2,5-Bis(ethylenedioxy)-12-(2-thienyl)-12-deuterio-(*E*)-dodec-9-ene (13a). To 20.23 g (32 mmol) of phosphonium salt **12**[3] in 75 mL of tetrahydrofuran (THF) was added 16 mL of phenyllithium (2 N solution) at 0 °C under a nitrogen atmosphere. At −70 °C 5.0 g (32 mmol) of **11a** in 5 mL of THF was added, followed by a second equivalent of C_6H_5Li. The mixture was maintained between −30 and −50 °C during 1 h, after which 7 mL of ethanol was added. The mixture was poured into water from which the product was extracted with petroleum ether. Chromatography yielded 4.7 g (40%) of **13a:** NMR (CCl_4) δ 1.23 (s, 3, diox CH_3), 1.65 (s, 4, $O_2CCH_2CH_2CO_2$), 3.79 (s, 8, 4 OCH_2), 5.20–5.50 (m, 2, C**H**=C**H**), 6.61–7.04 (m, 3, ThH).

2,5-Bis(ethylenedioxy)-12-(3-thienyl)-(*E*)-tridec-9-ene (13b) was prepared as for **13a:** yield 42%; NMR (CCl_4) δ 1.22 (d, 3, $CHCH_3$), 1.23 (s, 3, diox CH_3), 1.62 (s, 4, $O_2CCH_2CH_2CO_2$), 2.48–3.17 (m, 1, $CHCH_3$), 3.88 (s, 8, 4 OCH_2), 5.20–5.40 (m, 2, C**H**=C**H**), 6.77–7.28 (m, 3, ThH).

2-[6-(2-Thienyl)-6-deuterio-(*E*)-hex-3-enyl]-3-methylcyclopent-2-enone (14a). A mixture of 2.75 g (7.5 mmol) of diketal **13a,** 30 mL of 0.5 N HCl, and 60 mL of ethanol was refluxed under a nitrogen atmosphere of 1.5 h, whereupon the solution was rendered alkaline with 1 g of sodium hydroxide and refluxed for another 1.5 h. After evaporation of the ethanol and extraction with pentane, chromatography yielded 1.7 g (88%) of pure product **14a:** NMR (CCl_4) δ 1.30–2.52 (m, 13, aliphatic H), 2.52–3.04 (m, 1, CHD), 5.20–5.47 (m, 2, C**H**=C**H**), 6.45–7.20 (m, 3, ThH). Anal. Calcd for $C_{16}H_{19}DOS$: C, 73.51; H, 8.10. Found: C, 73.45; H, 7.82.

2-[6-(3-Thienyl)-(*E*)-hept-3-enyl]-3-methylcyclopent-2-enone (14b) was prepared as for **14a:** yield 80%; NMR (CCl_4) δ 1.18 (d, 3, $CHCH_3$), 1.67–2.52 (m, 13, aliphatic H), 2.52–3.00 (m, 1, $CHCH_3$), 5.12–5.37 (m, 2, C**H**=C**H**), 6.72–7.17 (m, 3, ThH). Anal. Calcd for $C_{17}H_{22}OS$: C, 74.40; H, 8.08. Found: C, 74.25; H, 8.18.

2-[6-(2-Thienyl)-6-deuterio-(*E*)-hex-3-enyl]-3-methylcyclopent-2-enol (1a). 2-[6-(3-Thienyl)-(*E*)-hept-3-enyl]-3-methylcyclopent-2-enol (3). At −30 °C 2 mmol of $LiAlH_4$ was added in small portions to a solution of 2.0 mmol of ketone **14a** or **14b.** After 1 h 0.5 N sodium hydroxide was added. The mixture was filtered, dried, and concentrated at low temperature. Due to their susceptibility to dehydration, the cyclopentenols were used immediately for cyclization experiments.

