pad and the solvent evaporated. The residue was distilled at 70–100 °C (0.25 mm) to give 4.90 g (27%) of a **7a–10a** mixture (11%, 13%, 51%, and 25%, respectively, by GLC). Part of this material was submitted to preparative GLC on a 13% OV-17 column (20 ft × $^3/_8$ in. Chromosorb W support) at 200 °C with a nitrogen flow of 120 mL/min. The first three products were collected separately and identified as **8a**, **10a**, and **9a** in the order of elution. **10a**: $^1$H NMR ($CDCl_3$) 5.7–6.0 (m, 2 H), 2.88 (d, 1 H, $J$ = 6 Hz), 1.9–3.0 (m, 3 H), 1.48 (s, 3 H), 1.43 (d, 3 H, $J$ = 7 Hz). Each one of the three products was separately hydrolyzed and recrystallized from water, the corresponding diacids were esterified with diazomethane, and the dimethyl estes **13–15** were distilled. The NMR data for each of these compounds and compound **12** can be found in Tables II and III.

**13**: IR (film) 1735, 1205 cm$^{-1}$; mass spectrum, $m/e$ (relative intensity) 226 (2) 195 (8), 194 (7), 166 (31), 107 (100). Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.94; H, 8.04.

**14**: IR (Nujol) 1720, 1660 cm$^{-1}$; mass spectrum, $m/e$ (relative intensity) 226 (2), 195 (5), 194 (6), 166 (17), 107 (100).

**15**: IR (Nujol) 1730, 1190 cm$^{-1}$; mass spectrum, $m/e$ (relative intensity) 226 (1), 195 (6), 194 (7), 166 (27), 107 (100).

Part of the initial mixture of anhydrides was hydrolyzed, recrystallized from water, and esterified with diazomethane. This product mixture was submitted to preparative GLC on a 13% OV-17 column (20 ft × $^3/_8$ in. Chromosorb W support) at 220 °C with a nitrogen flow of 120 mL/min. The fourth peak was collected and distilled at 80–90 °C (0.25 mm) to give **12**; IR (film) 1730, 1200 cm$^{-1}$; mass spectrum, $m/e$ (relative intensity) 226 (2), 195 (6), 194 (7), 166 (28), 107 (100). Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.68; H, 8.02.

**Comparative Reactions of *trans*-Piperylene with Maleic Anhydride and *N*-Phenylmaleimide.** A solution of maleic anhydride (98 mg, 1 mmol) and *trans*-piperylene (136 mg, 2 mmol) in benzene (2 mL) was prepared. A separate solution of *N*-phenylmaleimide (173 mg, 1 mmol) and *trans*-piperylene (136 mg, 2 mmol) in benzene (2 mL) was also prepared at the same time. The two solutions were then immediately set up for reflux and heated simultaneously in the same preheated oil bath for 10 min. The two reaction systems were rapidly cooled to room temperature, and the benzene and excess *trans*-piperylene were removed by evaporation. The two products were dissolved in $CDCl_3$ and analyzed by NMR: first reaction, product (**9c**)/maleic anhydride (**5c**) ratio of 3.0:1; second reaction, product (**9d**)/*N*-phenylmaleimide (**5d**) ratio of 1.9:1.

**Acknowledgment.** We thank FAPESP (Brazil) for a graduate research fellowship (to M.G.C.) and the CNPq (Brazil)–NAS (Washington) bilateral program in chemistry for financial aid. We also thank the Nucleo de Pesquisas de Produtos Naturais (Brazil) for some of the NMR and mass spectra and the IQ-USP, São Paulo, where this work was carried out.

