magnetically stirred under N_2 in THF (0.2 mL) at room temperature. After 3 days, a large portion of **1c** remained unchanged, and dimer **2** appeared as the only product in a significant amount (TLC, S_7). A small amount of deoxy derivative **1d** was also present. Relative proportions of materials were unchanged after 1 week.

Acknowledgment. Thanks are due to Dr. D. P. Lin, J. Hsu, and S. Grunfeld for measurements of the NMR, mass, and GC/MS spectra, partly supported (NMR) by Biomedical Research Support Grant SO-7-RR-05529 from the National Institutes of Health. Sublimed magnesium was generously furnished by Dow Chemical Co.

Registry No. **1a**, 69832-48-0; **1a** triflate, 79068-95-4; **1b**, 79068-96-5; **1c**, 79068-97-6; **1d**, 26293-58-3; **2**, 79068-98-7; **3a**, 4099-85-8; **3a** triflate, 70209-11-9; **3b**, 38838-06-1; **3c**, 32471-59-3; **3c** triflate, 79068-99-8; **3d**, 79083-82-2; **4**, 79069-00-4; **5a**, 4026-28-2; 5b, 4026-27-1; 6b, 61252-75-3; DL-**7a**, 22323-83-7; DL-**7a** triflate, 79120-24-4; DL-**7b**, 23737-52-2; **8**, 79069-01-5; **9**, 79069-02-6; **10**, 79101-57-8; **11a**, 33861-65-3; **11b**, 79069-03-7; *N*-phthaloyl-L-phenylalanine, 5123-55-7; lithium *N*-phthaloyl-L-phenylalaninate, 79069-04-8; 1,2:5,6-di-*O*-isopropylidene-3-*C*-methylene-α-D-ribohexofuranose, 21665-16-7; 1,2:5,6-di-*O*-isopropylidene-3-deoxy-3-oxo-α-D-ribohexofuranose, 2847-00-9; 2',3'-*O*-isopropylideneuridine, 362-43-6.

Notes

Synthetic Methods and Reactions. 104.[1] Silylations with in Situ Generated Trimethylsilyl Triflate Reagent Systems

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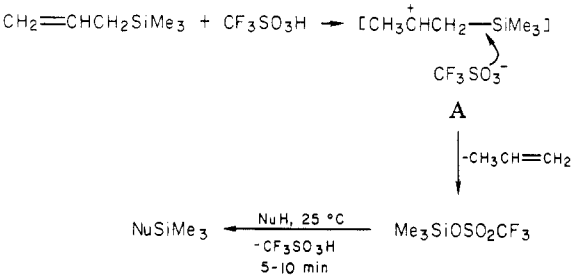
The trimethylsilyl group is a widely used protecting group for carboxylic acids, alcohols, mercaptans, carbonyl, and nitro compunds.[2] Recently, its usefulness was also demonstrated as an activating group, for example, for carboxylic acids, in the transesterification of carboxylic esters under essentially neutral conditions.[3] Although there are numerous reports on different silylation methods, most of them involve basic conditions.[2,4] Recently, silylations under acidic conditions with hexamethyldisiloxane have been reported. This method, however, necessitates high temperatures and long reaction times. Previously, we have reported a very mild silylation method with chlorotrimethylsilane/lithium sulfide.[4]

We also carried out extensive studies in an attempt to prepare stable trivalent silicenium ions such as $(CH_3)_3Si^+$. So far these attempts have been unsuccessful, due to the high affinity of the developing silicenium ion toward fluorine and oxygen containing donors, even in sysems of low nucleophilicity where related carbocations are stable. In these systems we instead observed quenching of the incipient silicenium ions by fluoride, fluorosulfonate, or triflate ions present in the medium. Trimethylsilyl trifluoromethanesulfonate (triflate)[6] is a powerful silylating reagent. However, it is expensive and highly moisture sensitive, thus making it difficult to handle. As a continuation of our interest in the development of in situ equivalents of trimethylsilylating agents, we have now studied the silylation of carboxylic acids, alcohols, phenols, mercaptans, and ketones with trimethylsilyl triflate, generated in situ from allyltrimethylsilane and trifluoromethanesulfonic acid.

