mL of 10% H_2SO_4 was added. The organic layer was separated, and the aqueous layer was extracted with two 100-mL portions of ether. The combined organic layers were dried over $MgSO_4$ and evaporated to give the crude product, which was chromatographed on 100 g of neutral Al_2O_3. The third and fourth 50-mL fractions yielded 9.03 g (81%) of light yellow liquid upon rotary evaporation and oil pump evacuation: ^1H NMR ($CDCl_3$) δ 0.97 (3 H, s), 1.47 (8 H, s, broad), 1.75–2.25 (2 H, complex m).

Reaction of 1a–c with Me_3CuLi_2. General Procedure. The 25-mL round-bottom flasks used were rinsed with concentrated HNO_3, water, concentrated NH_4OH, water, Alconox solution, distilled water, and acetone. They were dried in an oven (120 °C) and, immediately before use, in a Bunsen burner flame. After the flasks were cooled in a desiccator over P_2O_5, small stirring bars were added to them, they were charged with 0.25–0.50 mmol of substrate and flushed with N_2, and a rubber septum was fastened on with wire. A 30-μL volume of *n*-nonane was injected (all substances were weighed to the nearest 0.1 mg), and the flask was cooled to dry ice temperature under N_2. Ether (2.5 mL, freshly distilled from sodium benzophenone ketyl) was added by syringe followed after 30 min by 2.5 mL of 0.30 M ethereal Me_3CuLi_2, prepared at −20 °C from 570 mg of CuI (Alfa, ultrapure grade) and 7.2 mL of 1.25 M ethereal MeLi–LiBr diluted to 10.0 mL. After being stirred rapidly for several minutes at −70 °C, the reaction mixtures were warmed to their final temperatures and stirred for 20 h. Quenching with 1 mL of 2 M HCl (deoxygenated with N_2) and drying the ether layer by passing it through a Pasteur pipet plugged with a small wad of cotton and containing a layer of anhydrous Na_2SO_4 over Celite gave the product solution which was analyzed by GLC. With a 30 mL/min flow rate of He, a 10 ft × 0.25 in. 5% OV101 on Chromosorb WHP (80–100 mesh) column at 40 °C gave the following retention times (min) for the products: **4** (3.3), **5** (4.6), **6** (5.2), **7** (6.6), **8** (7.7), and standard (22).

Photolysis of 9. A mixture of 26.5 mg of **9** and 21.1 mg of *n*-nonane in 2.5 mL of Et_2O was treated with 2.5 mL of 0.30 M Me_3CuLi_2. It was placed in a 0 °C isopropyl alcohol bath and photolyzed using the 350-nm bulbs in a Rayonet reactor. After 24 h, TLC showed some **9** still present. GLC analysis showed <1% **4**, 14% **5**, 3% **6**, 4% **7**, and <1% **8**. In a companion experiment which contained no cuprate, <1% **4**, 25% **5**, 14% **6**, 15% **7**, and <1% **8** were measured. In the absence of light, none of these products were observed when Me_3CuLi_2 and **9** were stirred together.

Control experiments were performed as closely as possible to the "General Procedure". The amounts of LiI required by the stoichiometries in Table I (entries 2, 3, and 8) were added to the flasks containing the substrates in a glove bag under dry N_2, and the experiments were continued in the usual way.

Aliquots (0.25 mL) of a red solution of diazocyclohexane prepared from 176 mg of cyclohexanone hydrazone, 256 mg of Ag_2O, and 74 mg of $MgSO_4$ in 1.0 mL of alumina-dried xylenes were added to the reagents prepared from 140 mg of CuI and 0.6, 1.2, and 1.8 mL of 1.25 M MeLi. The final volumes were adjusted to 4 mL with Et_2O.

To 1.5 mL of 0.38 M 1-cyclohexenyllithium in 10 mL of Et_2O was added 3.0 mL of 0.50 M Me_3CuLi_2. The reaction mixture was stirred at room temperature under Ar; aliquots were removed and quenched with deoxygenated (N_2) water.

A mixture of 34.4 mg of 1-methylcyclohexene and 28.8 mg of *n*-nonane was treated with 3.0 mL of 0.25 M Me_3CuLi_2. After a day it was quenched with 1 mL of deoxygenated 2.0 M HCl. GLC analysis showed 98% starting material and <1% methylenecyclohexane. Similar treatment of a mixture of 32.3 mg of methylenecyclohexane and 29.6 mg of *n*-nonane gave 97% starting material and <1% isomeric olefin.

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Registry No. **1a**, 4545-18-0; **1b**, 49661-10-1; **1c**, 72003-87-3; **4**, 110-83-8; **5**, 108-87-2; **6**, 1192-37-6; **7**, 591-49-1; **8**, 590-66-9; **9**, 40571-39-9; cyclohexanone azine, 4278-87-9; Me_3CuLi_2, 61278-42-0.