**Registry No.** **4**, 1574-41-0; **5a**, 616-02-4; **5b**, 3120-04-5; **5c**, 108-31-6; **5d**, 941-69-5; **5e**, 41702-49-2; **6**, 2004-70-8; **7a**, 82112-10-5; **7c**, 35438-82-5; **7c** diacid, 40469-18-9; **7d**, 63427-62-3; **7e**, 82112-11-6; **8a**, 82112-12-7; **8e**, 82112-13-8; **9a**, 82112-14-9; **9a** diacid, 82166-42-5; **9c**, 35438-81-4; **9c** diacid, 40469-16-7; **9d**, 69979-93-7; **9e**, 82112-15-0; **10a**, 82112-16-1; **10e**, 82112-17-2; **12**, 82112-18-3; **13**, 82112-19-4; **14**, 82166-40-3; **15**, 82166-41-4.

# Silyl Phosphites. 21. A New Method for the Synthesis of L-Ascorbic Acid 2-*O*-Phosphate[1] by Utilizing Phosphoryl Rearrangement

Mitsuo Sekine, Tetsuaki Futatsugi, and Tsujiaki Hata*

*Department of Life Chemistry, Nagatsuta, Midoriku, Yokohama 227, Japan*

Friedrich Cramer

*Abteilung Chemie, Max-Planck-Institut für Experimentelle Medizin, 3400 Göttingen, FRD*

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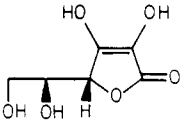
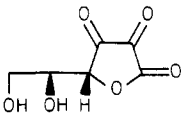
A stablilized form of vitamin C, L-ascorbic acid 2-*O*-phosphate (**1**), was successfully synthesized by a new method via a fully trimethylsilylated L-ascorbic acid (**4**) that was prepared in high yield by silylation of L-ascorbic acid with hexamethyldisilazane. Bromination of **4** gave an adduct (**6**) that was isomerized during distillation to a trimethylsilylated bicyclic half acetal (**8**) of dehydroascorbic acid. Addition of tris(trimethylsilyl) phosphite (TMSP) to **8** gave carbonyl addition compounds **9a** and **9b**, which underwent thermal rearrangement to give a mixture of bis(trimethylsilyl)-3,5,6-tris-*O*-(trimethylsilyl)-L-ascorbic acid 2-*O*-phosphate (**10**) and its 3-*O*-isomer **13** in the ratio of 88:12. Treatment of the mixture with cyclohexylamine in methanol gave selectively tricyclohexylammonium salt of L-ascorbic acid 2-*O*-phosphate in 53% yield.

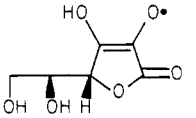
L-Ascorbic acid is well-known to be susceptible toward thermal and oxidative degradation, and hence various stable derivatives of L-ascorbic acid have been searched for and prepared in a number of laboratories.[2-10] Among these derivatives L-ascorbic acid 2-*O*-phosphate (**1**) has the promising property of generating antiscorbutic activity in vivo through enzymic degradation to free L-ascorbic acid. Cutolo and Larizza[4] first reported the synthesis of **1** by the reaction of 5,6-isopropyridene-L-ascorbic acid with phos-



L-ascorbic acid



**2**



**3**

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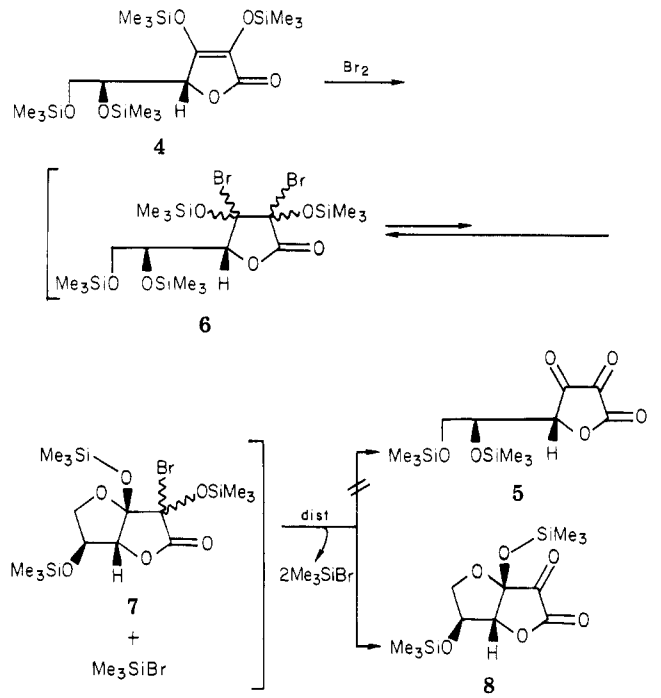
phorus oxychloride in pyridine. The structure of 1 was described originally as the 3-*O*-phosphate in the reports of Cutolo[4] and other groups.[5-8] Very recently, Radford[12] has definitely determined its structure as the 2-*O*-phosphate by means of $^{13}C$ NMR. At the same time, Jernow[11] reported the structural determination of vitamin C phosphate formed via acid hydrolysis of an ascorbic 3-*O*-phosphinate by employing X-ray and UV spectral analysis. Because of the pharmaceutical interest of 1, several modifications of Cutolo's procedure for the synthesis of 1 have been reported. However, these methods involve multistep purification procedures for separation of 1 from the simultaneously formed byproducts, and the yields of 1 were only moderate.

