Tetrahedron Letters,Vol.23,No.19,pp 1979-1982,1982 0040-4039/82/191979-04$03.00/0
Printed in Great Britain

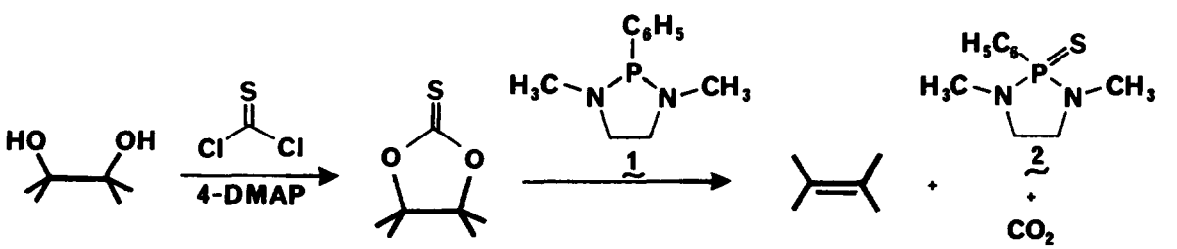
A MILD PROCEDURE FOR THE CONVERSION OF 1,2-DIOLS TO OLEFINS

E. J. Corey and Paul B. Hopkins
Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138

Summary An improved procedure for the stereospecific synthesis of olefins from 1,2-diols via the corresponding thionocarbonate is described.

The introduction of the versatile olefinic function by deoxygenation of a 1,2-diol is a useful technique in organic synthesis. Although numerous procedures have appeared for the conversion of 1,2-diols to the corresponding olefins,[1] only a few possess the mildness, stereospecificity, and efficiency necessary for their use in multistep synthesis of complex molecules. In the course of a recent investigation of the chemistry of erythronolide A,[2] the aglycone of the important antibiotic erythromycin A, we attempted the 11,12-deoxygenation of the 3,5-acetonide of erythronolide A (table, entry 7). The most promising of the existing procedures[3,4] failed with this sensitive substrate and a milder method was required. Herein is reported a modification of the thionocarbonate olefin synthesis[3] which was successful in effecting the 11,12-deoxygenation of erythronolide A-3,5-acetonide. This process is applicable to the synthesis of a wide variety of olefins and seems especially suited to cases involving complex or sensitive molecules.

Conversion of a diol to the corresponding thionocarbonate has previously been accomplished with thiocarbonyldiimidazole at reflux in toluene (110°C) or xylene (140°C).[3] In the present modification, exposure of a stirred solution of 1.0 equiv of a diol (ca. 0.2M) and 2.4 equiv of 4-dimethylaminopyridine (4-DMAP)[5] in methylene chloride at 0°C to 1.2 equiv of thiophosgene[6] for 1 hr results in formation of the thionocarbonate (TLC analysis, SiO_2). Isolation of the product is conveniently accomplished by addition of silica gel, evaporation of the solvent, and elution of the adsorbed material through a short silica gel column. The relatively non-polar thionocarbonate is rapidly eluted; any trace of starting diol (usually not present) and all side products are retained on the silica.[7]



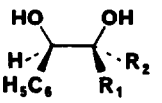
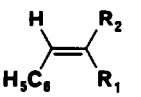
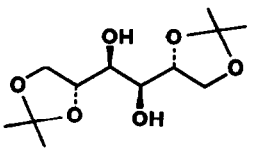
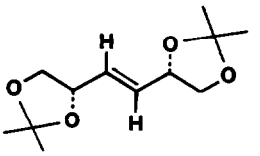
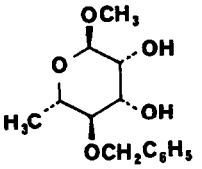
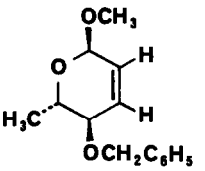
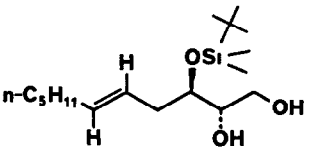
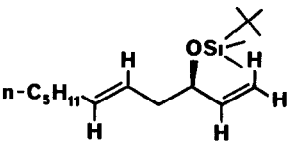
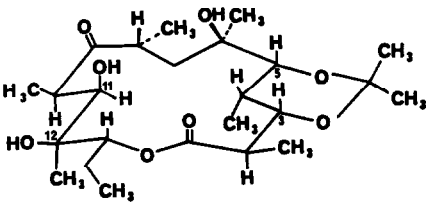
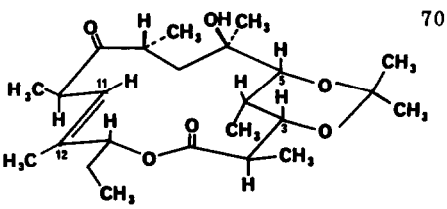
As shown in the table, this procedure is successful with a variety of vicinal diols Secondary-tertiary diols (entry 7) may require warming to 25°C as well as the use of chloroform (ethanol free) as reaction solvent, in which the bright orange 4-DMAP-thiophosgene adduct has somewhat greater solubility Ditertiary diols (pinacol) are recovered unchanged even upon prolonged reflux in chloroform