5-Methyl-11-deuterio-12,13[*b*]-thienotricyclo[7.4.0.0^{4,8}]tridec-4-ene (2a). To a solution of 500 mg of unsaturated alcohol **1a** in 10 mL of dichloromethane at −95 °C, 1.2 equiv of $SnCl_4$ was added dropwise. After 1 h the solution was poured into saturated ammonium chloride and the product was extracted with dichloromethane. Chromatography yielded 230 mg of product (50%): NMR (CCl_4) δ 1.60 (s, 3, CH_3), 1.80–2.65 (m, 14, aliphatic H), 6.66–6.95 (AB, 2, ThH). Anal. Calcd for $C_{16}H_{19}DS$: C, 78.31; H, 8.62. Found: C, 78.47; H, 8.67.

The cyclization of **3** was analogous to **1a:** yield 50%; NMR (CCl_4) δ 1.00–3.00 (m, 14, aliphatic H), 1.22 (d, 3, $CHCH_3$), 1.60 (s, 3, $C{=}CH_3$), 6.60–6.90 (AB, 2, ThH), 6.70 (s, 2, ThH). Anal. Calcd. for $C_{17}H_{22}S$: C, 79.07; H, 8.53. Found: C, 79.42; H, 8.85.

Acknowledgment. The authors are indebted to Dr. P. A. Leclercq and Dr. J. W. de Haan from the Department of Instrumental Analysis for recording and interpretation of the mass and ^{13}C NMR spectra, respectively. This investigation has been supported by the Netherlands Foundation for Chemical Research with financial aid from the Netherlands Organization for the Advancement of Pure Research (ZWO).

Registry No.—**1a,** 65121-21-3; **2a** α-isomer, 65121-22-4; **2a** β-isomer, 65166-18-9; **3,** 65121-23-5; **6a,** 42006-95-1; **6b,** 14861-60-0; **7a,** 42007-08-9; **7b,** 1468-83-3; **8a,** 65121-24-6; (*E*)-**8b,** 65121-25-7; (*Z*)-**8b,** 65121-26-8; **9a,** 65121-27-9; **9b,** 65121-28-0; **10a,** 65121-29-1; **10b,** 65121-30-4; **11a,** 65121-31-5; **11b,** 65121-32-6; **12,** 33548-59-3; **13,** 65121-33-7; **13b,** 65121-34-8; **14a,** 65121-35-9; **14b,** 65121-36-0; 2-thiophenecarboxylic acid methyl ester, 5380-42-7; 3-bromothiophene, 872-31-1; acetaldehyde, 75-07-0; triethyl phosphonoacetate, 867-13-0.

References and Notes

(1) Part 1: A. A. Macco, R. J. de Brouwer, and H. M. Buck, *J. Org. Chem.*, **42,** 3196 (1977).
(2) E. J. Corey and J. W. Suggs, *Tetrahedron Lett.*, 2647 (1975).
(3) W. S. Johnson, M. B. Gravestock, and B. E. McCarry, *J. Am. Chem. Soc.*, *93,* 4332 (1971).
(4) M. Schlosser and K. F. Christman, *Angew. Chem., Int. Ed. Engl.*, **5,** 126 (1966).
(5) A. Corvers, J. H. van Mil, M. M. E. Sap, and H. M. Buck, *Recl. Trav. Chim. Pays-Bas,* **96,** 18 (1977).
(6) J. W. de Haan and L. J. M. van de Ven, *Org. Magn. Reson.*, **5,** 147 (1973).
(7) A. Corvers, Thesis, Eindhoven University of Technology, March 1977.
(8) S. Gronowitz, *Acta Chim. Scand.*, **13,** 1045 (1959).
(9) E. J. Corey and J. W. Suggs, *Tetrahedron Lett.*, 2647 (1975).
(10) G. Wittig and D. Wittenberg, *Justus Liebigs Ann. Chem.*, **606,** 1 (1977).
(11) P. A. Bartlett, J. I. Brauman, W. S. Johnson, and R. A. Volkman, *J. Am. Chem. Soc.*, **95,** 7502 (1973).