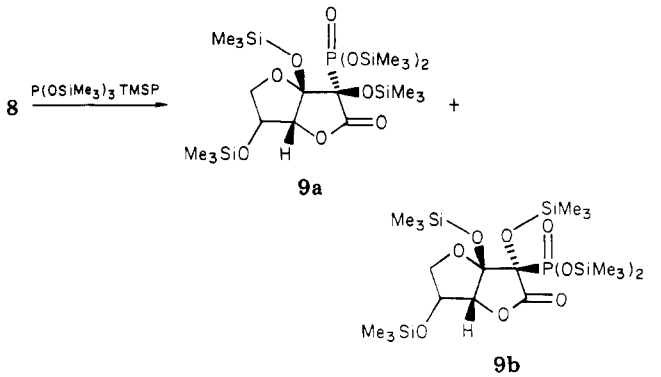
In this paper, we report a new method for the synthesis of 1 by introducing organosilicon chemistry.

## Results and Discussion

It is well-known that in a series of oxidative processes in vivo L-ascorbic acid is reversibly metabolized to dehydro-L-ascorbic acid (2) via monodehydro-L-ascorbic acid (3).[2] The redox reactions among these three ascorbates are closely related to revelation of their biological activity as vitamin C.[2] In connection with the synthesis of 1, our attention was focused on the α-diketo structure of 2, which might be available for introduction of a phosphoryl group into the 2-carbonyl oxygen by the reaction with tervalent phosphorus compounds.[13] However, 2 is so unstable that it has been obtained only as a dimer by the oxidation of 1 with iodine or quinone.[14-18] Monomeric 2 exists not only in an aqueous medium but also as a bicyclic hydrate species of 3,6-anhydro-L-xylohexulono-1,4-lactone hydrate[19] or dehydroascorbic acid dihydrate.[20,21] Therefore, 5,6-protected derivatives of 2 were required for our purpose as the starting materials. On the other hand, it was reported that the reaction of α-diketones with TMSP gave 1:1 carbonyl adducts or 2-[(trimethylsilyl)oxy]vinyl phosphates depending on the substituents of the α-diketones.[22,23] Initially, we considered that the reaction of a 5,6-protected derivative of 2 with TMSP would give selectively a 2-*O*-phosphorylated product since the 2-carbonyl group was expected to be the most reactive and capable of 1,2-addition[24] of TMSP followed by a C → O phosphoryl rearrangement which would lead to the 2-*O*-phosphate derivative. However, the problem in our project is that oxidation of 5,6-protected derivatives such as L-ascorbic acid 5,6-acetonide led to racemization at the $C^4$ carbon via an enol form, thereby losing activity as vitamin C.[20] Therefore, a method to avoid the racemization will be required. Considering that 2 tends to form a ring close to a half acetal,[14-19] the configuration of which is rigidly fixed, we tried to protect 2 with a movable protecting group, i.e., the trimethylsilyl group. A tetrakis-trimethylsilylated derivative (4) of L-ascorbic acid was prepared readily in 90% yield by silylation with hexamethyldisilazane. This compound was obtained on a large scale by distillation, and during the distillation no racemization was observed. In order to obtain a bis-trimethylsilylated derivative (5) of 2, the oxidation of 4 with bromine was performed. The bromination of 4 in $CH_2Cl_2$ proceeded smoothly. The $^1H$ NMR of the reaction mixture showed that a 1:1 bromine adduct (6) was mainly formed and only a small amount of trimethylsilyl bromide was formed. This suggests that the equilibrium between 6 and the bicyclic lactone 7 might exist and be substantially in favor of the former at room temperature. After removal of the solvent, distillation of the residual oil gave a yellow liquid, which soon crystallized. The product was negative for the Beilstein test, and its elemental analysis suggested that the α,β-diketo ester 5 was formed. Its NMR spectrum showed that the proton at $C^4$ was not shifted as compared with the NMR spectrum of 4, while the protons at $C^5$ and $C^6$ were shifted to lower field. The $^{13}C$ NMR spectrum of the product showed that one peak appeared in the region of keto carbonyl groups at 186 ppm and a new peak corresponding to an acetal carbon appeared at 99.8 ppm. Furthermore, its mass spectrum suggested a monomeric structure having $m/e$ 245 ($M^+ - SiMe_3$). From these results, we concluded that the product was not 5 but a bis-trimethylsilylated half ketal (8).

