acetyl bromide generated in situ to give the 2′,(3′)-*O*-acetyl derivative **7**, which would then cyclize to **3**. The formation of silyl halides and alkyl acetates by the action of acetyl halides on alkoxysilanes has been reported.[7] Attempts to prepare **4** by treatment of **1b** with acetic anhydride and phosphorus tribromide in the presence of boron trifluoride etherate in acetonitrile were unsuccessful, and resulted in the formation of 2′,3′,5′-tri-*O*-acetyladenosine as a major product, although a small amount of **4** could be detected (NMR) in the reaction.

The work presented in this note provides an alternative method for the transformation of the 2′,3′-cis diol function of purine nucleosides to the trans halo acetates.

Experimental Section

Melting points are uncorrected. NMR spectra were recorded on a Hitachi Perkin-Elmer R20A spectrometer and are reported in parts per million downfield from an internal standard of tetramethylsilane. UV spectra were measured on a Hitachi EPS-3T spectrometer. Thin-layer chromatography (TLC) was performed on Merck silica gel $60F_{254}$. Spots were detected by UV examination. Column chromatography was done using Merck silica gel 60.

Reaction of 3′,5′-Di-*O*-acetyladenosine (1a) with Lithium Bromide. Lithium bromide (5.0 g, 57 mmol) and boron trifluoride etherate (2.9 mL, 23 mmol) were added to a suspension of **1a**[4] (1.0 g, 3 mmol) in dry acetonitrile (100 mL). The resulting clear solution was kept at room temperature for 21 h. The solution was then neutralized with saturated aqueous sodium bicarbonate (20 mL) and concentrated to dryness. The residue was partitioned between chloroform (60 mL) and water (40 mL). The organic layer was washed with water (five 15-mL portions), dried ($MgSO_4$), and evaporated, leaving a solid residue. Crystallization of the residue from chloroform–hexane gave 300 mg (26%) of 9-(3-bromo-3-deoxy-2,5-di-*O*-acetyl-β-D-xylofuranosyl)adenine (**4**) with mp 165–167 °C. An analytical sample from the same solvent had mp 166–167 °C: UV λ_{max} (EtOH) 261 nm (ε 14 700); NMR (Me_2SO-d_6) δ 2.10 (s, 3, OAc), 2.17 (s, 3, OAc), 4.3–4.8 (m, 3, $C_{5'}$ H_2, $C_{4'}$ H), 4.9–5.1 (m, 1, $C_{3'}$ H), 5.9–6.1 (m, 1, $C_{2'}$ H), 6.28 (d, J = 3 Hz, 1, $C_{1'}$ H), 7.3–7.7 (br s, 2, NH_2), 8.29 (s, 1, C_2H or C_8 H), 8.41 (s, 1, C_2 H or C_8 H). Anal. Calcd for $C_{14}H_{16}N_5O_5Br$ (414.23): C, 40.59; H, 3.89; N, 16.91; Br, 19.29. Found: C, 40.45; H, 3.99; N, 16.80; Br, 19.69. This compound was identical (IR, NMR) with an authentic sample prepared by an alternate route (vide infra).

Alternative Synthesis of 4. To a suspension of 9-(2-*O*-acetyl-3-bromo-3-deoxy-β-D-xylofuranosyl)adenine[1f] (190 mg, 0.5 mmol) in pyridine (2.5 mL) was added acetic anhydride (250 mg, 2.5 mmol). The mixture was stirred at room temperature for 1.5 h and evaporated in vacuo. The residue was crystallized from chloroform–isopropyl ether to give 170 mg (80%) of **4** with mp 165–166 °C.

Reaction of 1a with Phosphorus Tribromide. Boron trifluoride etherate (2.2 mL, 17.5 mmol) and phosphorus tribromide (0.2 mL, 2.1 mmol) were added to a suspension of **1a** (700 mg, 2 mmol) in dry acetonitrile (30 mL). The resulting clear solution was kept at room temperature for 2 h and worked up as above to give a solid foam. Crystallization of the solid foam from methyl *n*-propyl ketone gave 450 mg (55%) of **4** with mp 166–167 °C. This compound was identical with the sample prepared as above.

