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DIISOPROPYLSILYL DITRIFLATE AND DI-*tert*-BUTYLSILYL DITRIFLATE NEW REAGENTS FOR THE PROTECTION OF DIOLS

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Summary Diisopropylsilyl ditriflate and di-*tert*-butylsilyl ditriflate, each available from the appropriate dialkylchlorosilane and triflic acid, react with 1,2-, 1,3-, and 1,4-diols usually at 25°C in the presence of 2,6-lutidine to provide the corresponding dialkylsilylene derivatives in high yield. These derivatives, which are readily deprotected under mild conditions, can be utilized for selective reactions of polyhydroxy compounds

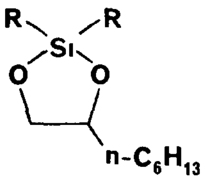
Several years ago, in connection with the study of the total synthesis of erythronolide A,[1] we investigated the use of di-*tert*-butyldichlorosilane as a reagent for the protection of diols as their di-*tert*-butylsilylene derivatives We found di-*tert*-butyldichlorosilane to be relatively unreactive under standard silylation conditions and because of this to be of limited applicability In agreement with these findings is the report of Trost[2] that only under forcing conditions (65-95°C, catalytic 1-hydroxybenzotriazole, CH_3CN or DMF) does di-*tert*-butyldichlorosilane react with even relatively unhindered diols to provide the silylene derivatives The recent use of trialkylsilyl triflates[3] for the silylation of hindered alcohols under mild conditions suggested a solution to this problem In this paper, we describe the synthesis and use of diisopropylsilyl ditriflate and di-*tert*-butylsilyl ditriflate, two highly effective reagents for the protection of a wide range of 1,2-, 1,3-, and 1,4-diols under mild conditions.

Diisopropylsilyl ditriflate and di-*tert*-butylsilyl ditriflate are conveniently prepared as follows Diisopropylchlorosilane,[4] 4 5g (30 mmol), stirred at 22°C in a flask equipped with a dropping funnel and gas outlet tube connected to a bubbler was treated with 8 0 ml (13 5g, 90 mmol) of triflic acid over 20 min After an additional 10 min at 22°C, the dropping funnel was replaced with a reflux condenser, and the mixture was heated at reflux for 2 h Direct distillation from the reaction flask afforded 9.6g (77%) of diisopropylsilyl ditriflate as a pale yellow liquid, b p. 61.5 - 63.5° (0.30 mm), ρ 1.406, pmr ($CDCl_3$, 270 MHz) δ 1.24

$$R_2SiHCl + 2\,CF_3SO_3H \longrightarrow R_2Si(OSO_2CF_3)_2 + H_2 + HCl$$

(12H, d, J=7.6 Hz), 1.59 (2H, septet, J=7.6 Hz) Similar treatment of di-<u>tert</u>-butylchlorosilane[2,5] 5 3g (30 mmol), afforded 9.4g (71%) of di-<u>tert</u>-butylsilyl ditriflate as a pale yellow liquid, b.p 73 5 - 74 5° (0.35 mm), ρ 1 358, pmr ($CDCl_3$, 80 MHz) δ 1.25 (s).[6] Both reagents were stored under dry argon.

The formation of diisopropylsilylene compounds **1a**-**7a** was readily effected by treatment of a solution of diol (1 0 equiv, <u>ca</u> 0.5 <u>M</u>) and 2,6-lutidine (3.0 equiv) in $CDCl_3$ at 0°C with diisopropylsilyl ditriflate (1.2 equiv) and warming to 25°C Analysis by pmr after 5 min revealed the essentially quantitative formation of the silylene derivative. It is noteworthy that even pinacol reacts to form **4a** rapidly at 25°C The five- and seven-membered diisopropylsilyl derivatives of diols are rapidly cleaved during tlc separation on silica gel. In contrast, the six-membered ring derivatives of 1,3-diols **5a** and **6a** are stable to tlc Most of the diisopropylsilyl derivatives could be isolated by passing the reaction mixture through a plug of Florisil (5% ethyl acetate-hexane as eluant)[7] Although derivatives **1a**, **3a**, and **4a** are extremely sensitive to water (5 1 THF-water at pH 7 for 1 h at 25°C resulted in hydrolysis to hydroxysilyl mono ethers **8a**), the six-membered ring derivatives showed much greater stability (**6a** being recovered unchanged after exposure to 5 1 THF-water at pH's 4 - 10 for 12 h at 25°C), the stability of **7a** was intermediate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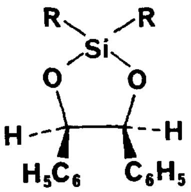
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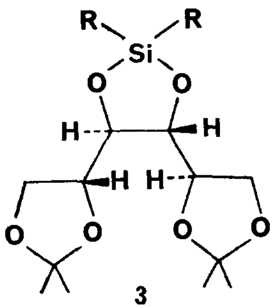
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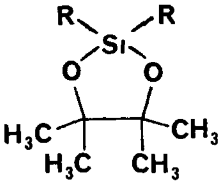
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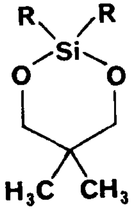
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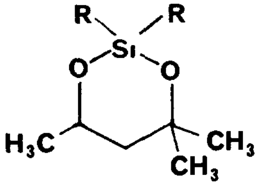
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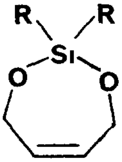
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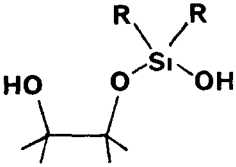
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a, R = <u>i</u>-Pr