Since the 3-carbonyl function was masked by an intermolecular ketalization, the reaction of 8 with TMSP was

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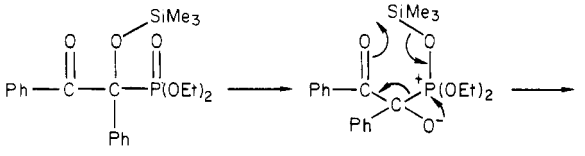
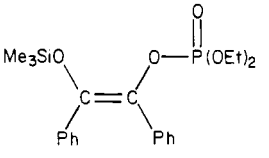
expected to take place regioselectively at the 2-carbon. When TMSP was added to **8** in $CH_2Cl_2$ at 0 °C, the addition reaction proceeded smoothly, and the $^{31}P$ NMR spectrum of the reaction mixture showed a ca. 1:1 mixture of two products having chemical shifts of +4.42 and +19.92 ppm. From considerations of the CPK model, TMSP can attack on the carbonyl group of **8** equally from both the upper and lower sides. The two products were assigned to the diastereoisomers of the addition compound. Kiss[25] reported that the reaction of L-ascorbic acid with 3-(hydroxymethyl)indol under acidic conditions gave diastereomers of a bicyclic 2-substituted lactone derivative having a similar structure to that of **9**. It seems that the adducts of the 2-carbonyl group of dehydroascorbic acid are more stable as bicyclic lactones than lactones having an open side chain. It is also known that the reaction of sodium L-ascorbate with benzyl chloride gave a similar $C^2$-benzylated bicyclic lactone.[26] The structure of **9** was finally confirmed by its $^1H$ NMR and $^{13}C$ NMR spectra. The $^1H$ NMR showed that the two signals of the $C^6$ methylene appeared at 3.76 and 4.32 ppm as doublets. The protons at $C^6$ and $C^5$ appeared at higher field than those of **4**, while the $C^4$ protons of the isomers were separated at 4.11 and 4.78 ppm. The distinct difference between the chemical shifts of the isomeric $C^4$ protons might be attributed to the interaction between the $C^4$ protons and the phosphoryl group, which was enhanced when they were in a 1,3-diaxial relation. On the other hand, the $^{13}C$ NMR showed clearly two kinds of bicyclic $C^5$ and $C^6$ carbons, which appeared generally in the region of more than 85 and 75 ppm, respectively. These results strongly suggest the formation of the diastereomers of the carbonyl adduct.