Reaction of Adenosine (1b) with Tetraacetoxysilane and Phosphorus Tribromide. Phosphorus tribromide (2.0 mL, 20.6 mmol) was added to a solution of tetraacetoxysilane[2] (9.9 g, 37.5 mmol) in dry acetonitrile (200 mL). The solution was kept at room temperature for 3 h. To this solution, **1b** (5 g, 18.7 mmol) and boron trifluoride etherate (42 mL, 0.326 mol) were added and the mixture was stirred at room temperature for 18 h. The resulting clear solution was poured into saturated aqueous sodium bicarbonate (500 mL), and the acetonitrile was largely removed in vacuo. The aqueous residue was extracted with chloroform (three 100-mL portions), and the organic phase was dried ($MgSO_4$). Evaporation of the solvent left a syrup which was crystallized from ethanol (30 mL). The crystals were collected, washed with ether, and dried thoroughly in vacuo at 80–90 °C to give 3.7 g (47%) of **4** with mp 165–167 °C, identical (IR, NMR) with that above. The mother liquors from the crystallization were evaporated, and the residue was chromatographed on a column of silicic acid (2.5 × 40 cm). The required fraction was eluted with chloroform–methanol (95:5). The eluate was evaporated and the residue (1.8 g) was crystallized from methyl *n*-propyl ketone to give 270 mg (3%) of 9-(2-bromo-2-deoxy-3,5-di-*O*-acetyl-β-D-arabinofuranosyl)adenine (**5**) with mp 138–140 °C: UV λ_{max} (MeOH) 260 nm (15 500); NMR (Me_2SO-d_6) δ 2.07 (s, 3, OAc), 2.17 (s, 3, OAc), 4.1–4.7 (m, 3, $C_{4'}$ H, $C_{5'}$ H_2), 5.0–5.3 (m, 1, $C_{2'}$ H), 5.8–6.1 (m, 1, $C_{3'}$ H), 6.49 (d, J = 6 Hz, 1, $C_{1'}$ H), 7.2–7.6 (br s, 2, NH_2), 8.20 (s, 1, C_2 H or C_8 H), 8.30 (s, 1, C_2 H or C_8 H). Anal. Calcd for $C_{14}H_{16}N_5O_5Br$ (414.23): C, 40.59; H, 3.89; N, 16.91; Br, 19.20. Found: C, 40.72; H, 4.08; N, 16.56; Br, 19.52. The mother liquors from the crystallization of **5** were evaporated and the residue was crystallized from ethanol, giving 120 mg (2%) of 2′,3′,5′-tri-*O*-acetyladenosine with mp 167–168 °C. This compound was identical with the sample prepared by an alternate route.[6]

Conversion of 5 to 9-(2,3-Anhydro-β-D-ribofuranosyl)adenine. To a suspension of **5** (500 mg, 1.2 mmol) in methanol (25 mL) was added 1 M methanolic sodium methoxide (3.6 mL). The resulting solution was stirred and heated at 50–55 °C for 20 min. After cooling, the mixture was neutralized with acetic acid and evaporated in vacuo. The crystalline residue was washed with water, then methanol, and dried, giving 220 mg (73%) of 9-(2,3-anhydro-β-D-ribofuranosyl)-adenine with mp ~180 °C dec. This material was identical (IR, NMR) with an authentic sample prepared by a different route.[1f]

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Registry No.—**a**, 6554-24-1; **b**, 58-61-7; **4**, 62805-48-5; **5**, 62805-49-6; 9-(2-*O*-acetyl-3-bromo-3-deoxy-β-D-xylofuranosyl)adenine, 42867-78-7; 2,3′,5′-tri-*O*-acetyladenosine, 7387-57-7; 9-(2,3-anhydro-β-D-ribofuranosyl)adenine, 2627-64-7.

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Bridgehead Free Radicals. The Tri-*n*-butyltin Hydride Reduction of Bridgehead Halides

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Some years ago, we reported on the stability of bridgehead free radicals as measured by the rates of unimolecular decomposition of *tert*-butyl peresters, and suggested that the results (included in Table I) were in accord with a preferred planar geometry for carbon-free radicals.[1] We ourselves, and Ruchardt (among others),[2] expressed some concern that the transition state for perester decomposition (1) might have

1

some charge separation, which would cause the rates to reflect carbonium ion, rather than radical, stabilities. This concern was reinforced by our measurement of a ρ^* of −1.6 for decomposition of some substituted adamantyl peresters.[3]

Consequently, we sought a reaction free of such complications, and settled upon the tri-*n*-butyltin hydride reduction of halides (eq 1).[4] This reduction is known to be a radical chain