b, R = <u>t</u>-Bu

Although di-*tert*-butylsilyl ditriflate is somewhat less reactive than the diisopropyl analogue, reaction with various diols (1.0 equiv) in the presence of 2,6-lutidine (3.0 equiv) in $CDCl_3$ with di-*tert*-butylsilyl ditriflate (1.2 equiv) (conveniently monitored by pmr) occurs at a reasonable rate at 0 - 25°C After plug filtration through silica gel (10% ethyl acetate-hexane as eluant) ethers **1b** and **2b** of 1,2-diols were obtained in 84 and 83% yield, respectively Similarly, products **5b** and **6b** from 1,3-diols were obtained at 25°C in 95 and 96% yield, respectively. The ether **7b** from a 1,4-diol was prepared at 25°C in 79% yield. The more hindered silylene **3b** was available in 88% yield after 24 h at 50°C Even the ditertiary diol pinacol afforded **4b** (70%) after 24 h at 100°C

Di-*tert*-butylsilylene derivatives of 1,3- and 1,4-diols were found to be considerably more stable than those of 1,2-diols The 1,2-diol derivatives **1b** - **3b** undergo rapid hydrolysis under basic conditions (5 1 THF-pH 10 buffer, 22°C, 5 min) to form hydroxysilyl mono ethers of the parent diol Hydrolysis of 1,2-diol derivatives **1b** - **3b** in 5 1 THF-water at pH 7 was relatively slow, requiring several hours. The six- and seven-membered cyclic derivatives **5b** and **7b**, in comparison, were unaffected at pH's 4 - 10 and 22°C over several hours

Deprotection of the dialkylsilylene derivatives can be accomplished satisfactorily with aqueous hydrofluoric acid in acetonitrile [8,9] Treatment of diisopropylsilylene derivative **6a** with 1 7 48% aqueous HF-acetonitrile for 15 min at 25°C afforded the deprotected diol in 95% yield. Similarly, the di-*tert*-butyl derivative **6b** was deprotected in 88% yield after 12 h at 25°C.

The ease of formation, stability toward hydrolysis, and mild conditions for deprotection of the dialkylsilylene derivatives of 1,3- and 1,4-diols suggest that these protecting groups will be useful in the selective transformation of polyhydroxy compounds For example, pyridinium dichromate oxidation[10] (2.5 equiv PDC, CH_2Cl_2, 27 h, 25°C) of a 1 1 mixture of *cis*-4-*tert*-butylcyclohexanol and **6b** resulted in the near quantitative formation of 4-*tert*-butylcyclohexanone and recovery of **6b** Similarly, tosylation (3 equiv TsCl, pyridine, 27 h, 25°C) of the same mixture provided the corresponding tosylate and recovered **6b**, each in over 90% yield [11,12]

References and Notes

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7. Satisfactory infrared and pmr spectral data have been obtained for the silylene derivatives reported herein.
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9. Trost has described the use of pyridinium hydrofluoride for this purpose.[2]
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11. For the use of a hindered bifunctional disiloxane for 1,3-diol protection, see M. J. Robins and J. S. Wilson, *J. Am. Chem. Soc.*, **103**, 932 (1981).
12. This research was assisted financially by the National Institutes of Health.

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