Next, we examined the conversion of the carbonyl addition product **9** into the fully trimethylsilylated derivative (**10**) of **1**. In a previous paper, we reported that diethyl α-benzoyl-α-[(trimethylsilyl)oxy]benzylphosphonate (**11**)

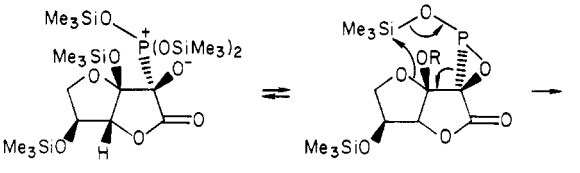


**11**

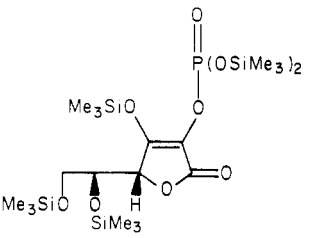


**12**

underwent thermal rearrangement to give (*Z*)-diethyl 1-phenylvinylphosphate **12** in high yield.[23] Therefore, we expected that **9** would undergo a similar rearrangement under certain conditions to give **10**. As expected the thermal rearrangement of **9** proceeded to afford **10** when **9** was melted at 60 °C and then allowed to react with TMSP at 160 °C. In this thermal rearrangement, one of the isomers (**9a**) disappeared faster than the other (**9b**). The diastereomer formed by attack of TMSP from the back side could be expected to undergo the pyrolysis more effectively than the other since in the case of the former a six-membered-ring transition state could be easily considered for the rearrangement. Therefore, **9a** was determined as the isomer formed by attack of TMSP from the back side.

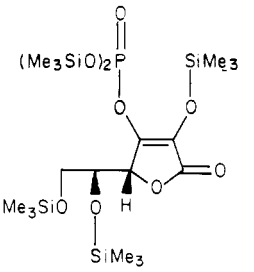


R = $SiMe_3$



**10**

Since **9a** and **9b** might be in equilibrium with the starting materials of **8** and TMSP at elevated temperatures, **9b** could be converted to **10** via a route of **9b** → **8** → **9a** → **10** under the conditions where the thermal rearrangement occurred. The progress of this rearrangement could be followed by the NMR spectra of the reaction mixture. The proton at $C^4$ appeared as a sharp quartet at 4.67 ppm, having a coupling constant $J_{H^4\text{-}P}$ = 2.8 Hz. The clear quartet suggested no isomerization at the $C^4$ carbon during the rearrangement. At about the end of the rearrangement, a new quartet peak at 5.08 ppm appeared. This peak was assigned to an isomer of 3-*O*-phosphate derivative **13** as compared with Jernow's report[11] that the



**13**

$C^4$ proton of 3-*O*-[bis(morpholine)phosphinyl]-5,6-*O*-isopropylidene-L-ascorbate, the structure of which was confirmed by X-ray analysis, appeared at 4.99 ppm. It is found that the quartet peak at 5.08 ppm increased gradually when the mixture was further heated for a prolonged time after the rearrangement was completed. This result implied that the 2-*O*-phosphate **10** was isomerized to the 3-*O*-phosphate **13** at temperatures where the rearrangement occurred. So that the isomerization could be avoided, the heating was continued at 105 °C for 5 h, which was found to be the best conditions after several screenings. Thus, a mixture of **10** and **13** was obtained in the ratio 88:12. The distillation of the reaction mixture gave a mixture of **10** and **13** in the ratio 79:21 owing to the above

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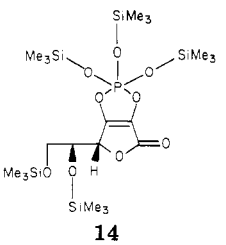
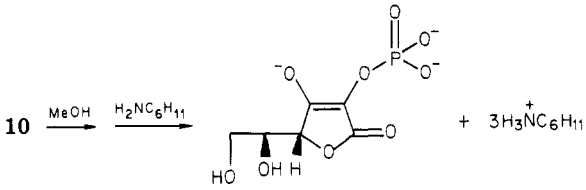
(27) Rearrangement of **10** → **13** may occur via an intramolecular migration of phosphoryl group as follows:



**14**

A similar type of equilibrium between **10** and **14** has already been discussed in a previous paper.[23]

mentioned isomerization during the distillation. There-




1

fore, the reaction mixture was directly treated with methanol for removal of the trimethylsilyl groups without distillation procedure. The additon of cyclohexylamine in methanol to the reaction mixture followed by recrystallization gave the tricyclohexylammonium salt of 1 in 53% yield selectively. The structure of the isolated salt could be confirmed by its melting point and $^1H$ NMR and $^{13}C$ NMR spectra, which were compatible with the data of an authentic sample[11] and the other salts of 1 reported.[5,12]

## Experimental Section

Melting points and boiling points are uncorrected. $^1H$ NMR spectra were recorded on a JNM-PS-100 spectrometer using benzene ($\delta$ 7.24) as the internal standard. IR spectra were obtained with a Hitachi 260-50 spectrophotometer. $^{31}P$ NMR spectra were recorded on a JEOL PS-100 FT spectrometer at 40.50 MHz using 85% $H_3PO_4$ as the internal standard. $^{13}C$ NMR spectra were measured on a JEOL PS-100 FT spectrometer. $^{13}C$ chemical shifts were referenced to internal $CDCl_3$ ($\delta$ 77.0) and reported in parts per million downfield from $Me_4Si$.

L-Ascorbic acid was purchased from Nakarai Chemical Co. Ltd. Hexamethyldisilazane was kindly supplied by Chisso Co. Ltd. and was purified by distillation before use. Trimethylsilyl chloride was donated by Toray Silicon Co. Ltd. and purified by distillation over calcium hydride.

Elemental analysis was performed by Mikiko Aoki.

**2,3,5,6-Tetrakis-*O*-(trimethylsilyl) Ascorbate (4).** L-Ascorbic acid (101 g, 0.573 mol) was dissolved in 700 mL of dry pyridine. Hexamethyldisilazane (10 mL) was added to the solution, whereupon a white precipitate appeared immediately. The mixture was gradually heated to 100 °C, at which ammonia gas was evolved. To the mixture was further added 246 mL of hexamethyldisilazane at 100 °C so slowly that vigorous stirring could be continued. After the addition was completed, the resulting solution was heated at 100 °C for an additional 2 h. After the solution was cooled to room temperature, the solvent and the excess reagent were removed in vacuo, and distillation of the residue gave 218 g (82%) of 4: bp 131–143 °C (0.01 mmHg); $^1H$ NMR ($CDCl_3$) $\delta$ 0.17 (s, 9 H, $Me_3Si$), 0.23 (s, 9 H, $Me_3Si$), 0.40 (s, 18 H, $Me_3Si$), 3.53 (d, 1 H, $J_{H^5\text{-}H^6}$ = 6.8 Hz, $H_a^6$), 3.56 (d, 1 H, $J_{H^5\text{-}H^6}$ = 7.2 Hz, $H^6_b$), 3.85 (dt, 1 H, $J_{H^4\text{-}H^5}$ = 1.6 Hz, $H^5$), 4.58 (d, 1 H, $H^4$); IR (NaCl) 1255, 1370, 1685, 1775, 2900, 2960 $cm^{-1}$; $^{13}C$ NMR ($CDCl_3$) $\delta$ −1.1, −0.3, 0.3, and 0.6 (Me–Si), 62.5 ($C^6$), 69.7 ($C^5$), 75.4 ($C^4$), 120.9 ($C^3$), 154.4 ($C^4$). Anal. Calcd for $C_{18}H_{40}O_6Si_4$: C, 46.51; H, 8.67. Found: C, 46.28; H, 8.30.