Table I. Relative Rates of Bridgehead Radical Formation

Reaction	Relative rate, R = 1-Methylcyclohexyl	3-Ethylpentyl	1-Adamantyl	1-Bicyclooctyl	1-Bicycloheptyl
RCO_3-*t*-Bu, Δ		1.00	0.52	0.045	3.5×10^{-4}
RCl, *n*-Bu_3SnH	1.0		0.24	0.12	0.010
RBr, *n*-Bu_3SnH	1.0		0.42	0.32	0.019

reaction,[4] in which the two chain-propagating steps are eq 2 and 3.

$$RX + (n\text{-}Bu)_3SnH \xrightarrow{Q\cdot} RH + (n\text{-}Bu)_3SnX \quad (1)$$

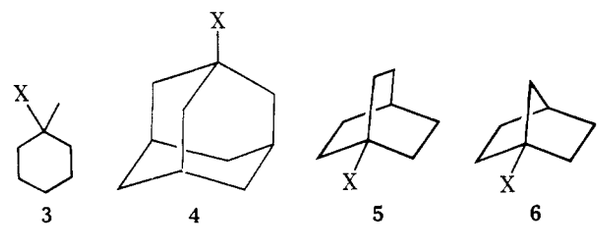
$$(n\text{-}Bu)_3Sn\cdot + RX \rightarrow (n\text{-}Bu)_3SnX + R\cdot \quad (2)$$

$$R\cdot + (n\text{-}Bu)_3SnH \rightarrow RH + (n\text{-}Bu)_3Sn\cdot \quad (3)$$

If eq 2 is the rate-limiting step, then the overall ease of reduction ought to be sensitive to the stability of R·; indeed, the ease of reduction of simple alkyl halides is tertiary > secondary > primary.[4] Furthermore, if the transition state is at all polarized, the electronegativities[5] of carbon (2.5) and tin (1.8) suggest that it is more likely to be in the sense of positive *tin* (**2**) than positive carbon.[4b] Thus, a correspondence between this reaction and perester decomposition would be evidence for the absence of appreciable charge separation in either reaction.

$$R^{\delta-}\cdots X\cdots{}^{\delta+}Sn(n\text{-}Bu)_3$$
2

We therefore set about synthesizing the series of bromides[6] **3a–6a.** Methylcyclohexane was chosen as a standard because



3 **4** **5** **6**

a, X = Br b, X = Cl

it should reflect reasonably well the inductive stabilization of the intermediate radical by the carbon skeletons of the bridged molecules. During those preparations, Ingold[7] published the results of a kinetic examination of tin hydride reductions in which he employed the rotating-sector method to obtain absolute rate constants for the individual propagation steps. He found that for most primary, secondary, and tertiary alkyl *bromides,* eq 3 is the rate-determining step; however, for all alkyl *chlorides,* eq 2 is rate limiting. We immediately included the chlorides (**3b–6b**) in our synthetic scheme, but, having the bromides, determined to reduce them as well.

The halides were allowed to compete for an insufficient amount of tri-*n*-butyltin hydride in trimethylpentane solution, and relative rates were calculated from the proportions of products, as determined by gas chromatography (see Experimental Section). Our data, which are given in Table I, are in complete accord with the data obtained by perester decomposition.

We conclude that: (a) at least in these unsubstituted bridgehead systems, there is no appreciable charge separation in the transition states for either tin hydride reduction or perester decomposition; (b) the stability order of bridgehead free radicals is that previously determined;[1] and (c) this stability order is determined by the preference of simple carbon free radicals for a planar configuration.

Experimental Section

Commercial chloro- and bromadamantane were purified by repeated sublimation. Commercial trimethylpentane was washed twice with concentrated sulfuric acid and three times with water, dried over anhydrous magnesium sulfate, and distilled at 96–99 °C from calcium hydride. The 1-chlorobicyclo[2.2.2]octane,[8] 1-bromobicyclo[2.2.2]-octane,[9] 1-chlorobicyclo[2.2.1]heptane,[10] 1-bromobicyclo[2.2.1]-heptane,[11] 1-chloro-1-methylcyclohexane,[12] 1-bromo-1-methylcyclohexane,[13] and tri-*n*-butyltin hydride[14] all were prepared by literature methods. Authentic samples of the hydrocarbon reduction products were commercial materials or were on hand from earlier work.[1]

