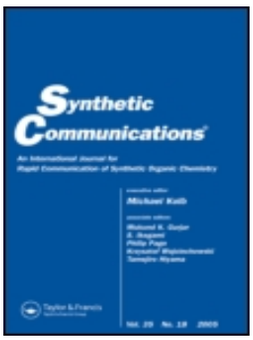

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Propylene Glycol Cyclic Sulfate as a Substitute for Propylene Oxide in Reactions with Acetylides

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ABSTRACT

Lithium acetylides react cleanly with propylene glycol cyclic sulfate to give, after acidic hydrolysis, homopropargylic alcohols in good yield. The benzyl and TBDPS protecting groups are stable to these conditions, but the THP, TBS, acetal and orthoester groups are not. The readily available (*S*)-cyclic sulfate gives the (*S*)-alcohol without loss of stereochemical integrity.

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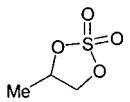
INTRODUCTION

Epoxides are widely used as electrophiles in synthetic organic chemistry.[1] Whilst they react with a wide range of nucleophiles, their reactions with many important carbon nucleophiles, in particular alkynyl lithium reagents,[1b] are complicated by the need to use a highly polar co-solvent[2] or a Lewis acid[3] such as $BF_3{\cdot}OEt_2$, or by prior conversion of the nucleophile to an aluminium derivative.[4]

Propylene oxide (methyl oxirane) **1** has found considerable use in organic synthesis to introduce a suitably functionalized methyl group.[5] Various syntheses of both the (*R*) and (*S*) enantiomers have been reported.[6] These materials are also commercially available. The particular disadvantage of this epoxide is its boiling point, 35°C, which makes its isolation, storage and use somewhat tricky.

(1)

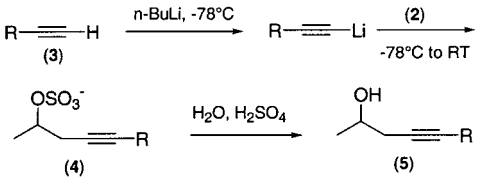


(2)

Recently, interest has grown in the use of cyclic sulfates.[7] They have been described as "like epoxides only more reactive."[8] Although there are numerous examples of ring opening of cyclic sulfates by heteroatom nucleophiles, the number of examples of carbon nucleophiles is small. It was surprising to find only a few examples of the reaction of a cyclic sulfate with an acetylide anion,[9] although the corresponding reaction of epoxides is a frequently used procedure. The cyclic sulfate of propylene glycol **2**[10] could be a useful and easily handled substitute for propylene oxide in this reaction, especially because the (*S*) enantiomer can be easily prepared from inexpensive (*S*)-methyl lactate (Sch. 1).

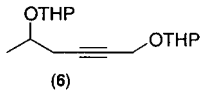
RESULTS AND DISCUSSION

The reaction between cyclic sulfate **2** and lithium acetylides is quite general (Sch. 2, Table 1) and, in all cases, only products arising from attack at the less substituted carbon of the cyclic sulfate were observed. Various lithium acetylides, generated by treatment of the acetylenes **3** in THF with n-butyl lithium at −78°C under N_2, reacted smoothly and rapidly with cyclic sulfate **2** to give the hemisulfate **4** which was then



a: R = Ph, **b**: R = $SiMe_3$, **c**: R = $CH(OEt)_2$, **d**: R = $C(OEt)_3$, **e**: R = CH_2OBn, **f**: R = CH_2OTHP, **g**: R = $CH_2OTBDMS$, **h**: R = $CH_2OTBDPS$, **i**: R = CO_2Et, **j**: R = CH_2OH.

Scheme 1.



Scheme 2.

Table 1. Yields of homopropargylic alcohols.

Entry	Alkyne	*R*	Product:yield
1	**3a**	Ph	**5a**:71%
2	**3b**	$SiMe_3$	**5b**:74%[a]
3	**3c**	$CH(OEt)_2$	**5c**:69%[b]
4	**3d**	$C(OEt)_3$	**5i**:81%
5	**3e**	CH_2OBn	**5e**:79%
6	**3f**	CH_2OTHP	**6**:19% + **5j**: 31%
7	**3g**	CH_2OTBS	**5g**:10% + **5j**: 48%
8	**3h**	$CH_2OTBDPS$	**5h**:90%

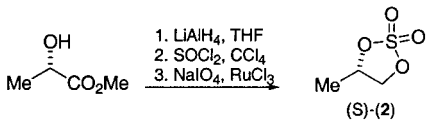
[a]For hydrolysis, the sulfuric acid must be added before the water, otherwise the lithium hydroxide generated can cause partial desilylation resulting in a yield of **5b** of 55% or less.
[b]After reprotection with ethanol, triethyl orthoformate and PPTS.

hydrolyzed with a small amount of water (1 equiv.) and conc. sulfuric acid (0.3 equiv.)[11] to give the homopropargyl alcohols **5**.

Phenyl acetylene **3a** and trimethylsilylacetylene **3b** reacted smoothly (Entries 1 and 2). With 3,3-diethoxypropyne **3c**,[12] not surprisingly, acetal hydrolysis occurred concurrently with sulfate hydrolysis, and reprotection was required to give the desired product **5c** (Entry 3). Use of 3,3,3-triethoxypropyne **3d**[13] resulted in hydrolysis of the *ortho* ester to

give the known ethyl ester **5i** cleanly, and in good yield (Entry 4).[14] The anion of **3d** is a convenient and stable alternative to the unstable anion of ethyl propiolate.

We also examined four different propargylic ethers to test the stability of some common protecting groups. The benzyl group was highly stable; the benzyl protected product **5e** was obtained in good yield and merely a trace of deprotected material **5j** was observed by TLC (Entry 5). The THP group was found to be too labile (Entry 6); both hydrolytic deprotection and scrambling were observed to give a complex mixture from which the known diol **5j**[15] and the *bis*-ether **6**, amongst others, could be isolated. In this case the epoxide method[5c] is clearly superior.



(S)-(2)

The TBS group was also found to be labile (Entry 7). A low yield of the desired compound **5g** was obtained, accompanied by a larger amount of diol **5j**. In contrast, the TBDPS group was found to be entirely stable to the hydrolysis conditions and compound **5h** was obtained in good yield (Entry 8).

When the (*S*)-enantiomer of cyclic sulfate **2** was used in the reaction with alkyne **3e**, subsequent analysis of the Mosher's ester of the product showed that the stereochemical integrity had been conserved and (*S*)-**5e** was obtained with an e.e. of >95%.[16] