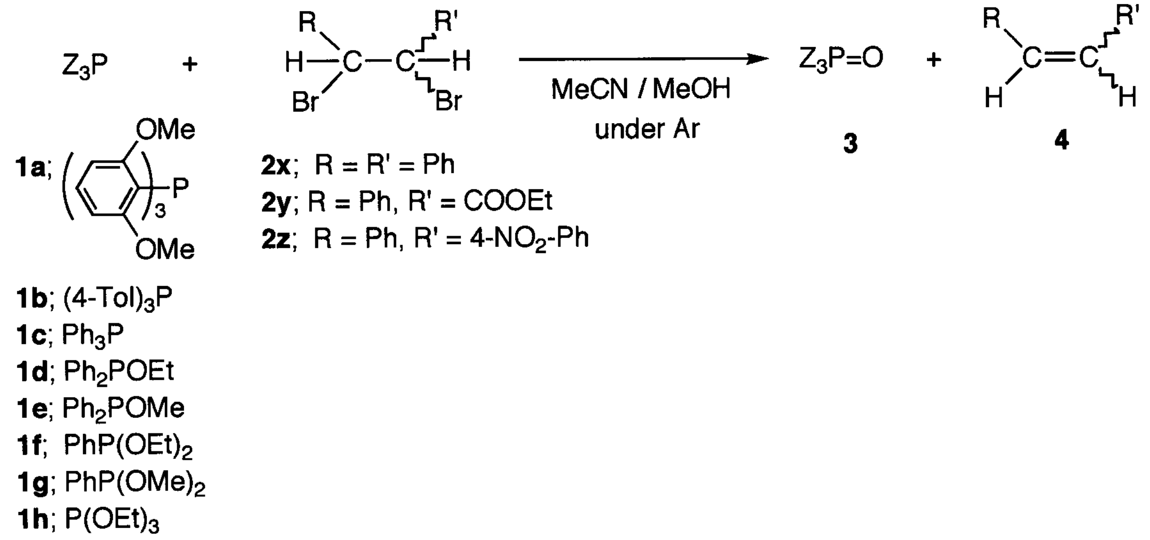
vic-Dibromides are debrominated by many reagents that exert Lewis base reactivity. For example, several types of nucleophiles bring about debromination of *vic*-dibromides by attacking a bromine of the starting *vic*-dibromide or a bromonium intermediate [1–4]. Meanwhile, mechanisms involving radical intermediates have been proposed for debromination of *vic*-dibromides with electron donors such as 1-benzyl-1,4-dihydronicotinamide [5] or sodium naphthalenide [6]. Cathodic reduction of *vic*-dibromides also results in the debromination [7].

Trivalent phosphorus compounds, which are known to be either nucleophiles or electron donors [8,9], have been shown to act as nucleophiles in reaction with *vic*-dibromides [10–13]. Such reactivity of these phosphorus compounds is due to their much higher oxidation potentials compared with the reduction potentials of *vic*-dibromides. Meanwhile, there are three possible electrophilic sites in *vic*-dibromides, upon which trivalent phosphorus compounds can attack nucleophilically, namely, bromine, hydrogen, or carbon. For example, triethyl phosphite can undergo the Arbuzov reaction with some 1,2-dibromoethanes by attacking the carbon of the dibromide; however, the phosphite attacks the bromine to result in debromination of *vic*-dibromides that have electron-withdrawing groups adjacent to both bromine atoms [12]. Furthermore, trivalent phosphorus compounds can attack the hydrogen atom of some *vic*-dibromides, resulting in the elimination of HBr [13].

A question arises as to what factors determine the relative ease of bromophilicity, carbophilicity, and basicity (affinity to a hydrogen) of the phosphorus of a given trivalent phosphorus compound. To seek an answer to this question, we carried out the reactions of trivalent phosphorus compounds **1a–h**

Correspondence to: Shinro Yasui.

Contract Grant Sponsor: Tezukayama Research Grant (to S. Y.).