Kinetic Method (Typical Example). A mixture of 0.256 g (1.5 mmol) of 1-chloroadamantane, 0.199 g (1.5 mmol) of 1-chloro-1-methylcyclohexane, 0.437 g (1.5 mmol) of tri-*n*-butyltin hydride, and 0.044 g of azobisisobutyronitrile was dissolved in 2.5 mL of trimethylpentane in a 5-mL ampule. The ampule was purged with nitrogen, sealed, and placed in a constant-temperature bath, held at 80 °C, for 96 h. (No tin hydride was detectable at the end of this time, and preparative experiments indicate essentially complete reduction in much less than this time.[4,6]) The ampule was then opened and the reaction mixture was introduced, without any isolation or purification, into a gas chromatograph.

Analytical Procedure. Chloride reaction mixtures were analyzed with a Barber-Colman gas chromatograph with Varian Aerograph recorder and digital integrator. This instrument was equipped with a 12 ft × 0.128 in. column packed with 10% DC-550 silicone oil on Chromosorb W HMDS, and a flame-ionization detector. Helium was the carrier gas, and analyses were conducted at an injector temperature of 200 °C, column temperature 120 °C, and detector temperature 220 °C. Bromide reaction mixtures were analyzed with a Perkin-Elmer 810 gas chromatograph equipped with a Leeds and Northrup recorder, a 150 ft × 0.010 in. Golay capillary column loaded with DC-550 silicone, and a flame-ionization detector. Helium was the carrier gas at an injector temperature of 200 °C, column temperature of 120 °C, and detector temperature of 220 °C.

The samples from each reaction were injected into the gas chromatograph until at least three reproducible chromatograms were recorded for at least two kinetic runs. Authentic samples were used for peak identification of all hydrocarbon products by both absolute retention time and peak enhancement. This was considered sufficient, since the identity of the reduction products is not in question.[6] Peak areas were measured either by the digital integrator or by means of a planimeter; detector responses to different hydrocarbons were closely similar, and no corrections were applied.

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Registry No.—**3a,** 931-77-1; **3b,** 931-78-2; **4a,** 768-90-1; **4b,** 935-56-8; **5a,** 7697-09-8; **5b,** 2064-03-1; **6a,** 13474-70-9; **6b,** 765-67-3; tributyltin hydride, 688-73-3.

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Reaction of Organo-Group 5A Compounds with *tert*-Butyl Hydroperoxide

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The rapid reduction of hydroperoxides by trivalent phosphorus compounds (eq 1) provides a useful qualitative[1] and quantitative[2] analytical tool. Yet little is known about the kinetics of this reaction. The early observation that the reduction occurs "essentially instantaneously" at −40 °C[3] has more recently been quantitated for some phosphites[4] and for triphenylphosphine.[5] But rate data are available only for those compounds which react slowly enough to permit quenching of aliquots and titration of unreacted peroxide[4] or for compounds which contain chromophores to provide for analysis by UV spectroscopy.[5]

$$\mathrm{ROOH} + \mathrm{R_3'P} \rightarrow \mathrm{ROH} + \mathrm{R_3'P{=}O} \qquad (1)$$

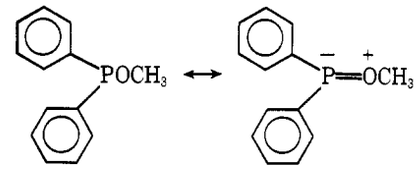
To circumvent these restrictions, we have used an in situ polarographic technique which allows the ready determination of the kinetics of hydroperoxide reactions with second-order rate constants ranging from 0.005 to >10 M^{-1} s^{-1}. This convenient kinetic technique has been used to study the reaction of *tert*-butyl hydroperoxide with a cross section of trivalent organo-group 5A compounds. We report herein our results in this area, including the first rate study of the trialkylphosphine–hydroperoxide reaction.

Results and Discussion

Polarography can be used to follow chemical reactions from the change of limiting currents with time as long as one component of the reaction mixture is electroactive.[6] Hydroperoxides possess such an electroactive handle.[7] We have found that the chemical reactivity of hydroperoxides with organo-group 5A compounds is sufficiently high that the electrochemical reaction at the dropping mercury electrode does not significantly perturb the concentration of the reactants. Thus, a chemical reaction and its electrochemical analysis can be run in the polarographic cell simultaneously.