Traditionally, the conversion of a thionocarbonate to the olefin has been conducted at reflux in trimethylphosphite (111°C) or triethylphosphite (156°C) [3] In contrast, the use of 3 0 equiv of neat 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine (1) (conveniently available in one step (70%) from sym-dimethylethylenediamine and dichlorophenylphosphine[8]) efficiently affords olefins from thionocarbonates at 25-40°C After the appropriate reaction time (2-24 hr at 40°C, TLC analysis[9]) the olefin produced is isolated by direct column chromatography on silica or alumina. Although in some cases (entries 1-4) the elimination reaction is initially heterogeneous, due to the partial insolubility of the thionocarbonate, efficient stirring permits smooth completion of the reaction The addition of a co-solvent such as dioxane or THF offers no advantage.

As illustrated, a variety of functional groups are compatible with this methodology A representative procedure follows.

1,2 5,6-Di-O-isopropylidene-D-mannitol-3,4-thionocarbonate. To a stirred solution of 262 mg (1.0 mmol) of 1,2:5,6-di-O-isopropylidene-D-mannitol[4] and 293 mg (2.4 mmol) of 4-DMAP in 4 0 ml of dry methylene chloride at 0° C under argon was added 108 μl (162 mg, 1.2 mmol) of 85% thiophosgene in carbon tetrachloride and the contents were stirred for 1.0 hr at 0°C. Silica gel (2 0 g, Merck) was added and the mixture was allowed to warm to 25°C After removal of the methylene chloride in vacuo, the remaining solid was loaded onto a column of 6.0 g of silica gel and eluted with 50% ethyl acetate in hexane. Concentration in vacuo afforded the thionocarbonate (284 mg, 93%) as a colorless solid, m.p. 152-156°, TLC R_f 0.51 (50% ethyl acetate in hexane), IR ($CHCl_3$) $1320 cm.^{-1}$ (C=S), ^1H NMR ($CDCl_3$, 80 MHz)· δ 1.34 (6H, s), 1.46 (6H, s), 4 15 (6H, m), 4.66 (2H, m).

trans-3,4-Didehydro-3,4-dideoxy-1,2.5,6-Di-O-isopropylidene-D-threo-hexitol. A suspension of 164 mg (0.54 mmol) of the above thionocarbonate in 0.29 ml (310 mg, 1.6 mmol) of 1 under argon was stirred at 40°C for 20 hr. After cooling to 25°C, the contents were directly chromatographed on a column of 20 g of silica gel (elution with 5% ether in methylene chloride) to afford 108 mg (88%) of pure trans olefin[4] as a colorless solid, m.p. 80-81°, TLC R_f 0.55 (17% ether in methylene chloride), ^1H NMR ($CDCl_3$, 80 MHz)· δ 1.35 (6H, s), 1.39 (6H, s), 3.55 (2H, t, J=7.7 Hz), 4 05 (2H, dd, J=8 0 and 6.2 Hz), 4.45 (2H, m), 5.77 (2H, m), $[\alpha]_D^{20}$ +56.7° (c 3 2, $CHCl_3$).[14]

Entry	Diol	Yield of Thionocarbonate[a]	Olefin	Yield of Olefin[e]
				