SCHEME 1

with *vic*-dibromides **2x–z**. The reactions took place, affording the products from debrominations of **2**, namely, olefins **4**, along with oxidation products from **1**, namely, pentavalent oxo-compounds **3** (Scheme 1). The results from quantitative analyses including kinetics on the reactions showed that an initial step of each reaction is nucleophilic attack by the phosphorus of **1** upon the bromine of **2**. Based on this mechanism, we herein discuss the relative ease of bromophilicity, carbophilicity, and basicity exerted by each of the trivalent phosphorus compounds in reactions with the *vic*-dibromides.

TABLE 1 Debromination of **2** with Ph_3P (**1c**)[a]

		Yield/%				
2	*time/min*	**2**[b]	*trans*-**4**	*cis*-**4**	**1c**	**3**[b]
meso-**2x**	180	13	87	[c]	12	88
dl-**2x**	240	88	5	[c]	85	5
erythro-**2y**	210	6	94	[c]	6	77

[a] In MeCN:MeOH (10:1 v/v) at 70°C under Ar in the dark. [**1c**] = [**2**] = 1.00×10^{-2} M.
[b] Recovered.
[c] Not detected.

RESULTS

Reactions of Triphenylphosphine 1c *with vic-Dibromides* 2

Triphenylphosphine **1c** (1.00×10^{-2} M) was reacted with an equimolar amount of **2** in acetonitrile containing methanol (MeCN:MeOH = 10:1 v/v) under an argon atmosphere. Due to the poor solubility of *meso*-**2x** in the solvent at room temperatures, the reactions were carried out at an elevated temperature (70°C). After an appropriate reaction period, the reaction mixture was analyzed by gas chromatography (GC) and gas chromatography–mass spectrometry (GC-MS). As reported in Table 1, *meso*-**2x** and *erythro*-**2y** were debrominated to give *trans*-**4x** and *trans*-**4y**, respectively, in nearly quantitative yields, without giving the *cis*-isomers. Also, *dl*-**2x** afforded *trans*-**4x**, but the yield was much lower. In these reactions, **1c** was converted to a theoretical amount of triphenylphosphine oxide **3c**. No evidence for the formation of dibromotriphenylphosphorane Ph_3PBr_2 was obtained in these reactions.

The time course of the reaction of **1c** with *meso*-**2x** was examined with GC, as shown in Figure 1, which indicated a 1:1 stoichiometry. The examination allows us to estimate roughly the second-order rate constant k_2 of this reaction to be 6×10^{-2} $M^{-1}s^{-1}$. In Figure 1 are shown theoretical curves based on this value of k_2, along with experimental data points.

Kinetics

For the reactions of **1a–h** with **2z**, kinetics investigations were carried out at 25°C under pseudo-first-order conditions in which **1** was present in large excess. The progress of each reaction was followed by monitoring the increase in the absorbance at 351 nm of the olefin **4z**, which gave pseudo-first-order rate constants with correlation coefficients > 0.999. With experiments with different concentrations of **1**, the

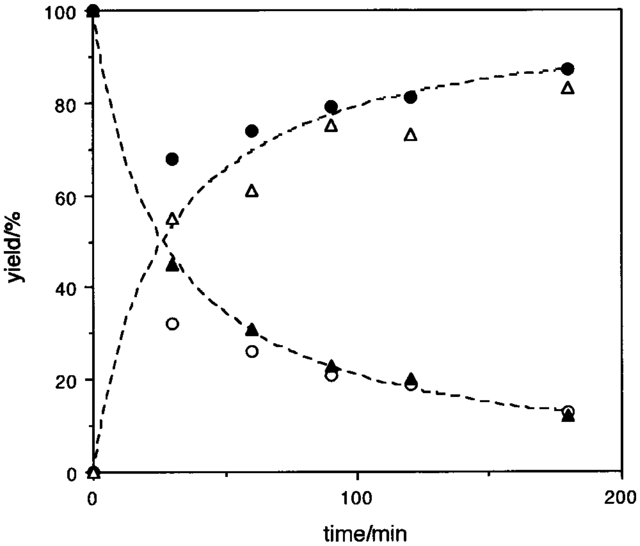


FIGURE 1 Time-course for the reaction of **1c** with *meso*-**2x**. Closed triangles and open triangles represent **1c** and **3c** respectively. Open circles and closed circles represent *meso*-**2x** and *trans*-**4**, respectively. Dashed lines are theoretical ones; see the text.

TABLE 2 Rate Constants for the Reaction of **1** with *meso*-4-nitro-stylbene dibromide (*meso*-**2z**) in the Presence of MeOH[a]

1	$k_2/M^{-1}\ s^{-1}$	E_p^{ox}/V^b
1a	1.38×10	0.36
1b	1.20	0.82
1c	1.71×10^{-1}	0.94
1d	1.65×10^{-1}	1.20
1e	1.10×10^{-1}	1.24
1f	2.98×10^{-2}	1.50
1g	5.77×10^{-3}	1.52
1h	1.24×10^{-4}	1.90

[a] In MeCN at 25°C under Ar in the dark. [**1**] = (~1.0–6.0) × 10^{-3} M, [*meso*-**2z**] = 5.0 × 10^{-5} M, [MeOH] = 0.1 M.

[b] Peak oxidation potential vs Ag/Ag$^+$.

second-order rate constant k_2 was obtained for each reaction, as summarized in Table 2.

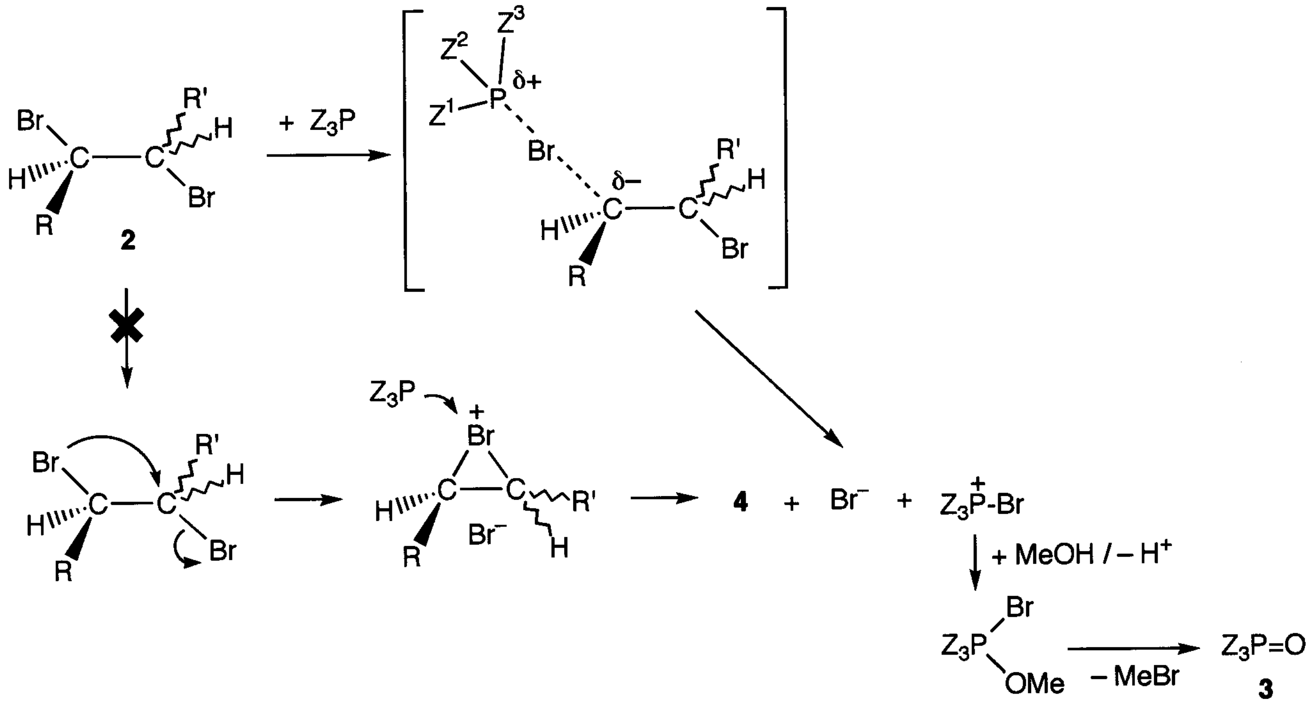
DISCUSSION

vic-Dibromides undergo reductive debromination either by nucleophilic attack by nucleophiles [1–4] or through the single electron transfer (SET) mechanism [5–7]. Although trivalent phosphorus compounds can act sometimes as electron donors [8], peak oxidation potentials of **1** (ranging from 1 to 2 V vs. Ag/Ag$^+$) [14] are much higher than peak reduction potentials of **2** (determined by cyclic voltammetry; −2.14 V, −2.07, and −1.49 V vs. Ag/Ag$^+$ for *meso*-**2x**, *erythro*-**2y**, and *erythro*-**2z**, respectively), predicting that the SET from **1** to **2** would be highly endothermic if it were to occur. Besides, use of an oxygen atmosphere was found to exhibit no effect on the yields of the debromination products. Therefore, the debromination of **2** with **1** observed here cannot be explained by an SET mechanism, but **1** acts as a nucleophile in the present reactions.

With this premise, we first examined a possibility of a bromonium mechanism as depicted in the lower part of Scheme 2. That is, **2** initially releases a bromide ion to form a bromonium cation intermediate, which is followed by nucleophilic attack by **1** upon the resulting intermediate to afford the product **4**. This mechanism predicts the formation of *cis*-**4x** from *dl*-**2x** because complete stereospecificity in a bromonium mechanism is well known [2,4]. However, this is not the case, as shown in Table 1, thus eliminating further consideration of this mechanism for the present reaction. In addition, we can hardly imagine what could cause initial elimination of a bromide ion to form the bromonium intermediate.

