alkylphosphate); NMR ($CDCl_3$) δ 1.33 (t, 6 H, J = 7 Hz, $\mathbf{CH_3}CH_2O$), 4.10 (m, 4 H, J = 7 Hz, $CH_3\mathbf{CH_2}O$), 5.10 (m, 1 H, CH═C). This enol phosphate ester was then immediately reduced as in the above procedure for 4 h to afford 0.077 g (84%) of cholest-3-ene (**15D**): mp 71.5–72.5 °C [lit.[17] mp 72.0–7.25 °C]; IR ($CHCl_3$) 1660 cm^{-1} (CH═CH); NMR ($CDCl_3$) δ 5.28 (m, 1 H, CH═CH) and 5.60 (m, 1 H, CH═CH).

Method e. 5-Methyl-5β-cholest-3-ene (15E). To a solution of lithium dimethyl cuprate [prepared from purified CuI (0.190 g, 1.00 mmol) and methyllithium (1.25 mL, 2.00 mmol, 1.6 M in ether)] in ether (10 mL) at −40 °C was added 4-cholesten-3-one (0.192 g, 0.50 mmol) in ether (1.0 mL). This mixture was then allowed to warm to room temperature and diethyl phosphorochloridate (0.344 g, 2.00 mmol) was added. After stirring for 3 h at room temperature the reaction mixture was then poured into an ice-cold mixture of equal volumes of saturated aqueous NH_4Cl solution, saturated aqueous NH_4OH solution, and water. The mixture was then extracted with ether. The combined etheral extracts were then dried ($MgSO_4$) and concentrated in vacuo to give 0.185 g of a yellow oil. Chromatography on silica gel gave 0.149 g (56%) of the enol phosphate ester: IR ($CHCl_3$) 1675 (C═CH), 1250, 1025, and 975 cm^{-1} (trialkyl phosphate); NMR ($CDCl_3$) δ 1.33 (t, 6 H, J = 7 Hz, $\mathbf{CH_3}CH_2O$), 4.10 (m, 4 H, J = 7 Hz, $CH_3\mathbf{CH_2}O$), and 5.10 (m, 1 H, C═CH). This enol phosphate ester was then immediately reduced as in the above procedure for 4 h to afford 0.090 g (84%) of 5-methyl-5β-cholest-3-ene (**15E**): mp 78–80 °C [lit.[1,18] bp 150 –180 °C (0.05 mm)]; IR ($CHCl_3$) 1660 cm^{-1} (CH═CH); NMR ($CDCl_3$) δ 5.27 (m, 1 H, CH═C) and 5.60 (m, 1 H, C═CH).

Method f. $\Delta^{2,4}$-Androstadiene-17β-ol (16F).[19] To a cold (−30 °C) solution of lithium diisopropylamide prepared from diisopropylamine (0.144 g, 1.42 mmol) and *n*-butyllithium (0.5 mL, 1.0 mmol, 1.0 M in hexane) in THF (5.0 mL) was added testosterone (0.144 g, 0.500 mmol) in THF (1.0 mL) dropwise with vigorous stirring. After the addition was completed the cooling bath was removed and the mixture was allowed to warm to 0 °C. Diethyl phosphorochloridate (0.344 g, 2.00 mmol) was added and the stirring was continued for an additional 30 min. The mixture was then poured into water (20 mL) and extracted with ether. The combined etheral extracts were then dried ($MgSO_4$) and concentrated in vacuo: The resulting oil, 0.203 g, was chromatographed on silica gel to give 0.102 g (48%) of the desired enol phosphate ester: IR (thin film) 3450 (OH), 1655 (C═C), 1250, 1025, and 960 cm^{-1} (trialkyl phosphate); NMR ($CDCl_3$) δ 1.35 (t, 6 H, J = 7 Hz, $\mathbf{CH_3}CH_2O$), 4.20 (m, 4 H, J = 7 Hz, $CH_3\mathbf{CH_2}O$), 5.10 (s, 1 H, C═CH), and 5.40 ppm (m, 1 H, CH═C). This enol phosphate ester was then immediately reduced as in the above procedure for 4 h to afford 0.056 g (86%) of $\Delta^{2,4}$-androstadien-17β-ol (**16F**): mp 170–171 °C [lit.[19] mp 171–173 °C]; UV (EtOH) λ_{max} 266 (ϵ 6030), 273 (ϵ 5720) nm; IR ($CHCl_3$) 3450 (OH), 1640, and 728 cm^{-1} (CH═CHCH═C); NMR ($CDCl_3$) δ 3.80 (m, 1 H, **CH**OH), and 5.55 (m, 3 H, CH═CHCH═C).