1.	R_1=H, R_2=C_6H_5	95%		94%[f]
2.	R_1=C_6H_5, R_2=H	90%[b]		85%[g]
3.	R_1=C_6H_5, R_2=CH_3	86%		87%[h]
4.		93%		88%[l]
5.		90%		75%[j]
6.		97%[c]		85%[k]
7.		87%[d]		70%[l]

a. Except for entry 7, the diol (0.2-0.25 M, CH_2Cl_2) and 2.4 equiv 4-DMAP at 0°C were treated with 1.2 equiv of thiophosgene and stirred 1 hr at 0°C. After addition of silica gel (ca. 0.5 g per mmol 4-DMAP) and concentration to dryness, the adsorbed thionocarbonate was loaded onto a silica gel column (1-4 g per mmol 4-DMAP) and eluted with an appropriate solvent. b. m.p. 159-160° (rec. CCl_4, 81%); lit 162-163°[10]. c. The starting diol was prepared in the course of a previous synthesis[11]. d. 2.5 equiv Cl_2C=S, 5.25 equiv 4-DMAP, $CHCl_3$, 25°, 3.5 hr[2]. e. 3.0 equiv 1, 40°C 2-24 hr, followed by direct chromatography of the reaction mixture. f. m.p. 121-122°, VPC analysis > 98% purity. g. VPC analysis, > 96% purity. h. m.p. 46-47° (lit 48°[12]), VPC analysis > 99% purity. i. m.p. 80-81° (lit 82°), $[\alpha]_D^{20}$ +56.7° (c 3.2, $CHCl_3$) (lit $[\alpha]_D$ +60°[4]). j. $[\alpha]_D^{20}$ -167.6° (c 9.5, $CHCl_3$) (lit $[\alpha]_D^{23}$ -168°[13]). k. $[\alpha]_D^{20}$ -9.7° (c 2 1, $CHCl_3$). l. IR ($CHCl_3$): 1715 cm^{-1} (C=O); pmr ($CDCl_3$, 80 MHz). δ 1.70 (3H, d, J=1.3 Hz, CH_3C=C), 5.35 (1h, dq, J=7 and 1.3 Hz, HC=C), MS: m/e 424, M^+, $[\alpha]_D^{20}$ -70.8° (c 0.63, $CHCl_3$); cis-hydroxylation (1. OsO_4/THF/H_2O, 2. $NaHSO_3$/pyr) reafforded erythronolide A-3,5-acetonide (68%).[14]

References and Notes

1. "Compendium of Organic Synthetic Methods," Vol. I, pp. 488, 511, 512, Vol. II, pp. 197, 204; Vol. III, pp. 310, 311; Vol. IV, pp. 315, 316, 331, John Wiley, New York.

2. E. J. Corey, P. B. Hopkins, S. Kim, S. Yoo, K. P. Nambiar, and J. R. Falck, J. Am. Chem. Soc., 101, 7131 (1979); D. Schomburg, P. B. Hopkins, W. N. Lipscomb, and E. J. Corey, J. Org. Chem., 45, 1544 (1980).

3. E. J. Corey and R. A. E. Winter, J. Am. Chem. Soc., 85, 2677 (1963); E. J. Corey, F. A. Carey, and R. A. E. Winter, J. Am. Chem. Soc., 87, 934 (1965); review: "Reactions of Organosulfur Compounds," E. Block, Academic Press, 1978, pp. 229-235.

4. S. Hanessian, A. Bargiotti, and M. LaRue, Tetrahedron Letters, 737 (1978).

5. Review: G. Höfle, W. Steglich, and H. Vorbrüggen, Angew. Chem. Int. Ed., 17, 569 (1978).

6. Review S. Sharma, Synthesis, 803 (1978).

7. Satisfactory infrared, pmr, and mass spectral data have been obtained for all new compounds reported herein.

8. M. K. Das and J. J. Zuckerman, Inorg. Chem., 10 (5), 1028 (1971). We are pleased to acknowledge the help of Dr. C. C. Cumbo who performed some preliminary experiments with $\underset{\sim}{1}$ in these laboratories. The reagent should be stored under argon or nitrogen at -20°.

9. A sample of the co-product $\underset{\sim}{2}$ for TLC comparison is conveniently prepared by treatment of $\underset{\sim}{1}$ in benzene at 25° with elemental sulfur. R_f $\underset{\sim}{2}$: 0.3 (CH_2Cl_2).

10. R. A. E. Winter, Ph. D. Thesis, Harvard University, Cambridge, Massachusetts, 1965

11. E. J. Corey, P. B. Hopkins, J. E. Munroe, A. Marfat, and S. Hashimoto, J. Am. Chem. Soc., 102, 7986 (1980).

12. J. W. Faller and K. J. Laffey, Organomet. Chem. Syn., 471 (1972).

13. A. H. Haines, Carbohyd. Res., 21, 99 (1972).

14. This research was assisted financially by the National Institute of Health.

(Received in USA 11 February 1982)