**Preparation of Bicyclic Lactone 8.** To a solution of 4 (23.9 g, 51.4 mmol) in 50 mL of dry $CH_2Cl_2$ at 0 °C was added dropwise bromine (2.63 mL, 51.4 mmol) in 8 mL of dry $CH_2Cl_2$. After the mixture was stirred at room temperature for 1 h, 5.6 mL (51.4 mmol) of dimethyl phosphonate was added at 0 °C, and the mixture was kept at room temperature overnight. The solution changed from orange to red. The solvent was removed in vacuo, and the residue was distilled to afford 12 g (73%) of 8: bp 99–101 °C (0.01 mmHg); mp 52–56 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 0.25 (s, 9 H, $Me_3Si$), 0.31 (s, 9 H, $Me_3Si$), 4.19 (d, 2 H, $J_{H^5\text{-}H^6}$ = 3.3 Hz, $H^6$), 4.53 (dt, 1 H, $J_{H^4\text{-}H^5}$ = 1.0 Hz, $H^5$), 4.67 (d, 1 H, $H^4$); IR (NaCl) 1155, 1220, 1262, 1812 (C=O), 2250, 2950 $cm^{-1}$; $^{13}C$ NMR ($CDCl_3$) $\delta$ −0.3 and 1.0 (Me–Si), 74.5 ($C^4$), 78.2 ($C^6$), 89.2 ($C^5$), 99.8 ($C^3$), 158.0 ($C^1$), 186.6 ($C^2$); mass spectrum, $m/e$ 245 ($M^+ - SiMe_3$). Anal. Calcd for $C_{12}H_{22}O_6Si_2$: C, 45.26; H, 6.97. Found: C, 45.43; H, 6.88.

Table I. Spectral Data of 9a and 9b

| | | 9a | 9b |
|---|---|---|---|
| $^1H$ NMR ($CDCl_3$) | H-4 | 4.11 (s) | 4.78 (s) |
| | H-5 | 4.32 (m) | 4.32 (m) |
| | H-6 | 3.76 (d, $J$ = 3.2 Hz) | 4.00 (d, $J$ = 2.7 Hz) |
| $^{13}C$ NMR ($CDCl_3$) | C-4 | 71.03 | 74.19 |
| | C-5 | 89.81 | 87.65 |
| | C-6 | 76.65 | 76.47 |
| $^{31}P$ NMR ($CDCl_3$) | | +19.92 | +4.42 |

**Reaction of Bicyclic $\alpha$-Keto Lactone 8 with TMSP.** To a solution of 514 mg (1.61 mmol) of 8 in 4 mL of dry $CH_2Cl_2$ at 0 °C was added 0.534 mL (1.61 mmol) of TMSP by a syringe. The solution turned immediately from yellow to colorless. After the solvent was removed in vacuo, the residue was dissolved in $CDCl_3$ and measured by $^1H$ NMR, $^{13}C$ NMR, and $^{31}P$ NMR. The spectral data of the products **9a** and **9b** are summarized in Table I.

**Preparation of 10.** To the bicyclic $\alpha$-keto lactone 8 (3.48 g, 10.9 mmol) melted at 60 °C was added 3.6 mL (10.9 mmol) of TMSP. The mixture turned light yellow. The mixture was heated at 105 °C. After 5 h, 8 disappeared and a mixture of **10** and **13** was formed in the ratio 88:12 ($^1H$ NMR). Distillation gave a mixture of **10** and **13** in the ratio 79:21, bp 141–143 °C (0.02 mmHg).

**10**: $^1H$ NMR ($CDCl_3$) $\delta$ 0.13 (s, 9 H, $Me_3SiOC^5$), 0.17 (s, 9 H, $Me_3SiOC^6$), 0.38 (s, 18 H, $Me_3SiOP$), 0.43 (s, 9 H, $Me_3SiOC^3$), 3.58 (d, 1 H, $J_{H^5\text{-}H^6}$ = 7 Hz, $H^6_a$), 3.62 (d, 1 H, $J_{H^5\text{-}H^6}$ = 7 Hz, $H^6_b$), 3.91 (dt, 1 H, $J_{H^4\text{-}H^5}$ = 1.4 Hz, $H^5$), 4.71 (dd, 1 H, $J_{P\text{-}H^4}$ = 2.8 Hz, $H^4$); IR (NaCl) 1684 $cm^{-1}$; $^{31}P$ NMR ($CDCl_3$) $\delta$ +24.04 (d, $J_{P\text{-}H^4}$ = 2.7 Hz).