Acknowledgments. We graciously thank the National Institute of General Medical Sciences (Grant No. GM 18759) and the Robert A. Welch Foundation (Grant No. E-518) for the funds to support this research program.

Registry No.—$TiCl_3$, 7705-07-9; 1-acetoxy-2-methylcyclohexene, 1196-73-2; diethyl phosphorochloridate, 814-49-3.

References and Notes

(1) R. E. Ireland and G. Pfister, *Tetrahedron Lett.*, 2145 (1969).
(2) M. Fetizon, M. Jurion, and N. T. Anh, *Chem. Commun.*, 112 (1969).
(3) R. E. Ireland, C. J. Kowalski, J. W. Tilley, and D. M. Walba, *J. Org. Chem.*, **40,** 990 (1975); R. E. Ireland, D. C. Muchmore, and U. Hengartner, *J. Am. Chem. Soc.*, **94,** 5098 (1972).
(4) Generation of the thermodynamic enolate anion can be accomplished either by treatment of the ketone with 0.95 equiv of lithium diisopropylamide in THF followed by an appropriate amount of time at room temperature for equilibration or treatment of the corresponding enol acetate with 2 to 2.2 equiv of methyllithium in THF: see ref 6.
(5) Generation of the kinetic enolate anion can be accomplished by treatment of the ketone with 1.1 equiv of lithium diisopropylamide in THF: see ref 6.
(6) J. M. Conia, *Rec. Chem. Prog.*, **24,** 43 (1963); H. O. House, *Rec. Chem. Prog.*, **28,** 99 (1967); H. O. House, M. Gall, and H. O. Olmstead, *J. Org. Chem.*, **36,** 2361 (1971).
(7) For an excellent review of "The Chemistry of Low Valent Titanium", see: J. E. McMurry, *Acc. Chem. Res.*, **7,** 281 (1974).
(8) S. Tyrlik and I. Wolochowicz, *Bull. Soc. Chim. Fr.*, 2147 (1973); *J. Chem. Soc., Chem. Commun.*, 781 (1975); T. R. Nelson and J. J. Tufariello, *J. Org. Chem.*, **40,** 3159 (1975).
(9) J. E. McMurry and M. P. Fleming, *J. Org. Chem.*, **41,** 896 (1976); J. A. Marshall and M. E. Lewellyn, *ibid.*, **42,** 1311 (1977).
(10) G. L. Larson, E. Hernandez, C. Alonso, and I. Nieves, *Tetrahedron Lett.*, 4005 (1975).
(11) R. H. Shapiro and M. J. Heath, *J. Am. Chem. Soc.*, **89,** 5734 (1967).
(12) L. Dorfman, *Chem. Rev.*, **53,** 47 (1953); F. C. Chang and N. F. Wood, *Steroids*, **4,** 55 (1964); H. C. Barrett and G. Büchi, *J. Am. Chem. Soc.*, **89,** 5665 (1967); W. G. Dauben, M. E. Lorber, N. D. Vietmeyer, R. H. Shapiro, J. H. Duncan, and K. Tomer, *J. Am. Chem. Soc.*, **90,** 4762 (1968); W. G. Dauben and D S. Fullerton, *J. Org. Chem.*, **36,** 3277 (1971).
(13) W. S. Johnson and W. P. Schneider, "Organic Syntheses", Collect. Vol. IV, Wiley, New York, N.Y., 1963, p 132.
(14) L. Ruzecka and H. A. Boekenoogen, *Helv. Chim. Acta*, **14,** 1319 (1931).
(15) W. A. Mosher, *J. Am. Chem. Soc.*, **62,** 552 (1940).
(16) E. A. Braude, W. F. Forbes, B. F. Gofton, R. P. Houghton, and E. S. Waight, *J. Chem. Soc.*, 4711 (1957).
(17) D. H. R. Barton and W. J. Rosenfelder, *J. Chem. Soc.*, 1048 (1951).
(18) D. C. Muchmore, *Org. Synth.*, **52,** 109 (1977).
(19) B. Berkoz, A. D. Cross, M. E. Adame, H. Capiro, and A. Bowers, *J. Org. Chem.*, **28,** 1976 (1963).
(20) J. Sicher, F. Šipoš, and M. Tichy', *Collect. Czech. Chem. Commun.*, 847 (1961); S. Winstien and N. J. Holness, *J. Am. Chem. Soc.*, **77,** 5562 (1955).
(21) I. I. Bardyshev, V. V. Bazylchik, and E. N. Manukov, *Zh. Org. Khim.*, **3,** 829 (1967).
(22) A. T. Bloomquist, L. H. Liu, and J. C. Bohrer, *J. Am. Chem. Soc.*, **74,** 3643 (1952).
(23) A. T. Bloomquist, R. E. Burge, Jr., and A. C. Sucsy, *J. Am. Chem. Soc.*, **74,** 3636 (1952).
(24) A. W. Schmidt, V. Schoeller, and V. Eberlein, *Ber.*, **74B** 1313 (1941).
(25) S. F. Birch, R. A. Dean, F. A. Fidler, and R. A. Lowry, *J. Am. Chem. Soc.*, **71,** 1362 (1949).