Methylation of Pyrimidines, the Corresponding Nucleosides, and Inosine with Trimethyloxosulfonium Hydroxide

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The methylation of nucleic acid components is being actively pursued. The most interesting aspects of the problem have arisen from the discovery of various kinds of methylated ribonucleosides from RNA,[1-3] and from studies of the interaction of alkylating agents with nucleic acids and their components.[4-6]

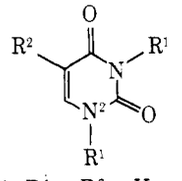
We wish to describe the methylation of pyrimidines (**1, 2,** and **5**), the corresponding nucleosides (**7, 10,** and **16**), and inosine (**13**), using trimethyloxosulfonium hydroxide (MOSH) as a new alkylating agent. Although the preparation of MOSH was reported about two decades ago,[7] its chemistry has been little studied. We prepared MOSH in methanol by a modified procedure, finding that this reagent is potentially very useful for methylation of a wide variety of compounds.

Results and Discussion

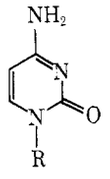
The general procedure consists of heating pyrimidines or nucleosides with MOSH at 40–140 °C in dimethylformamide (DMF). The reaction was followed by thin-layer chromatography and the products were isolated through a very simple workup of the reaction mixture. The results are summarized in Table I.

This method converted uracil (**1**), thymine (**2**), and cytosine (**5**) to the corresponding *N*-methylated derivatives in excellent yields.

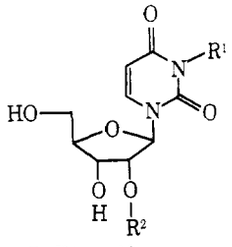
Similarly, uridine (**7**), thymidine (**10**), and inosine (**13**)



1, $R^1 = R^2 = H$
2, $R^1 = H$; $R^2 = Mo$
3, $R^1 = Me$; $R^2 = H$
4, $R^1 = R^2 = Me$



5, R = H
6, R = Me



7, $R^1 = R^2 = H$
8, $R^1 = Me$; $R^2 = H$
9, $R^1 = R^2 = Me$

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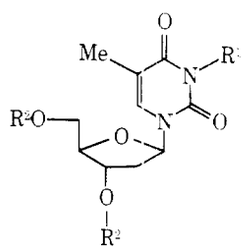
Table I. Methylation of Pyrimidines, the Corresponding Nucleosides, and Inosine with MOSH

Compound	Registry no.	Mole ratio,[a] MOSH/compd	React. temp, °C	React. time, h	Product[b]	Registry no.	Yield,[c] %	λ_{max} (log ϵ)[d] (pH 7)	R_f'/R_f[e]
Uracil (1)	66-22-8	4 (DMF)	80	2	1,3-Me_2-Ura (3)	874-14-6	96 (81)	267.0 (3.92)	3.4
Thymine (2)	65-71-4	4 (DMF)	80	2	1,3-Me_2-Thy (4)	4401-71-2	92 (77)	272.0 (3.97)	4.5
Cytosine (5)	71-30-7	4 (DMF)	80	2	1-Me-Cyt (6)	1122-47-0	87 (80)	275.0 (4.02)	2.1
Uridine (7)	58-96-8	1.4 (DMF)	60	3	3-Me-Urd (8)	2140-69-4	78 (60)	262.0 (3.95)	2.0
					3,$O^{2'}$-Me_2-Urd (9)[f]	7103-27-7	12	262.0 (3.95)	3.1
7		3 (Me_2SO)	60	3	8		83		
					9		5		
7		4 (MeOH)	64	5	8		56		
					9		4		
Thymidine (10)	50-89-5	1.4 (DMF)	60	4	3-Me-dThd (11)	958-74-7	90 (75)	269.5 (3.96)	1.6
					3,$O^{3'}$,$O^{5'}$-Me_3-dThd (12)	65150-68-7	2	270.0 (3.88)	2.6
Inosine (13)	58-63-9	1.4 (DMF)	60	7	1-Me-Ino (14)	2140-73-0	67 (50)	249.5 (4.00)	1.3
					1,$O^{2'}$-Me_2-Ino (15)[f]	65150-69-8	5	250.0 (4.01)	1.7
Cytidine (16)	65-46-3	3 (DMF)	100	5	$O^{2'}$-Me-Cyd (17)[f]	2140-72-9	53 (43)	270.0 (3.96)	1.9
16		2 (DMF)	60	8	17		40 (31)		

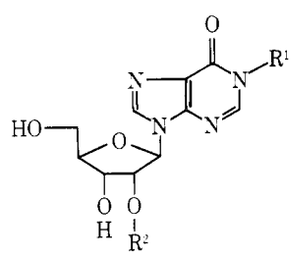
[a] Solvents used are shown in parentheses: DMF, dimethylformamide; Me_2SO, dimethyl sulfoxide. [b] Ura, Thy, Cyt, Urd, dThd, Ino, and Cyd refer to uracil, thymine, cytosine, uridine, thymidine, inosine, and cytidine, respectively. [c] Yields were calculated by spectroscopic method. Yields in parentheses were obtained based on isolated amounts of purified products. [d] UV spectra in acidic (pH 1) and basic (pH 13) conditions were identical with those reported in the literature. [e] R_f and R_f' refer to mobilities of starting materials and products, respectively: aluminum oxide TLC, solvent B for the reaction mixtures of 1 and 2; silica gel TLC, solvent A for the reaction mixtures of 7 and 10; solvent C for the reaction mixtures of 5, 13, and 16. [f] A trace of the $O^{3'}$-methyl isomer was present in the reaction mixture.

underwent smooth methylation with MOSH to produce the corresponding *N*-methylated nucleosides (**8, 11, and 14**) in good yields and the *O'*-methylated nucleosides (**9, 12, and 15**) in small amounts. Here, the use of high reaction temperature and a large excess of MOSH gave numerous products which might have arisen from random methylation of nitrogen atoms and carbohydrate hydroxyls. In general, however, *N*-methylated nucleosides were formed exclusively when the reactions were conducted at 40–60 °C, using about 40% excess of MOSH.

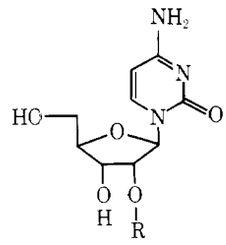
In cytidine (**16**), on the other hand, methylation did not take place on the pyrimidine ring, but MOSH methylated selectively the 2′ OH group, furnishing $O^{2'}$-methylcytidine (**17**) in fairly good yield. Failure of MOSH to methylate the 3 position of **16** is also shown by the absence of 1,3-dimethylcytosine in the reaction of **5** with excess reagent.



10, $R^1 = R^2 = H$
11, $R^1 = Me$; $R^2 = H$
12, $R^1 = R^2 = Me$

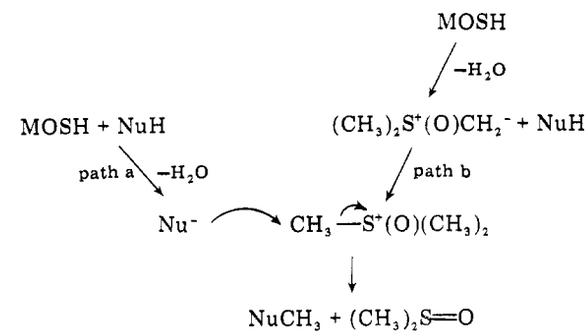


13, $R^1 = R^2 = H$
14, $R^1 = Me$; $R^2 = H$
15, $R^1 = R^2 = Me$



16, R = H
17, R = Me

Scheme I



There was no evidence of methylation of the carbonyl group oxygen or the external amino groups of the pyrimidines and nucleosides examined.