Bis(trimethylsilyl) Monoperoxysulfate: Convenient Baeyer–Villiger Oxidant

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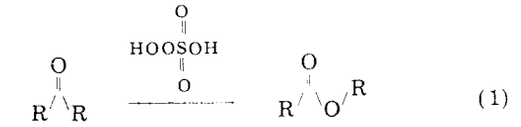
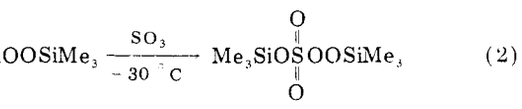
Caro's acid or monoperoxysulfuric acid serves as a common reagent for the conversion of ketones into esters (eq 1), a reaction known as Baeyer–Villiger oxidation.[3] Some



(1)

of the short comings of this important reagent in preparative applications include (i) the use of aqueous conditions, (ii) the presence of strong acid, and (iii) undesirable side reactions. Since the bis(trimethylsilyl) derivative of Caro's acid is known[4] and conveniently prepared via the reaction of sulfur trioxide with bis(trimethylsilyl) peroxide at −30 °C (eq 2), we explored the potential and utility of



(2)

this interesting substance as a Baeyer–Villiger oxidant. The solubility of this reagent in nonprotic and nonpolar media such as methylene chloride and the bis(trimethylsilyl)-buffered sulfuric acid product that is formed after oxygen transfer constitute obvious advantages over the Caro's acid reagent.

Indeed, as the results in Table I confirm, bis(trimethylsilyl) monoperoxysulfate exhibits a great propensity as a Baeyer–Villiger oxidant. From the examples listed in the table, the reagent displays general scope, since aliphatic, aromatic, acyclic, and cyclic ketones are readily oxidized to their corresponding esters in high yield.

Some of the limitations of this novel oxidant are that α,β-unsaturated ketones react sluggishly, that double bonds are oxidized, and that aralkyl ketones such as *p*-bromoacetophenone are hydrolyzed to the corresponding phenols. Furthermore, as with Caro's acid, the oxidation of cyclohexanone proves problematic, affording the ω-hydroxy acid. However, in general the bis(trimethylsilyl) monoperoxysulfate affords higher yields and purer product than Caro's acid. The preparation of the potentially useful silyl reagent and the general procedure for the Baeyer–Villiger oxidation are described below.

Experimental Section

Melting points are uncorrected. NMR spectra were run on a Hitachi Perkin-Elmer R-24B instrument and IR spectra on a Perkin-Elmer Model 283 infracord. Solvents and reagents were purified according to standard literature procedures.

Bis(trimethylsilyl) Monoperoxysulfate.[4] A 100-mL, three-necked, round-bottomed flask, equipped with a pressure-equalizing addition funnel, Teflon spinbar, rubber septum cap, and a three-way stopcock, was attached to a nitrogen manifold. Under a nitrogen atmosphere, a solution of 1.0 g (5.6 mmol) of bis(trimethylsilyl) peroxide[5] in 20 mL of dry CH_2Cl_2 was syringed

(1) NIH Career Development Awardee (1975–1980).
(2) Graduate Fellow in the Support for University Biomedical Education (SUBE) program sponsored by NIH-MBS.
(3) Hassall, C. H. *Org. React.* **1957**, *9*, 73.
(4) Bressel, B.; Blaschette, A. *Z. Anorg. Allg. Chem.* **1970**, *377*, 182.

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Table I. Yields of Baeyer-Villiger Product

ketone	ester	% yield[a]
4-heptanone	*n*-propyl butyrate	96
benzophenone	phenyl benzoate	83
p-bromoacetophenone	*p*-bromophenol	98
fluorenone	2'-hydroxydiphenyl 2-acid lactone	74
adamantanone	4-oxahomoadamantan-5-one	88
tetracyclone	tetraphenyl-α-pyrone	76

[a] Isolated yields except *n*-propyl butyrate which was quantitated by VPC.

into the above reaction vessel. After the mixture was cooled to −30 °C, with stirring, 25 mL of a 0.2 M solution of SO_3 in CH_2Cl_2 was added dropwise from the addition funnel over a period of 15 min, carefully maintaining the reaction mixture at −30 °C. The reaction progress was monitored by NMR, observing the appearance of the trimethylsilyl product signal as a singlet at δ 0.40. After completion of the reaction (ca. 30 min), this solution was utilized directly for the Baeyer–Villiger oxidations.

General Method for the Baeyer–Villiger Oxidation. To the above prepared solution of the bis(trimethylsilyl) monoperoxysulfate was added 1.4 mmol of the ketone to be oxidized in 10 mL of dry CH_2Cl_2 at −30 °C over 45 min. The reaction mixture was allowed to warm up to room temperature (ca. 30 °C) and kept at this temperature for 8 h. To the mixture was added 5 mL of H_2O, the solution was transferred to a separatory funnel, the aqueous layer was syphoned off, and the CH_2Cl_2 layer was washed with 2 × 20 mL of 5% aqueous $NaHCO_3$ and dried over $MgSO_4$. Rotoevaporation of the solvent and purification of the crude product by silica gel chromatography gave the results summarized in Table I. The identity of the products was confirmed by comparison of physical constants and IR and NMR spectra with the authentic materials.