Oxidation with Supported Oxidants. 2. Preparation of Sulfoxides by Alumina-Supported Sodium Metaperiodate

Kwang-Ting Liu* and Yung-Chien Tong

Department of Chemistry, National Taiwan University, Taipei, Republic of China

Received December 5, 1977

Recent interest in utilizing reagents impregnated on inorganic solid supports has been proved to be successful for organic synthesis in a number of aspects, such as selectivity, reactivity, and manipulative convenience.[1-10] We have engaged in the study of selective oxidations of a variety of functional groups based on this concept. In this note we wish to report our results on a facile preparation of sulfoxides from sulfides by using sodium metaperiodate supported on acidic alumina.

The development of efficient reagents for selective oxidation of sulfides to sulfoxides has been a challenge for many years. The most commonly employed reagent for this purpose is sodium metaperiodate,[11,12] for which a careful control of reaction temperature and the quantity of oxidant is in general of necessity. The use of alumina-supported thallium(III) nitrate may circumvent such inconvenience but the reagent is toxic and is reactive toward many other functional groups, and the reaction is sensitive to steric hindrance.[10] None of these disadvantages exists, however, in the newly developed procedure using supported sodium metaperiodate.

The supported oxidant can readily be prepared by soaking the inorganic support with a hot 1.67 M solution of sodium metaperiodate and then evaporating to dryness. The oxidation is carried out simply by vigorous stirring of this solid oxidant with the solution of a sulfide at room temperature. The products were isolated by removal of the solid reagents by filtration and then evaporation of the solvent. Systematic study on some ten inorganic supports, including alumina, celite, charcoal, florisil, montmorillonite clays, and silica gel, indicated that the acidic alumina and the acidic clays, Girdler Catalyst K-10 and KO, are by far the most effective ones. The readily available chromatographic adsorbent, Merck acidic Aluminium oxide 90 for column chromatography, was then employed for the present purpose. Solvent also plays an im-

Table I. Preparation of Sulfoxides from Sulfides by Oxidation with Alumina-Supported Sodium Metaperiodate[c]