The above results are comparable with or superior to methylations by other alkylating agents such as dimethyl sulfate,[8] methyl iodide,[9] diazomethane,[10] etc.[11,12] The present method is unique in the highly selective formation of **17** from **16**; by contrast, all other methods have been reported to convert **16** inefficiently to a mixture of **17**, $O^{3'}$-methyl-, and $O^{5'}$-methylcytidines, and di- and tri-*O'*-methylated cytidines.[13–16]

Me_2SO as a reaction medium gave results similar to those observed in DMF. Less polar solvents such as acetone and dioxane were unsuitable because of solubility problems. Employment of protic solvents such as methanol and ethanol decreased the yields.

Although kinetics were not examined, methylation occurs most likely in a bimolecular fashion between trimethyloxosulfonium ion and anionized forms (Nu^-) of pyrimidines or nucleosides (NuH) (path a of Scheme I). Involvement of an ylide, $[(CH_3)_2S^+(O)CH_2^-]$, as an alkylating agent[17] (path b) is not likely since its formation would require the action of a very strong base such as sodium hydride on $(CH_3)_3S^+{=}O$ in an anhydrous environment, a condition which would not be realized because methylation would result in formation of water in amounts equal to the concentration of NuH.

Experimental Section

Melting points were uncorrected. Thin-layer chromatography was performed on silica gel [GF_{254} (Type 60), Merck] or aluminum oxide [GF_{254} (Type 150), Merck], using a mixture of chloroform and methanol in the following volume ratios: solvent A, 17:3; B, 5:1; C, 5:2. Column chromatography was carried out using silica gel [Merck (art. 7734), 70–230 mesh].

Commercially available uracil (**1**), thymine (**2**), cytosine (**5**), uridine (**7**), thymidine (**10**), inosine (**13**), and cytidine (**16**) were used without further purification.

Preparation of Trimethyloxosulfonium Hydroxide (MOSH). Trimethyloxosulfonium iodide[7] (5.0 g, 22.7 mmol) was dissolved in a hot mixture of methanol and water (500 mL–1 mL). Excess silver oxide (5.3 g, 23.0 mmol) was added to the solution and the mixture was stirred at room temperature. After 1 h, a few drops of the supernatant was removed, acidified with dilute nitric acid, and tested for iodide with a silver nitrate solution. The checking was repeated until the reaction was complete. The reaction mixture was filtered, concentrated to 100 mL, and used for the subsequent methylation reactions. The concentration of MOSH was determined by titration with 0.1 N hydrochloric acid to be 0.216 N; the yield was calculated as 95%. MOSH was stable in methanol for several months upon storage in a refrigerator.

The neat sample of MOSH gave the following spectral data: IR (KBr) 3350 (s), 2950 (m), 1645 (bm), 1480 (m), 1210 (s), 1105 (s), 1047 (s), and 950 (m) cm^{-1}; NMR (Me_2SO-d_6) τ 2.98 (s, CH_3); mass spectrum (75 eV) *m/e* 92 (M − H_2O), 78 (92 − CH_2), 77 (92 − CH_3) and 63 ($CH_3S{=}O$).

Reaction of the methanol solution of MOSH with equivalent amounts of hydrochloric acid or hydroiodic acid gave trimethyloxosulfonium chloride or iodide, respectively, in quantitative yields.

Methylation Reactions. The following are isolation procedures. The mobilities (R_f) of products in thin-layer chromatography are shown in Table I with references on the UV spectral peak at pH 7. UV spectra at pH 1 and 13 as well as the melting points of all known compounds agreed in most cases with literature values. The NMR spectra were obtained in all compounds and coincided with the assigned structures. Yields are calculated after recrystallization and are based on the isolated amounts of products. Spectroscopic yields of products in reaction mixtures were determined in a manner similar to that employed in our previous study.[18]

Products (**9**, **12**, and **15**) were identified by a comparison of R_f values and UV spectra of the aqueous extracts of the corresponding spots in thin-layer chromatography of reaction mixtures with those of authentic samples.[19]

Reaction conditions and results are summarized in Table I.