As shown in Table I, the reactivity of trivalent phosphorus compounds with *tert*-butyl hydroperoxide decreases as the substituents on phosphorus become increasingly electron withdrawing, i.e., in the order: trialkylphosphines (entries 1 and 2) > triarylphosphines (entries 6–10) > trialkyl phosphites (entries 11–14) > triphenyl phosphite (entry 15). This is as expected, since by far the predominant pathway of the reaction for both phosphites[8] and triphenylphosphine[3,5] is nucleophilically induced cleavage of the peroxide linkage. Approximately one order of magnitude separates the contiguous classes in the above reactivity series.

Diphenylmethoxyphosphine (entry 3) represents an anomaly in the above series in that inductive effects alone do not explain its reactivity toward *tert*-butyl hydroperoxide. Whereas the replacement of a phenyl group of triphenylphosphine by an electron-withdrawing methoxyl would be expected to decrease the oxophilicity of the resulting compound, the opposite effect is observed. A similar observation was made by Denney et al.,[9] who found that in competitive reactions triphenylphosphine and diphenylethoxyphosphine possess approximately equal oxophilicities toward benzoyl peroxide. These results can be attributed to the resonance effect of a methoxyl group more than counterbalancing its inductive effect, thereby enhancing the oxophilicity of phosphorus. Such a process is possible because of the well-known



ability of phosphorus to expand the octet in its outer electron shell. Alternatively, the increased reactivity of phosphinite esters may be a manifestation of the α effect.[10] In any case, replacing a second phenyl group in triphenylphosphine by methoxyl causes a balancing of inductive and resonance/α effects, so that dimethoxyphenylphosphine (entry 5) is essentially equal to triphenylphosphine in oxophilicity.

Our results with trialkyl phosphites (entries 11–14) show the expected[11] dependence of oxophilicity on inductive effects (e.g., triethyl phosphite > trimethyl phosphite) as long as steric factors do not interfere. However, triisopropyl (entry 13) and tri-2-ethylhexyl (entry 14) phosphites react with *tert*-butyl hydroperoxide more slowly than would be predicted by inductive effects alone, which suggests that steric factors do play a part in this reaction. Interestingly, the relative reactivity of trimethyl and triethyl phosphites toward *tert*-butyl hydroperoxide (0.65) is the same as that toward singlet oxygen.[12]

A Hammett plot (Figure 1) for para-substituted triarylphosphines (entries 6–10) shows a reasonable correlation of rate with σ constants (r = 0.967). Using the Yukawa–Tsuno[13] treatment to blend fractional amounts of σ^+ into the relationship does not improve the straight-line fit. This is consistent with the hypothesis[5] that little positive charge is present on phosphorus in the transition state of the phosphine–hydroperoxide reaction. However, the lack of σ^+ con-

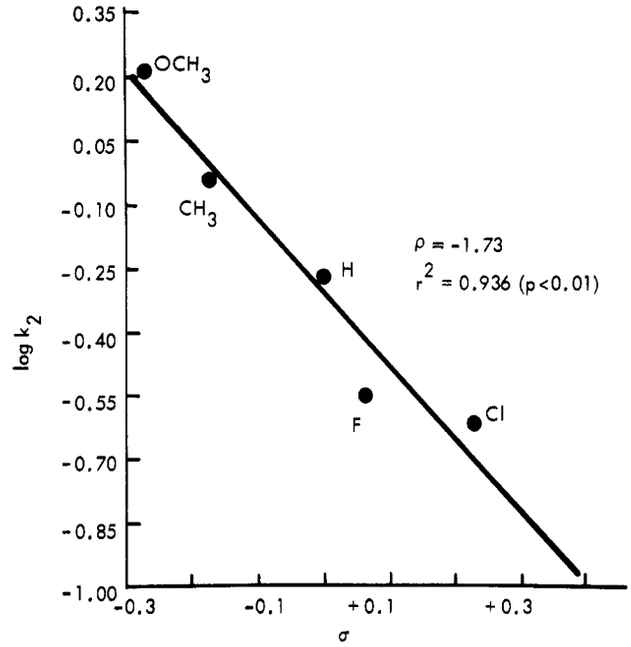


Figure 1. Relationship between Hammett σ and log k_2 for the reaction of triarylphosphines with *tert*-butyl hydroperoxide.