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Registry No. Bis(trimethylsilyl) monoperoxysulfate, 23115-33-5; 4-heptanone, 123-19-3; benzophenone, 119-61-9; *p*-bromoacetophenone, 99-90-1; fluorenone, 486-25-9; adamantanone, 700-58-3; tetracyclone, 479-33-4; *n*-propyl butyrate, 105-66-8; phenyl benzoate, 93-99-2; *p*-bromophenol, 106-41-2; 2'-hydroxydiphenyl 2-acid lactone, 2005-10-9; 4-oxahomoadamantan-5-one, 21898-84-0; tetraphenyl-α-pyrone, 33524-67-3; bis(trimethylsilyl) peroxide, 5796-98-5; SO_3, 7446-11-9.

(5) Davis, A. G.; Cookson, P. G.; Farzel, N. *J. Organomet. Chem.* **1974**, *99*, C-31.

A Mild Method of Hydrolysis of 2,4-Dialkoxy-6-substituted Pyrimidines to 6-Substituted Uracils

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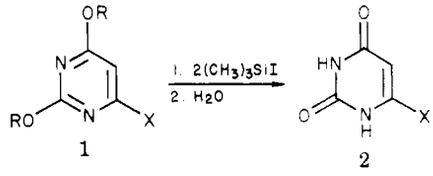
We are interested in synthesizing certain 6-substituted uracils for our enzymatic studies of new antitumor agents. Many of these compounds have been prepared by acid hydrolysis of the corresponding 2,4-dialkoxy-6-substituted pyrimidines;[1-3] however, the conditions required to hydrolyze these substituted pyrimidines can sometimes lead to decomposition of the products. For example, the hydrolysis of 2,4-dimethoxy-6-pyrimidinesulfonic acid with 0.1 N HCl was reported[1] to cause at least partial hydrolysis with loss of bisulfite to give barbituric acid. In our hands, under a wide variety of hydrolytic conditions, essentially all barbituric acid and little uracil-6-sulfonic acid was obtained. Acid hydrolysis of 2,4-dimethoxy-6-fluoropyrimidine was reported[2] to result in complete loss of fluoride ion, yielding only barbituric acid. The synthesis of 6-fluorouracil was later reported[4] in moderate yield by hydrogenolysis of 2,4-dibenzyloxy-6-fluoropyrimidine. Uracil analogues sometimes are protected as their corresponding 2,4-dialkoxypyrimidines in order to carry out chemical transformations on the ring. It is, then, important to have mild methods of deprotection to obtain the newly functionalized uracils. Since uracil-6-sulfonic acid was one of the compounds we wished to study, a mild hydrolysis method of 2,4-dimethoxy-6-pyrimidinesulfonic acid was sought. As a result of this investigation, we wish to report a general method of hydrolysis of 2,4-dialkoxy-6-substituted pyrimidines in high yields.

Table I. Hydrolysis of 2,4-Dialkoxypyrimidines by Iodotrimethylsilane[a]



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compd no.	R	X	reaction time	% yield[b]
1a	CH_3	SO_3H	<15 min	quantitative
1b	CH_3	SO_2NH_2	<15 min	94
1c	CH_3	Cl	10 h	quantitative
1d	CH_3	CH_3	<15 min	87
1e	CH_3	F	6 h	67
1f[c]	C_2H_5	H	1 h	35
			2 h	53
			14 h	quantitative
1g	$C_6H_5CH_2$	Cl	<15 min	quantitative

[a] All reactions were carried out in dry sulfolane at 40–45 °C. [b] The yields are for crude products which had IR spectra identical with pure compounds. [c] There was no shift in the methylene resonances in the NMR spectrum during the reaction.

Iodotrimethylsilane has been used for the dealkylation of esters,[5] ethers,[6] and phosphate esters.[7] We have found that this reagent smoothly dealkylates 2,4-dialkoxypyrimidines to uracils in high yields. Table I summarizes the compounds used in the study, reaction times, and yields of products obtained.

It is interesting to note that unlike the reported aqueous acid hydrolysis of 2,4-dimethoxy-6-pyrimidinesulfonic acid,[1], iodotrimethylsilane dealkylation produces uracil-6-sulfonic acid in quantitative yield. The lower yield ob-

(1) S. B. Greenbaum and W. L. Holmes, *J. Am. Chem. Soc.*, **76**, 2899 (1954).
(2) J. P. Horowitz and A. J. Tomson, *J. Org. Chem.*, **26**, 3392 (1961).
(3) S. B. Greenbaum, *J. Am. Chem. Soc.*, **76**, 6052 (1954).
(4) I. Wempen and J. J. Fox, *J. Med. Chem.*, **7**, 207 (1964).
(5) M. E. Jung and M. A. Lyster, *J. Am. Chem. Soc.*, **99**, 968 (1977).
(6) M. E. Jung and M. A. Lyster, *J. Org. Chem.*, **42**, 3761 (1977).
(7) G. M. Blackburn and D. Ingleson, *J. Chem. Soc., Chem. Commun.*, 870 (1978).

0022-3263/79/1944-4970$01.00/0