Scheme I[a]



[a] NuH = RC(=O)OH or ROH.

Trimethylsilylation of carboxylic acids and alcohols took place almost instantaneously when 2–3 drops of triflic acid was added to a mixture of the substrate (10 mmol) and allyltrimethylsilane (12 mmol) in carbon tetrachloride solution, with the immediate liberation of propene (Scheme I). Recently, Morita et al.[7] have also reported a similar approach, using *p*-toluenesulfonic acid catalyst. However, under their reaction conditions silylation of alcohols and carboxylic acids was achieved only by heating at 70–80 °C for 1.5–3.0 h. The authors suggested that an ionic tosylated intermediate related to A may be the active silylating agent in the reactions. We believe, under our reaction conditions, the silylations are taking place via in situ formed trimethylsilyl triflate, which must be causing the instantaneous silylations in the case of carboxylic acids and alcohols. The formation of trimethylsilyl triflate from allyltrimethylsilane and triflic acid was confirmed by ^1H, ^{13}C, and ^{29}Si NMR spectroscopy.

The wide utility and general superiority of the present silylating system have been further demonstrated by the silylaton of mercaptans and thiophenols, albeit at a higher

(1) For part 103, see G. A. Olah, S. C. Narang, and L. D. Field, *J. Org. Chem.* **46**, 3727 (1981).
(2) (a) C. B. Reese, *Prot. Groups Org. Chem.*, 95–143 (1973); (b) J. F. Klebe, *Acc. Chem. Res.*, **3**, 299 (1970); (c) B. E. Cooper, *Chem. Ind.*, 194 (1978).
(3) G. A. Olah, S. C. Narang, G. F. Salem, and B. G. B. Gupta, *Synthesis*, 142 (1981).
(4) G. A. Olah, B. G. B. Gupta, S. C. Narang, and R. Malhotra, *J. Org. Chem.*, **44** 4272 (1979), and references cited therein.
(5) H. W. Pinnick, B. S. Bal, and N. N. Lajis, *Tetrahedron Lett.*, 4261 (1978).
(6) G. Simchen and W. Kober, *Synthesis*, 259 (1976).
(7) T. Morita, Y. Okamoto, and H. Sakurai, *Tetrahedron Lett.*, 835 (1980).
(8) H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **34**, 2324 (1969).
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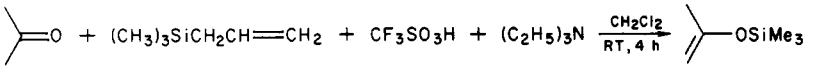
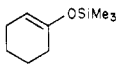
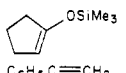
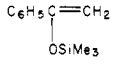
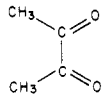
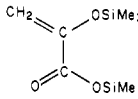
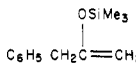
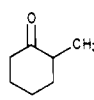
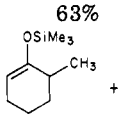
Table I. Preparation of Trimethylsilyl Ethers. Thioethers and Esters form the Corresponding Alcohol or Thiol or Carboxylic Acids

substrate	product	% yield	obsd bp or mp, °C (torr)	lit bp or mp, °C (torr)
cyclohexanol	cyclohexyl trimethylsilyl ether	95	42-43 (50)	58-60 (12)[4]
benzyl alcohol	benzyl trimethylsilyl ether	98	65-66 (4.5)	92 (19)[4]
phenol	phenyl trimethylsilyl ether	95	65 (10)	72 (14)[4]
α-toluenethiol	trimethylsilyl thiobenzoxide	95	110-113 (2.5)	
benzenethiol	trimethylsilyl thiophenoxide	95	92-95 (3.5)	
m-toluenethiol	trimethylsilyl thio-*m*-tolyl ether	90	85-87 (1.0)	
benzoic acid	trimethylsilyl benzoate	70	43-45 (0.75)	97-99 (10)[7]
acetic acid	trimethylsilyl acetate	91	102-104 (760)	102-103 (760)[9]
indole-2-carboxylic acid	trimethylsilyl indole-2-carboxylate	98	133.3 dec	