A. Pyrimidines (1, 2, and 5). These heterocycles (5.0 mmol) were dissolved in the methanol solution of MOSH prepared as above (20.0 mmol). The solvent was removed under reduced pressure and the residues were dissolved in DMF (30 mL) and warmed at 80 °C for 2 h. The reaction mixtures were concentrated and the resulting substances were purified by recrystallization from suitable solvents (ethanol–diethyl ether, ethanol–water, and water for **3**, **4**, and **6**, respectively).

B. Uridine (7). The nucleoside (1.22 g, 5.0 mmol) was mixed with the methanol solution of MOSH (7.0 mmol). The solvent was removed from the mixture and the residue in DMF (30 mL) was heated at 60 °C for 3 h. The reaction mixture was concentrated under reduced pressure and applied to a silica gel chromatograph (1.5 × 55 cm) using chloroform–methanol (8:1 v/v) as a solvent. The fraction (200–530 mL) gave crude 3-methyluridine (**8**), which was recrystallized from ethyl acetate–methanol: 0.78 g (60%); mp 118.5–119 °C (lit.[20] 119–120 °C).

C. Thymidine (10). The treatment of **10** (1.21 g, 5.0 mmol) with MOSH (7.0 mmol) in DMF (30 mL) at 60 °C for 4 h provided 3-methylthymidine (**11**) after processing the reaction mixture in a manner similar to that mentioned above: 0.95 g (75%); mp 130–131 °C (chloroform) (lit.[21] 128.5–132 °C).

D. Cytidine (16). Compound **16** (1.22 g, 5.0 mmol) was allowed to react with the methanol solution of MOSH (7.0 mmol) in DMF (30 mL) at 100 °C for 1 h. Thereafter, 3 mmol, 3 mmol, and 2 mmol of the reagent solution were added at hourly intervals to the reaction mixture. After the last of the MOSH solution was added, heating was continued for 2 h. The resulting solution was concentrated and applied to a silica gel column chromatograph (1.5 × 70 cm), using a mixture of chloroform and methanol (3:1 v/v) as a solvent. $O^{2'}$-Methylcytidine (**17**) was eluted in the fraction (70–110 mL): 0.54 g (43%); mp 257–258 °C (ethanol) (lit.[14] 256–257 °C).

E. Inosine (13). The nucleoside (1.34 g, 5.0 mmol) was treated with MOSH (7.0 mmol) in DMF (30 mL) at 60 °C for 7.5 h. The reaction mixture was concentrated under reduced pressure to give the residue, which was washed with diethyl ether and then extracted with hot acetone. 1-Methylinosine (**14**) was obtained as a white precipitate from the cooled extract: 0.70 g (50%); mp 207–208 °C (ethanol–methanol) (lit.[22] 209–210 °C).

Registry No.—3-Methylcytidine, 2140-64-9; trimethyloxosulfonium hydroxide, 65150-70-1; trimethyloxosulfonium iodide, 1774-47-6.

