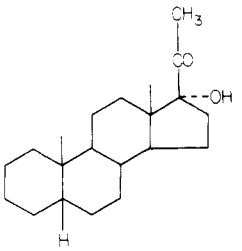
Table III. Molecular Rotations of 17α-Hydroxy-5α-pregnan-20-one at 330 nm in Mixtures of Heptane and Dioxane[a]

solvent	$[\phi]_{330}$	solvent	$[\phi]_{330}$
heptane	334	5% dioxane	2240
1% dioxane[b]	1140	10% dioxane	2960
3% dioxane	1690	dioxane	4190

[a] [Steroid] = 5×10^{-4} M; $T = 25.0 \pm 0.1$ °C. [b] Volume/volume.

another polarity scale with the data in Table I, but it can be reasonably predicted that such a scale would provide better correlations over the entire solvent range for systems not containing ionic, basic, or acidic functionalities (e.g., NR_3^+, COOH, OH, NH_2, and R_3C^+).

In related work, we examined the conformationally mobile 17α-hydroxy-5α-pregnan-20-one whose ORD spectra likewise respond markedly to the solvent (Table II). Thus, $[\phi]_{330}$ equals 4.2×10^3 in dioxane but only 0.33×10^3 in heptane. Interestingly, the molecular rotations of the steroid in Table II correlate miserably with those of the cyclohexanone in Table I (coefficient = 0.64). In particular, the steroid finds the oxygen-containing solvents (methanol, 2-propanol, dioxane, ether) much more polar relative to their effect on the cyclohexanone system. Hydrogen bonding by the steroidal hydroxy group, where the conformational mobility is centered, must play a key role. Chlorocarbons (methylene chloride, chloroform, and chlorobenzene) rank low in polarity in Table II but not so in Table I. In contrast to the protic solvents, the chlorocarbons are relatively efficient in stabilizing the opposed dipoles that exist in the ee configuration of the cyclohexanone system.



Addition of only 5% dioxane to heptane elevates the molecular rotation of the steroid from 0.33×10^3 to 2.3×10^3 (Table III). In other words, the steroid in 5% dioxane–95% heptane behaves similarly to steroid in pure dioxane, a clear indication of a solvent-sorting phenomenon.[11] ORD would seem to provide a particularly sensitive method for assessing specific solvent effects.

Experimental Section

(+)-*trans*-2-Chloro-5-methylcyclohexanone was prepared by chlorinating (+)-3-methylcyclohexanone (Aldrich).[5] Synthesis of the steroid followed known procedures.[12] All ORD spectra were obtained with a Perkin-Elmer 241 MC polarimeter and a 10-cm quartz cell thermostated at 25.0 ± 0.1 °C. Solvents were either spectrophotometric grade or distilled immediately before use.

Acknowledgment. This work was supported by the National Science Foundation and the North Atlantic Treaty Organization.

Registry No. (+)-*trans*-2-Chloro-5-methylcyclohexanone, 89616-30-8; 17α-hydroxy-5α-pregnan-20-one, 2301-91-9.

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(12) Danilewicz, J. C.; Klyne, W. *J. Chem. Soc.* **1962**, 4950.

Reactions of (Silylamino)phosphines with Epoxides and Episulfides

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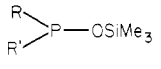
Received October 28, 1983

Recently, several authors[1-4] have reported the synthesis of *O*- and *N*-trimethylsilyl derivatives of phosphorus(III) compounds. Most prominent among these are the trimethylsilyl phosphites (**1**) and the [bis(trimethylsilyl)amino]phosphines (**2**). The silyl phosphites have proven



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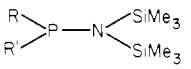
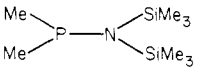


2

useful in various synthetic and mechanistic studies. For example, the reaction of diethyl trimethylsilyl phosphite with α-halo carbonyl compounds[5] has helped to clarify the mechanism of the Perkow reaction. 1,2-Adducts of silyl phosphites with α,β-unsaturated carbonyls have also been used as homoenolate equivalents.[6]

Recently, similar reactions of [(trimethylsilyl)amino]-phosphines have been reported.[7] In view of their ease of preparation,[8] relatively high reactivity, and the affinity of both silicon and phosphorus for oxygen, we decided to explore the reactions of these compounds with epoxides.