Table II. Preparation of Enol Silyl Ethers form Ketones



substrate	products	% yield[a]	mp/bp, °C (torr) (lit. mp/bp, °C (torr))[ref]
		81	70-72 (18-19) (74-75 (20))[6]
		72	48-49 (15) (158-159 (760))[8]
		76	89-92 (12-13) (89-91 (12))[8]
		64	78-79 (13-14) (74 (12))[6]
		73[b]	100-110 (14-15) (97-104 (10))[6]
		84[b]	79-85 (20) (90-93 (20))[8]

[a] Yield of isolated product. [b] Isomer ratio calculated from ^{1}H NMR in CCl_4. [c] Reaction time 10 h. [d] Reaction time 1 h. [e] Purity of the product as determined by ^{1}H NMR is <95%.

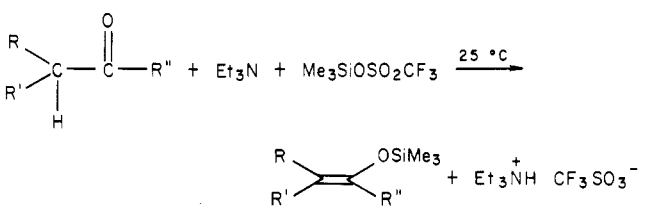
temperature. Thus, when a mixture of allyltrimethylsilane, mercaptan, and a catalytic amount of triflic acid was heated under reflux in carbon tetrachloride for 8–10 h, high yields of the corresponding trimethylsilyl thio derivatives were obtained.

The silylation of ketones under similar catalytic reaction conditions did not proceed. In these cases an equimolar amount of triflic acid was needed to completely perform the silylating reagent. To this in situ formed reagent was added a mixture of ketone and triethylamine by a dropping funnel, resulting in a facile reaction to give the desired silyl enol ethers (Scheme II, Table II), facile O-silylation being responsible for pushing the reaction in the forward direction.

Formation of silyl enol ethers takes place at room temperature, wheras previous reports[6] suggested use of preformed trimethylsilyl triflate at 80 °C (refluxing benzene). However, the present method employs methylene chloride, a more polar solvent.

For generation of trimethylsilyl triflate in situ, various other silanes can also be used. Phenyltrimethylsilane behaved smilarly, although silylations proceeded slower.

Scheme II



Similarly tetramethylsilane or trimethysilane also reacted with triflic acid to form trimethylsilyl triflate.

The silylations can be carried out in a variety of other solvents such as chloroform, methylene chloride, or acetonitrile, further underscoring the utility of the method. The above results clearly indicate the versatility and broad scope of the in situ method of forming trimethylsilyl triflate.

$$(CH_3)_4Si \xrightarrow{CF_3SO_3H} CH_4 + [(CH_3)_3Si^+CF_3SO_3^-] \rightarrow (CH_3)_3SiOSO_2CF_3$$

In conclusion, we have found versatile, economical, and

mild conditions for silylations with in situ formed trimethylsilyl triflate reagent.

Experimental Section

Typical Procedure for the Preparation of Trimethylsilyl Benzoate. To a mixture of benzoic acid (1.22 g, 10 mmol) and allyltrimethylsilane (1.4 g, 12 mmol) in carbon tetrachloride (20 mL) solution was added with good stirring 2–3 drops of triflic acid under nitrogen atmosphere. Immediate reaction took place, resulting in the dissolution of benzoic acid and the copious liberation of propene. the ^{1}H NMR of this clear solution revealed that the reaction was complete. To this solution 2–3 drops of pyridine was added to neutralize triflic acid and the evaporation of solvent afforded crude trimethylsilyl benzoate, which was distilled under reduced pressure to obtain pure product, bp 43–45 °C (0.75 mm) (lit. bp 97–99 °C (100 mm)), 1.4 g, 71% yield.