Trivalent phosphorus compounds that have a P–O–C linkage, phosphite **1h**, phosphonites **1f,g**, and phosphinites **1d,e** could undergo the Arbuzov reaction with **2**, in which case an initial step would be nucleophilic attack by **1** upon the carbon bonded to the bromine. Any possibility of such a reaction can be discarded, however, because there is no evidence for formation of the Arbuzov product. In addition, linearity in the log $k_2 - E_p^{ox}$ correlation shown in Figure 2 (vide infra) suggests strongly that the reactions of **1a–h** proceed according to a single mechanism; of these phosphorus compounds, phosphines **1a–c** cannot undergo the Arbuzov reaction in principle.

To elucidate further the mechanism, we here examine the results of kinetics investigations on the debromination of **2z** with **1a–h**. In Figure 2, the logarithm of k_2 (Table 2) is plotted against peak oxidation potential E_p^{ox} of **1**, a quantity that evaluates electronic effects of ligands on the phosphorus of **1**. Indeed, we have shown that E_p^{ox} values of trivalent phosphorus compounds Z_3P with open-chain structures (the compounds examined in this article) correlate linearly with the sum of the Taft's substituent constants σ^* of the ligands Z, $\Sigma\sigma^*$, with the slope $\Delta E_p^{ox}/\Delta\Sigma\sigma^* = 0.35$ [14]. That is, the plot in Figure 2 is equivalent to a Taft plot. There is a good linear correlation between log k_2 and E_p^{ox} (correlation coefficient $r = 0.96$), with the slope being −3.0. This value of the slope is converted to a reaction constant ρ^*, defined by an equation $\log k_2 = \rho^*\Sigma\sigma^* + \text{const.}$,