The deoxygenation of epoxides was first reported by Boskin and Denny,[9] who found that (*E*)- and (*Z*)-but-2-ene epoxides are deoxygenated by triphenylphosphine at 150 °C with inversion of configuration. The mechanism of this process is believed to involve a nucleophilic ring opening, rotation, and collapse of the betaine intermediate.[10] We herein report the results of our study of the reactions of [bis(trimethylsilyl)amino]dimethylphosphine (**3**) with epoxides.



3

Results and Discussion

When **3** was heated with 1 equiv of propylene oxide in a pressure tube to temperatures as high as 150 °C, no reaction occurred. However, on the addition of 5 mol % of $ZnBr_2$, a reaction occurred at 90 °C, as observed by ^{31}P NMR, to produce a 81% yield of trimethylsiloxy phosphine imide **4** as an easily distillable air- and moisture-sensitive liquid. This reaction was repeated with several other epoxides to produce the products shown in Table I.

A survey of the products obtained shows that, despite the zinc catalysis, the phosphorus exhibits a strong preference for attack at the least sterically hindered position. With butadiene monoxide, **3** reacted with attack of

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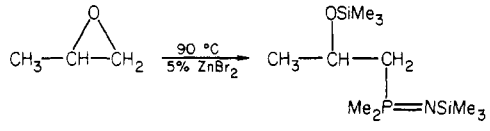

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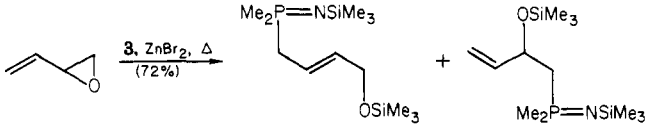
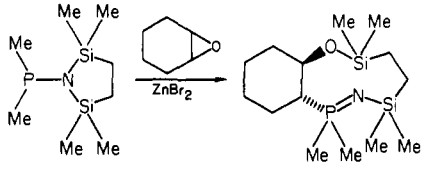
phosphorus at both primary carbons via S_N2 and S_N2' nucleophilic substitution. This result is in contrast to those obtained with other zinc-catalyzed epoxide openings[11] in which the nucleophile attacks primarily at the position more able to stabilize the positive charge. It is possible that the extreme bulkiness of the phosphine precludes this type of attack.



8a (1:3) 8b

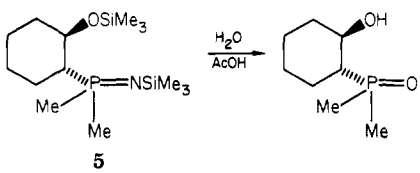
The precise role of zinc bromide is uncertain. Other catalysts including ZnI_2, $TiCl_4$, $SnCl_2$, and BF_3 were tried with lesser degrees of success. Since zinc(II) halides rapidly polymerize epoxides at room temperature, it seems likely that the zinc exists primarily as phosphorus complex. Zinc(II)–phosphine complexes with 1:1 stoichiometry have been observed and, very recently, spectroscopically characterized.[12] The use of such complexes to catalyze organophosphorus reactions has not been reported,[13] however.

With these observations in mind, we propose the mechanism shown in Scheme I, involving nucleophilic attack of free phosphine on the complexed epoxide, rotation, and intramolecular silicon transfer. In order to determine the nature of the silicon transfer, a reaction was performed with the phosphine[14] **9** and cyclohexene oxide. The formation of the cyclic phosphine imide **10** in 66% yield indicates that the reaction prefers intramolecular silicon transfer despite the unfavorable geometry that probably requires a chair to chair inversion after an initial trans diaxial ring opening.



9 10

Compound **5** was quantitatively hydrolyzed to the corresponding β-hydroxy phosphine oxide upon treatment with an acetic acid, THF, and water mixture. X-ray crystallography reveals the trans orientation of the substituents, confirming S_N2 type attack of phosphorus.[15]



5

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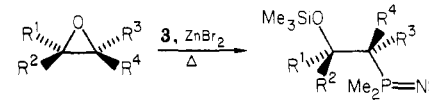
(15) Buynak, J. D.; Chu, S., manuscript in preparation.

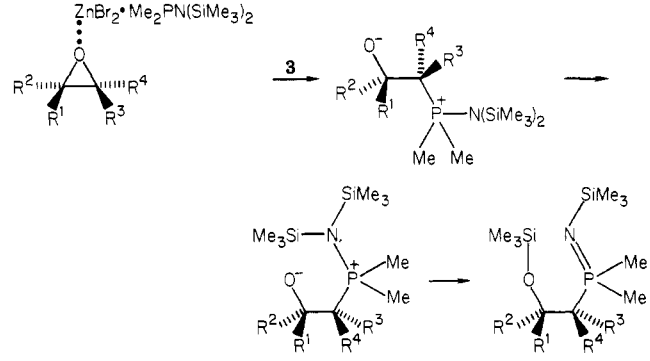
Table I. Products from the Reaction of 3 with Epoxides[a]



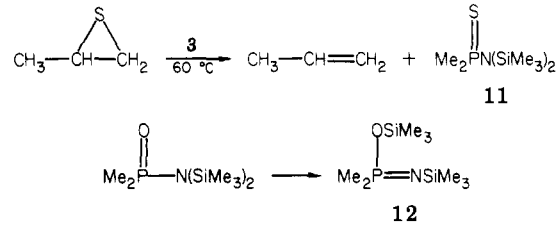
substituents	product	isolated yield, %	bp, °C (mm)
$R^1 = CH_3$; $R^2 = R^3 = R^4 = H$	4	81	57 (0.25)
$R^1 = R^3 = (CH_2)_4$; $R^2 = R^4 = H$	5	77	110 (0.4)
$R^1 = Ph$; $R^2 = Me$; $R^3 = R^4 = H$	6	75	132 (1.1)
$R^1 = Ph$; $R^2 = R^3 = R^4 = H$	7a	66%	130-140
$R^1 = R^2 = R^3 = H$; $R^4 = Ph$	7b	(7a:7b = 20:1)	(1.5)

[a] Satisfactory analytical data were obtained for all the compounds reported.

Scheme I



In contrast to the results with epoxides, episulfides react rapidly at 60 °C with (silylamino)phosphine **3**, producing the corresponding alkenes and the (silylamino)phosphine sulfide **11** in quantitative yield. This sulfide represents an unusual series of compounds since the corresponding phosphine oxides rearrange to the trimethylsiloxy phosphine imides[16] **12**.



11 12

Experimental Section

The [(trimethylsilyl)amino]phosphines **3** and **9** were prepared according to literature procedures.[8] Propylene sulfide and all epoxides, except α-methylstyrene oxide, were purchased from Aldrich Chemical Co. and distilled from CaH_2 prior to use. α-Methylstyrene oxide was prepared from MCPBA oxidation of α-methylstyrene (Dow Chemical Co.) and distilled from CaH_2 prior to use. Anhydrous zinc bromide was purchased from Aldrich and kept tightly sealed within a desiccator filled with $CaSO_4$. NMR spectra were recorded on an IBM/Bruker WP-200SY spectrometer using $CDCl_3$ as solvent. ^{31}P spectra used trimethyl phosphite as an external reference. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

General Procedure for the Reaction of (Silylamino)-phosphines 3 and 9 with Epoxides. A solution of **3** (7.0 g, 31.6 mmol) and cyclohexene oxide (3.72 g, 3.84 mL, 37.9 mmol) was

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prepared in a dry, bottle-cap type pressure tube under argon. Anhydrous $ZnBr_2$ (0.356 g, 1.6 mmol) was then added, the reaction vessel capped, and the slurry heated to 90 °C for 3 h. The contents of the flask were then transferred to a small, round-bottomed flask via a double-ended needle and distilled, bp 110 °C (0.4 mm).

Reaction of (Silylamino)phosphine 3 with Propylene Sulfide. **3** (3.03 g, 25.6 mmol) was added to propylene sulfide (2.0 g, 27.0 mmol) in a chilled (0 °C) sublimation device under argon. The reaction vessel was then allowed to stir at room temperature for 24 h. The excess propylene sulfide was then removed in vacuo and the product sublimed (90 °C (0.1 mm)) to produce a quantitative yield of a low-melting (25–30 °C) white solid.

Hydrolysis of Dimethyl[2-(trimethylsiloxy)cyclohexyl]-phosphine (Trimethylsilyl)imide (5). A solution of the phosphine imide (30 mmol) in acetic acid/H_2O/THF (10 mL/10 mL /10 mL) was allowed to stir at room temperature for 2–3 h and worked up by removing the solvent in vacuo and purifying the β-hydroxy phosphine oxide by flash chromatography (silica gel, 10% MeOH/CH_2Cl_2). The yield of white solid thus obtained was quantitative. The material could be recrystallized from ethyl acetate to yield plates with mp 155–156 °C.