General Procedure for the Preparation of Trimethylsilyl Enol Ethers. To an ice-cold solution of allyltrimethylsilane (1.5 mol equiv per mole of carbonyl group) in dry methylene chloride contained in a three-neck round-bottom flask was carfully added trifluoromethanesulfonic acid (1.5 mol equiv per mole of carbonyl group) under a nitrogen atmosphere. An exothermic reaction took place, generating trimethylsilyl triflate. The solution was stirred for 15–20 min during which time it was allowed to warm up to room temperature. From a dropping funnel, a solution of triethylamine (2 mol equiv per mole of carbonyl group) and the carbonyl compound in methylene chloride was slowly added to the above solution. After the addition was complete, the reeaction mixture was stirred for the required time. After the completion of the reaction, solvent was removed in vacuo. This resulted in two layers. The lighter product layer was separated and the denser layer was extracted with carbon tetrachloride. the extract was combined with product layer. Carbon tetrachloride was removed in vacuo and the resulting crude product was purified by fractional distillation under reduced pressure.

Acknowledgment. Support of our work by the National Science Foundation is gratefully acknowledged.

Registry No. Cyclohexanone, 108-94-1; cyclopentanone, 120-92-3; acetophenone, 98-86-2; 2,3-butanedione, 431-03-8; 1-phenyl-2-propanone, 103-79-7; 2-methylcyclohexanone, 583-60-8; (1-cyclohexen-1-yloxy)trimethylsilane, 6651-36-1; (1-cyclopenten-1-yloxy)-trimethylsilane, 19980-43-9; trimethyl[(1-phenylethenyl)oxy]silane, 13735-81-4; 1,1'-[[1,2-bis(methylene)-1,2-ethanediyl]bis(oxy)bis(trimethyl)silane, 31411-71-9; trimethyl[[(1-phenylmethyl)ethenyl]-oxy]silane, 59021-31-7; trimethyl[(1-methyl-2-phenylethenyl)oxy]silane, 43108-63-0; trimethyl[(6-methyl-1-cyclohexen-1-yl)oxy]silane, 19980-33-7; trimethyl[(2-methyl-1-cyclohexen-1-yl)oxy]silane, 19980-35-9; cyclohexanol, 108-93-0; benzyl alcohol, 100-51-6; phenol, 108-95-2; α-*oluenethiol, 100-53-8; benzenethiol, 108-98-5; *m*-toluenethiol, 108-40-7; benzoic acid, 65-85-0; acetic acid, 64-19-7; indole-2-carboxylic acid, 1477-50-5; cyclohexyl trimethylsilyl ether, 13871-89-1; benzyl trimethylsilyl ether, 14642-79-6; phenyl trimethylsilyl ether, 1529-17-5; trimethylsilyl thiobenzoxide, 14629-67-5; trimethylsilyl thiophenoxide, 4551-15-9; trimethylsilyl thio-*m*-tolyl ether, 79255-62-2; trimethylsilyl benzoate, 2078-12-8; trimethylsilyl acetate, 2754-27-0; trimethylsilyl indole-2-carboxylate, 79255-63-3; allyltrimethylsilane, 762-72-1; triflic acid, 1493-13-6.

Regio- and Stereoselective Cleavage of Epoxides with Cyanoborohydride and Boron Trifluoride Etherate[1]

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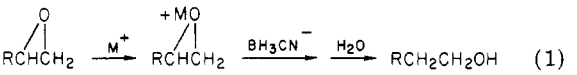
As expected for SN_2 processes, nucleophilic hydride transferring reagents attack epoxides at the less substituted position to afford the more highly substituted alcohol.[2] With electrophilic hydride reagents (i.e., BH_3, AlH_3, etc.), reverse opening is often observed to produce the less substituted alcohol, but mixtures usually result.[2,3]

We envisioned that the unique acid stability of cyanoborohydride[4] might be advantageous for regioselective opening of epoxides in which the less substituted alcohol would be preferentially produced by trapping of hydride at the site best able to accomodate a carbonium ion[5] (eq 1). Activation of epoxides toward nucleophilic attack by