SCHEME 2

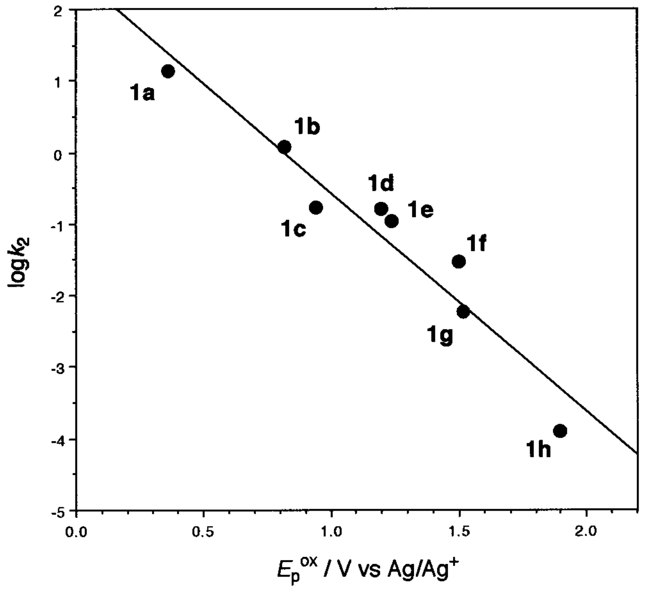


FIGURE 2 Plot of log k_2 vs E_p^{ox} for the reactions of **1a–h** with *meso*-**2x**.

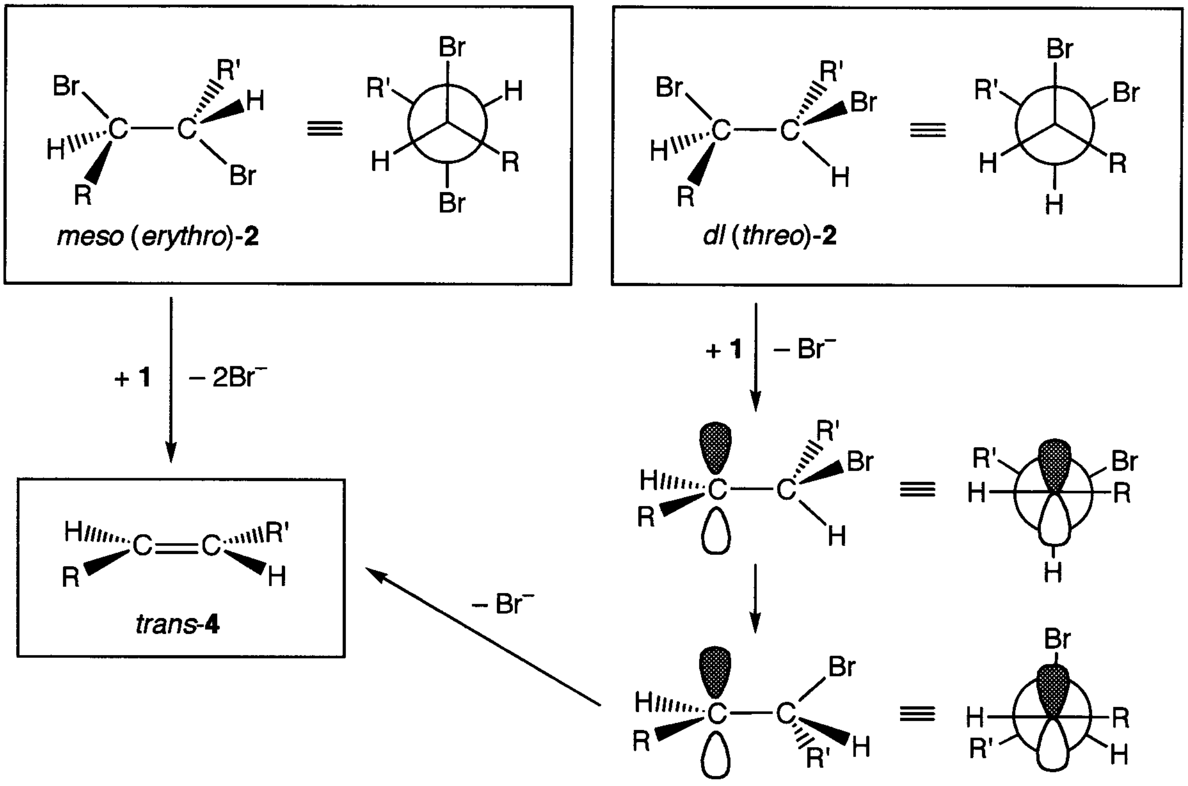
by using the relationship between E_p^{ox} and $\Sigma\sigma^*$. Thus, $\rho^* = -1.1$ is obtained, which clearly shows that a positive charge is developed largely on the phosphorus at the transition state of the debromination of **2z** with **1** [15].