Acknowledgment. We are grateful to the Robert A. Welch Foundation, the donors of the Petroleum Research Fund, administered by the American Chemical Society, and Research Corporation for supporting this work.

Registry No. **3**, 63744-11-6; **4**, 89618-64-4; **5**, 89618-65-5; **6**, 89618-66-6; **7a**, 89618-67-7; **7b**, 89618-68-8; **9**, 68437-96-7; **10**, 89618-69-9; **11**, 63744-10-5; $ZnBr_2$, 7699-45-8; *trans*-1-(dimethylphosphoryl)-2-hydroxy cyclohexane, 89618-70-2; propene, 115-07-1; methylthiirane, 1072-43-1; methyloxirane, 75-56-9; 7-oxabicyclo[4.1.0]heptane, 286-20-4; phenyloxirane, 96-09-3; 2-methyl-2-phenyloxirane, 2085-88-3.

Electrochemical Procedure for a Practical Preparation of Piperonal from Isosafrole

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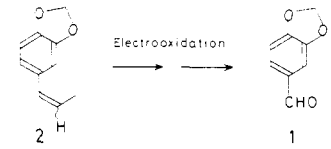
Piperonal (3,4-(methylenedioxy)benzaldehyde) (**1**), an important fragrance used as a soap additive and a synthetic precursor of Dopa, has been industrially prepared by ozonolysis[1] or chromic acid oxidation[2] of isosafrole **2**. Because of the environmental pollution associated with chromium species and the requirement of a large quantity of electricity and a carefully controlled reaction temperature (0–5 °C) for ozonolysis, these demerits have prompted us to develop a nonpolluting and more economical process. Recently, several attempts employing ruthenium tetroxide oxidation combined with m-periodate[3] and air-oxidation under γ-ray irradiation[4] have appeared.

On the other hand, an electrochemical oxidation would be a promising method for a piperonal synthesis from isosafrole because an electrooxidative bond cleavage of carbon–carbon double bonds is possible in principle. For example, an electrochemical conversion of cyclic enol acetates to keto esters in a MeOH–AcOH–$LiClO_4$ system has been achieved in satisfactory yield.[5] However, the direct bond cleavage method leads in some cases to overoxidation of the product aldehyde to give the corresponding carboxylic acid, as observed in the conversion of methyl eugenol to 3,4-dimethoxybenzoic acid.[6] A plausible reaction pathway for the electrochemical carbon–carbon bond cleavage would be initial oxygenation of the double bond to the corresponding glycol or a derivative followed by C–C bond cleavage. We describe a two-step electrochemical procedure that leads to a highly selective preparation of **1** from **2** via **3a**.



Epoxidation of olefins is efficiently achieved by the halide ion mediated electrochemical oxidation in which bromide ion is found to be the most useful.[7] Thus, **2** was subjected to the electrooxidation in MeCN–H_2O (7:2) containing 1.5–2.0 equiv of sodium bromide at room temperature. Platinum foils were employed as electrodes, and a constant current was passed (20 mA, 2.83 F/mol) in an undivided cell. The products were epoxide **4** (71%) and glycol **3a** (23%) after chromatography. Unlike the electrochemical epoxidation of isoprenoids, where the use of 0.1–1.0 equiv of sodium bromide was suitable to suppress the formation of the corresponding dibromide,[7] the use of more than 1 equiv of sodium bromide was required to provide **3a** and **4** in good yield. Dibromide **3c** was found to be spontaneously hydrolyzed to give **3b**, which collapsed to the epoxide **4** under the electrolysis conditions. Epoxide **4** is unstable under the reaction conditions and suffers partial hydrolysis resulting in the formation of **3a**.[8] After electrolysis, 1% aqueous sulfuric acid was added to the reaction mixture, which was stirred for 1 h to give **3a** (98%) as a diastereomeric mixture (25:75 by NMR). The glycol **3a** was subjected to acid-catalyzed dehydration (*p*-TsOH–benzene), affording ketone **5** (84%), which is a precursor of methyl Dopa.[8,9]

The efficiency of the epoxidation is dependent upon the pH of the reaction solution. In a MeCN–H_2O–NaBr system, the solution at the end of electrolysis was alkaline. On addition of a small amount of an acid, a mixture of **4**, **3a**, and the corresponding bromohydrin **3b** was obtained. Under more acidic conditions such as MeCN–H_2O–NaBr–H_2SO_4, **3b** was obtained quantitatively. The nature of the halide ion is also important in the product selectivity. In contrast to the successful results obtained with

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