(1)

complexation with a Lewis acid is required since this moiety is essentially inert toward cyanoborohydride in neutral or basic media.[6] After considerable exploration the combination of boron trifluoride etherate in dry THF was demonstrated to offer the most reliable and convenient reductive system. Other acidic reagents including protonic examples (H_2SO_4, CF_3COOH resulted in considerable polymerization of the epoxides while others (i.e., $SbCl_3$) were reduced by the reagent. Results using the BH_3CN^-/BF_3 system for a variety of epoxides are presented in Table I and illustrate important features of the conversions. First, the ring severing is highly regioselective and afford predominately the less substituted alcohols (entries 5–9) in good to excellent yields. Reactive epoxides (i.e., styrene oxide, cyclohexane oxide) are effectively reduced at 5 °C (ice bath), while aliphatic examples require ambient or refluxing (66 °C) temperatures for adequate conversions. In addition, the stereoselectivity greatly favors anti cleavage since 1-methylcyclohexane oxide (entry 5) produced almost exclusively *cis*-2-methylcyclohexanol resulting from backside diaxial opening of the intermediate complexed ring.

Limitations of the reductions were uncovered in that certain aryl and other epoxides prone to rearrangement gave products steming from migration. Thus, *trans*-stilbene oxide (entry 10) afforded predominately 2,2-diphenylethanol resulting from initial BF_3 induced rear-

(1) Presented in part at the 172nd National Meeting of the American Chemical Society, San Francisco, CA, Sept 1976; ORG 173.

(2) Discussions of reductive opening of epoxides with hydride reagents are contained in the following: (a) Hajos, A. "Complex Hydrides"; Elsevier: New York, 1979. (b) Carey, F. A.; Sundberg, R. J. "Advanced Organic Chemistry, Part B"; Plenum Press: New York, 1977. (c) House, H. O. "Modern Synthetic Reactions", 2nd ed.; W. A. Benjamin: Menlo Park, CA, 1972; pp 103–104.

(3) Electrophilic reagents which have been utilized with varying degrees of success include the following: (a) AlH_3; Yoon, N. M.; Brown, H. C.; Lamke, W. E. *J. Org. Chem.* **1967**, *32*, 537. Lansbury, P. T.; Sharf, D. J.; Pattison, V. A. *ibid.* **1968**, *32*, 1748. Ashby, E. C.; Cooke, B. J. *J. Am. Chem. Soc.* **1968**, *90*, 1625. (b) Diisobutylaluminum hydride; Zakharkin, L. I.; Khorlina, I. M. *Izv. Akad. Nauk. SSSR, Ser. Khim.* **1965**, 862. Lenox, R. S.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1973**, *95*, 957. (c) BH_3 + BF_3; Brown, H. C.; Yoon, N. M. *Chem. Commun.* **1968**, 1549. Lyle, R. E.; Krueger, W. E. *J. Org. Chem.* **1967**, *32*, 2873. (d) BH_3 + BH_4^-; Brown, H. C.; Yoon, N. M. *J. Am. Chem. Soc.* **1968**, *90*, 2686. Bessiere-Chretien, Y.; Meklati, B. *Tetrahedron Lett.* **1971**, 621. Fu, Y. L.; Bobek, M. *J. Org. Chem.* **1980**, *45*, 3836.

(4) For reviews of cyanoborohydride chemistry, see (a) Hutchins, R. O.; Natale, N. R. *Org. Prep. Proced. Int.* **1979**, *11*, 201. (b) Lane, C. F. *Synthesis* **1975**, 131.

(5) The use of acid in combination with cyanoborohydride to generate ions which are trapped by hydride has been successful for conversions of triphenylmethanol to triphenylmethane [Kreevoy, M. M.; Johnston, D. C. *Croat. Chem. Acta* **1973**, *45*, 511], acetals to ethers [Horne, D. A.; Jordan, A. *Tetrahedron Lett.* **1978**, 1357], and the conversion of certain reactive allylic alcohols to alkenes [Hutchins, R. O.; Kandasamy, D. *J. Org. Chem.* **1975**, *40*, 2530].

(6) Hutchins, R. O.; Kandasamy, D.; Maryanoff, C. A.; Masilamani, D.; Maryanoff, B. E. *J. Org. Chem.* **1977**, *42*, 82.

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