meso-4-Nitro-substituted stilbene dibromide, *meso*-**2z**, is debrominated by **1c** with $k_2 = 1.71 \times 10^{-1}$ M^{-1} s^{-1} at 25°C (Table 2). On the other hand, it has been roughly estimated that the debromination of the unsubstituted derivative, *meso*-**2x**, with **1c** takes place with $k_2 = 6 \times 10^{-2}$ $M^{-1}s^{-1}$ at 70°C. Since these k_2 values have been obtained for different temperatures and we have no data concerning activation parameters, direct comparison of these constants is impossible. However, clearly a 4-nitro-substituent in a *meso*-stilbene dibromide accelerates its debromination significantly; *meso*-**2z** is debrominated three times faster than the unsubstituted derivative, *meso*-**2x**, even at a temperature of 35° lower. This observation indicates a significant amount of a negative charge developed on the carbon at the transition state.

With the results previously stated in mind, we propose an E1CB-like mechanism for the debromination of **2** with **1**. As depicted in the upper part of Scheme 2, the phosphorus of **1** undergoes initial nucleophilic attack upon the bromine atom of **2** to give a carbanion-like intermediate (or a transition state), from which the second bromine is being eliminated as a bromide ion. At the transition state of this process, charge separation occurs, and fractional positive and negative charges are developed on the phosphorus of **1** and the carbon of **2**, respectively. Consistent with this mechanism is the observed stoichiometry, **1**:**2** = 1:1. Furthermore, as expected from this mechanism, *meso*-**2x** and *erythro*-**2y** give *trans*-**4** in high yields. Thus, anti-elimination of two bromines from a *meso*- (or *erythro*-) isomer takes place easily to give the *trans*-olefin because the anti conformation with respect to the two bromines is thermodynamically the most stable one for the *meso*- (or *erythro*-) isomer (Scheme 3).

For the *dl*-isomer, on the other hand, a conformation in which a bromine and a hydrogen are located at anti positions with respect to each other is the relatively highly stable (or possibly the most stable) one (Scheme 3). From this conformation, anti-elimination of HBr would be more favorable in energy than syn-elimination of two bromines. Nevertheless, *dl*-**2x** is in fact debrominated in reaction with **1c** to afford *trans*-**4**, although the yield is low, without giving a product resulting from HBr elimination (Table 1). This fact suggests strongly that nucleophilic attack by **1c** on the bromine of *dl*-**2x** is also the initial step in this case. The resulting carbanion-like intermediate from this isomer is transformed to a less crowded conformer, from which the second bromine is eliminated as a bromide ion to afford *trans*-**4**. Such syn-elimination would require more energy than the anti-elimination; that is, debromination from the *dl*-isomer would be more sluggish than that from the *meso*- (or *erythro*-) isomer. This is indeed reflected in the lower yield of *trans*-**4** from *dl*-**2x** (Table 1).

Emphasized here again is that the bromine atom in **2x–z** is preferred, irrespective of the configuration of **2**, over the hydrogen atom or the carbon atom as the site of nucleophilic attack by the phosphorus of **1**. The affinity of the phosphorus to the bromine may not be surprising when one takes into account the hard and soft acids and bases (HSAB) principle [17]; trivalent phosphorus compounds are soft bases, and a bromine is softer than a hydrogen or a carbon. However, such an argument is an oversimplification. Surveying literature presented so far, we find that, when treated with *vic*-dibromides, trivalent phosphorus compounds sometimes undergo reactions that are not predictable by the HSAB principle. In a series of reactions of triethyl phosphite **1h** with 1,2-dibromoethane derivatives, **1h** undergoes the Arbuzov reaction with unsubstituted 1,2-dibromoethane by attacking the carbon of this dibromide, whereas **1h** attacks the bromine when the 1,2-dibromoethane bears an electron-withdrawing substituent on the α-carbon [12]. This fact suggests that the bromine is preferred in nucleophilic attack by the phosphorus only when a carbanion center resulting from removal of the bromine is sufficiently stabilized. Also against prediction by the HSAB principle is the re-