Sulfoxide	Registry no.	Time, h	Isolated yield, %	Bp, °C (Torr) [mp, °C]
1,4-Oxathian 4-oxide	109-03-5	0.5	91	97–101 (1) [41–43]
Tetramethylene sulfoxide	1600-44-8	0.5	85	97–103 (3)
Di-*n*-butyl sulfoxide	2168-93-6	1	85	87–89 (1) [30–31]
Di-*sec*-butyl sulfoxide	13153-06-5	2.5	91	72–74 (1)
Di-*tert*-butyl sulfoxide	2211-92-9	1.5	85	[55–58]
Diallyl sulfoxide	14180-63-3	3	87	98–102 (3)
Benzyl isopropyl sulfoxide	33038-70-9	1.5	85	79–81 (1)
2-(Methylsulfinyl)ethanol	21281-74-3	0.5	67	130–133 (1) [33–35]
Methyl phenyl sulfoxide	1193-82-4	5	88	98–102 (1)
Isopropyl phenyl sulfoxide	4170-69-8	5	89	107–108 (1)
2-*exo*-Norbornyl phenyl sulfoxide[a]	65956-70-9	13	85	(38–40)
3-*endo*-Chloro-2-*exo*-norbornyl phenyl sulfoxide[a]	65956-71-0	34	85	(89–90)
Diphenyl sulfoxide	945-51-7	48	90	(69–71)
Benzo[*b*]thiophene *S*-oxide		48	0[b]	

[a] The structure was confirmed by IR, NMR, mass spectra, and satisfactory elemental analysis. [b] Recovery of starting material. [c] Registry no. 7790-28-5.

portant role in this oxidation. Ethanol (95%) was found to be superior to dichloromethane, dichloromethane saturated with water, benzene, benzene saturated with water, carbon tetrachloride, or tetrahydrofuran. An excess, 2 equiv, of the oxidant is required for complete conversion of sulfides to sulfoxides in a reasonable time. A variety of sulfides have been studied and the results are summarized in Table I. Although the yield is comparable with that which has been obtained from the oxidation with aqueous sodium metaperiodate,[11,12] in the present procedure the reaction is faster and easier to conduct.

The crude product was found to be essentially free from sulfone. Purification by the conventional distillation, recrystallization, or sublimation gave the pure sulfoxide, and the yield was in general no less than 85%. The inertness of benzo[*b*]thiophene is likely the consequence of its aromatic character. The relatively low yield, 67%, of 2-(methylsulfinyl)ethanol[13] might be due to the cleavage of the glycol-like carbon–carbon bond by sodium metaperiodate, similar to the case of thia derivatives of sugars.[15] Unsaturated functions[16] and chloro substituent can be tolerated. Unlike the oxidation of sulfides with iodobenzene dichloride[17] the electronic effect of the chloro and phenyl groups seems to be significant.

Evidently the facile oxidation of sulfides to sulfoxides with sodium metaperiodate supported on acidic alumina has the advantages of manipulative convenience, excellent yield, and wide application. Although the nature of the supported sodium metaperiodate or the principal factor responsible for its remarkable performance is not yet understood, the present method provides an additional example to illustrate the superiority of inorganic solid-supported reagents, which might soon become a new category of the most useful reagents in general organic synthesis.

Experimental Section

Preparation of the Supported Oxidant. Merck acidic Aluminium oxide 90 for column chromatography[18] (33.4 g) was added in one portion to a magnetically stirred solution of 21.4 g (0.1 mol) of sodium metaperiodate in 60 mL of water at 60 °C. The mixture was stirred for 20 min at 60 °C and then dried in a rotatory evaporator. The resulting white powder was heated at 120 °C for 16 h to get a constant weight. The concentration of the oxidant is 3 mmol on 1 g of alumina. This supported oxidant can be stored in a desiccator for months without losing its activity.