References and Notes

(1) R. H. Hall, *Biochim. Biophys. Acta*, **68**, 278 (1963); R. H. Hall, *Biochemistry*, **3**, 769, 876 (1964).
(2) L. Hudson, M. Gray, and B. G. Lane, *Biochemistry*, **4**, 2009 (1965).
(3) Y. Furuichi and K. Miura, *Nature (London)*, **253**, 374 (1975); C. M. Wei and B. Moss, *Proc. Natl. Acad. Sci. U.S.A.*, **72**, 318 (1975).
(4) A. M. Michelson and F. Pochon, *Biochim. Biophys. Acta*, **114**, 469 (1966); F. Pochon and A. M. Michelson, *ibid.*, **149**, 99 (1967).
(5) W. C. J. Ross, "Biological Alkylating Agents", Butterworths, London, 1962, p 45.
(6) R. H. Hall, "The Modified Nucleosides in Nucleic Acids", Columbia University Press, New York, N.Y., 1971.
(7) R. Kuhn and H. Trishmann, *Ann. Chem.*, **611**, 117 (1958).
(8) A. D. Broom et al., *Biochemistry*, **3**, 494 (1964); B. Singer, *ibid.*, **11**, 3939 (1972); P. Brookes and P. D. Lawley, *J. Chem. Soc.*, 1348 (1962).
(9) J. W. Jones and R. K. Robins, *J. Am. Chem. Soc.*, **85**, 193 (1963); Y. Furukawa et al., *Chem. Pharm. Bull. (Tokyo)*, **13**, 1273 (1965).
(10) J. A. Haines et al., *J. Chem. Soc.*, 1406 (1964); J. B. Gin and C. A. Dekker, *Biochemistry*, **7**, 1413 (1968); A. D. Broom and R. K. Robins, *J. Am. Chem. Soc.*, **87**, 1145 (1965).
(11) A. Vincze, R. E. L. Henderson, J. J. McDonald, and N. J. Leonard, *J. Am. Chem. Soc.*, **95**, 2677 (1973); R. Roe, Jr., J. S. Paul, and P. O'B. Montgomery, *J. Heterocycl. Chem.*, **10**, 859 (1973).
(12) According to a referee's suggestion, we examined the reaction of **7** (0.2 mmol) with trimethyloxosulfonium iodide (0.8 mmol) in the presence of potassium carbonate (0.8 mmol) in DMF (1.2 mL) at 60 °C. The reaction occurred in a heterogeneous phase to give **8** in 85% after 4 h. Under comparable conditions, **16** was converted to only 3,N^4-dimethylcytidine, which was isolated in the yield of 70%. The formation of **17** was negligible, the result of which is in contrast with methylation by MOSH. In addition to this characteristic reactivity of MOSH, the reagent has an advantage in allowing products to be isolated much more easily because Me_2SO is the only coproduct.
(13) D. M. G. Martin, C. B. Reese, and G. F. Stephenson, *Biochemistry*, **7**, 1406 (1968).
(14) J. T. Kusmierek, J. Giziewicz, and D. Shuger, *Biochemistry*, **12**, 194 (1973).
(15) L. Sun and B. Singer, *Biochemistry*, **13**, 1905 (1974).
(16) I. Tazawa, S. Tazawa, J. L. Alderfer, and P. O. P. Ts'O, *Biochemistry*, **11**, 4931 (1972).
(17) H. Metzger, H. König, and K. Seelert, *Tetrahedron Lett.*, 867 (1964); L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol. 1, Wiley, New York, N.Y., 1967, p 317.
(18) K. Yamauchi, T. Tanabe, and M. Kinoshita, *J. Org. Chem.* **41**, 3691 (1976).
(19) Authentic compounds **9** and **15** were prepared by reactions of trimethyl phosphate with **7** and **13**, respectively: K. Yamauchi and M. Kinoshita, *J. Chem. Soc., Perkin Trans. 1*, in press. **12** was synthesized according to the recent report of G. R. Pettit, P. Brown, J. J. Einck, K. Yamauchi, and R. M. Blazer, *Synth. Commun.*, **7**, 449 (1977).
(20) H. T. Miles, *Biochim. Biophys. Acta*, **22**, 247 (1956).
(21) H. T. Miles, *J. Am. Chem. Soc.*, **79**, 2565 (1957).
(22) J. Zemlicka, *Collect. Czech. Chem. Commun.*, **35**, 3572 (1970).

(*Z*)-2-Ethoxyvinyllithium: A Remarkably Stable and Synthetically Useful 1,2-Counterpolarized Species[1]

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(*Z*)-2-Ethoxyvinyllithium ((*Z*)-**1**) can easily be prepared by halogen/metal exchange between (*Z*)-2-ethoxyvinyl bromide and butyllithium in diethyl ether at −80 °C.[2] Addition of an aldehyde or a ketone followed by hydrolysis leads to the formation of (*Z*)-3-hydroxy enethers (**2**) which may be alkylated to afford alkenyl diethers (**3**) or to be converted, by acid treatment, into α,β-unsaturated aldehydes (**4**). Examples are listed in Table I.

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