SCHEME 3

action of triphenylphosphine **1c** with *erythro*-2,3-dibromobutyric acid, which results in elimination of HBr instead of elimination of two bromine atoms; the phosphorus of **1c** initially attacks the hydrogen of the *vic*-dibromide [13]. High acidity of the α-hydrogen due to the electronegative carboxyl group certainly accounts for this result.

These facts now allow us to conclude that an electronic character of a given *vic*-dibromide mainly determines the relative ease of bromophilicity, carbophilicity, and basicity exerted by the phosphorus of a trivalent phosphorus compound in a reaction with the dibromide. With increasing electronegativity of substituents on the carbon bonded to the bromine in a *vic*-dibromide, the bromine becomes more amenable to attack by the phosphorus; in other words, the bromophilicity of the phosphorus becomes higher. Introduction of electronegative substituents on the carbon bonded to the bromine atom also enhances the apparent carbophilicity of the phosphorus as well, but the influence of such substituents is larger in enhancing the bromophilicity [18]. The present work has revealed that bromophilicity of the phosphorus atom in trivalent phosphorus compounds is well exerted toward *vic*-dibromides **2** that bear phenyl and/or ethoxycarbonyl groups on the α-carbon. This reactivity of **2** results from a subtle balance in electronegativity effects of substituents of **2**. If the dibromide has less powerful electronegative substituents, the carbon would be preferred in nucleophilic attack by the phosphorus of **1**. On the other hand, if the substituents are highly electronegative, the α-hydrogen becomes so acidic that it would be easily removed by attack by the phosphorus reagent.

EXPERIMENTAL

Instruments

Gas chromatography analysis was accomplished with a Shimadzu GC-14B gas chromatograph. Mass spectra were obtained on a Shimadzu GCMS-QP2000A gas chromatograph–mass spectrometer equipped with a Shimadzu GC-MSPAC 200S data processor. UV-visible spectra were recorded on a Hitachi U-3212 spectrophotometer.

Materials

Trivalent phosphorus compounds (**1a–h**) and *vic*-dibromides (**2x,y**) were commercially available (Tokyo Chemical Industry). *erythro*-1,2-Dibromo-1-(4′-nitrophenyl)-2-phenylethane (**2z**) was prepared by the reaction of 4-nitrostilbene with pyridinium tribromide in dichloromethane at room temperature (86% yield).

Kinetics

Into a UV-vis quartz cell equipped with a silicon rubber stopper and filled with argon gas were added successively the solution of 1 in acetonitrile, the solution of *meso*-**2z** in acetonitrile, and methanol. The stock solutions of **1** and of *meso*-**2z** had been prepared under an argon atmosphere, with adjustment of their concentrations such that the concentrations of **1**, *meso*-**2z**, and methanol became $(\sim 1.0\text{–}6.0) \times 10^{-1}$ M, 5.0×10^{-5} M, and 0.1 M, respectively, after the mixing. Increase in the absorbance at 351 nm resulting from formation of *trans*-**4z** was followed on a spectrophotometer.

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[15] Debromination of **2z** with tris (2,6-dimethoxyphenyl)phosphine **1a** takes place undoubtedly through a nucleophilic mechanism because **1a** is an efficient nucleophile but a poor electron donor [16]. Therefore, the fact that the point for the reaction with **1a** fits the linear line given in Figure 2 confirms the nucleophilic mechanism occurring in the debromination also with other phosphorus compounds **1b–h**.

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