**13**: $^1H$ NMR ($CDCl_3$) $\delta$ 0.13 (s, 9 H, $Me_3SiOC^5$), 0.18 (s, 9 H, $Me_3SiOC^6$), 0.35 (s, 9 H, $Me_3SiOC^2$), 0.38 (s, 18 H, $Me_3SiOP$), 3.55 (d, 1 H, $J_{H^5\text{-}H^6}$ = 7.2 Hz, $H^6_a$), 3.57 (d, 1 H, $J_{H^5\text{-}H^6}$ = 7.2 Hz, $H^6_b$), 4.01 (dt, 1 H, $J_{H^4\text{-}H^5}$ = 1.6 Hz, $H^5$), 5.16 (dd, 1 H, $J_{P\text{-}H^4}$ = 2.8 Hz, $H^4$); IR (NaCl) 1775 $cm^{-1}$; $^{31}P$ NMR ($CDCl_3$) $\delta$ +24.22 (d; the $J$ value could not be assigned owing to the overlapping of the peakes of **10** and **13**).

**Tricyclohexylammonium Salt of L-Ascorbic Acid 2-*O*-Phosphate (1).** The above mentioned reaction mixture (1.456 g) containing **10** and **13** (88:12) was dissolved in 50 mL of ether and 8 mL of methanol. After the solution was kept at room temperature for 1 h, 2 mL (17 mmol) of cyclohexylamine was added. The solution was cooled to 0 °C. The precipitate was collected by filtration, washed with three 10-mL portions of ether, and dried over $P_4O_{10}$ in vacuo to give 1.64 g (53%) of the title compound: mp 173–175 °C (lit.[11] mp 173–176 °C); IR (KBr) 1615, 1732 $cm^{-1}$; $^1H$ NMR ($D_2O$–$Me_4Si$ (external reference)) $\delta$ 1.2–2.2 (m, 30 H, cyclohexylamine), 3.20 (m, 3 H, CH–N), 3.76 (d, 2 H, $J_{H^6H^{6'}\text{-}H^5}$ = 6.6 Hz, $H^6$ and $H^{6'}$), 4.07 (dt, 1 H, $J_{H^5\text{-}H^6}$ = 5.6 Hz, $J_{H^5\text{-}H^{6'}}$ = 7.6 Hz, $J_{H^4\text{-}H^5}$ = 2.0 Hz, $H^5$), 4.53 (br s, 1 H, $H^4$); $^{13}C$ NMR ($D_2O$–dioxane, 2:1, v/v) $\delta$ 24.8 ($C^3$ and $C^5$ of cyclohexylamine), 25.3 ($C^4$ of cyclohexylamine), 31.3 ($C^2$ and $C^6$ of cyclohexylamine), 51.0 ($C^1$ of cyclohexylamine), 63.3 ($C^6$), 70.4 $C^5$), 79.0 ($C^4$), 113.6, 113.4 (d, ($^{13}C$–$^{31}P$), $C^2$), 176.7 ($C^3$), 178.1 ($C^1$). Anal. Calcd for $C_{24}H_{48}O_9N_3P\cdot H_2O$: C, 50.43; H, 8.82; N, 7.35. Found: C, 50.56; H, 8.95; N, 7.68.

The $^{13}C$ NMR spectrum of the authentic sample tripotassium salt given by Takeda Chem. Co. Ltd. is as follows: ($D_2O$) $\delta$ 63.3 ($C^6$), 70.5 ($C^5$), 79.4 ($C^4$), 113.2, 113.3 (d ($^{13}C$–$^{31}P$), $C^2$), 176.3 ($C^3$), 178.1 ($C^1$).

**Registry No.** 1, 82134-96-1; 4, 55517-56-1; 8, 82134-97-2; **9a**, 82149-58-4; **9b**, 82189-07-9; **10**, 82134-98-3; **13**, 82134-99-4; L-ascorbic acid, 50-81-7.