General Oxidation Procedure. To a solution of 0.05 mol of the sulfide in 50 mL of 95% ethanol was added 54.8 g (0.1 mol) of the supported oxidant in one portion at room temperature. The mixture was stirred vigorously at the same temperature until the sulfide was completely consumed, as was detected by GC analysis on a Varian Model 1420 instrument with 6 ft × 1/8 in. 5% Carbowax 20M column. After filtration of the solid and removal of most of the ethanol from the filtrate, 25 mL of dichloromethane was added. The solution was dried over anhydrous sodium sulfate and the solvent was stripped off. The sulfoxide was purified by distillation, recrystallization, or sublimation. For the known sulfoxides IR and NMR spectra and bp and/or mp were found to be identical with literature data unless otherwise mentioned. For new sulfoxides satisfactory elemental analysis was obtained.

Acknowledgments. The financial support by the National Science Council is gratefully acknowledged. The authors also would like to thank Miss Chih-Fen Hsin for technical assistance.

Registry No.—1,4-Oxathiane, 15980-15-1; tetrahydrothiophene, 110-01-0; di-*n*-butyl sulfide, 544-40-1; di-*sec*-butyl sulfide, 626-26-6; di-*tert*-butyl sulfide, 107-47-1; diallyl sulfide, 592-88-1; benzyl isopropyl sulfide, 770-34-3; 2-(methylthio)ethanol, 5271-38-5; methyl phenyl sulfide, 100-68-5; isopropyl phenyl sulfide, 3019-20-3; 2-*exo*-norbornyl phenyl sulfide, 24584-22-3; 3-*endo*-chloro-2-*exo*-norbornyl phenyl sulfide, 13204-36-9; diphenyl sulfide, 139-66-2.

References and Notes

(1) P. J. Kakis, M. Fetizon, N. Douchkine, M. Golfier, P. Mourgues, and T. Prange, *J. Org. Chem.*, **39**, 523 (1974), and previous papers in this series.
(2) G. H. Posner, A. W. Runquist, and M. J. Chapdelaine, *J. Org. Chem.*, **42**, 1202 (1977), and previous papers in this series.
(3) N. H. Anderson and H. Uh, *Synth. Commun.*, **3**, 115 (1973).
(4) J. M. Lalancette and J. Lafontaine, *Chem. Commun.*, 815 (1973).
(5) J. M. Lalancette, M. J. Fournier-Breault, and R. Thiffault, *Can. J. Chem.*, **52**, 589 (1974).
(6) E. C. Taylor, C.-S. Chiang, A. McKillop, and J. F. White, *J. Am. Chem. Soc.*, **98**, 6750 (1976).
(7) S. L. Regen and C. Koteel, *J. Am. Chem. Soc.*, **99**, 3837 (1977).
(8) E. Keinen and Y. Mazur, *J. Am. Chem. Soc.*, **99**, 3861 (1977).
(9) J. S. Filippo, Jr., and C.-I. Chern, *J. Org. Chem.*, **42**, 2182 (1977).
(10) K.-T. Liu, *J. Chin. Chem. Soc.* (*Taipei*), **24**, 217 (1977).
(11) N. J. Leonard and C. R. Johnson, *J. Org. Chem.*, **27**, 282 (1962).
(12) C. R. Johnson and J. E. Keiser, "Organic Syntheses", Collect. Vol. V, Wiley, New York, N.Y., 1973, p 791.
(13) This compound was first reported by Price and Zomlefer.[14] However, their data on elemental analysis and bp (80–80.5 °C (9 Torr)) are highly suspicious. The IR, NMR, and mass spectra of 2-(methylsulfinyl)ethanol we obtained are consistent with the assigned structure.
(14) C. C. Price and J. Zomlefer, *J. Am. Chem. Soc.*, **72**, 14 (1950).
(15) L. Hough and M. I. Taha, *J. Chem. Soc.*, 3994 (1957).
(16) Professor Lilian Kao Liu of National Tsing Hua University informed us that alkenyl and alkynyl sulfoxides could be obtained in better than 80% yield from the corresponding sulfides by this method.
(17) G. Barbieri, M. Cinquini, S. Colonna, and F. Montanari, *J. Chem. Soc. C*, 659 (1968).
(18) The commercial adsorbent with particle size of 100–325 mesh was employed. The use of the more selected alumina, 170–325 mesh, did not show any improvement.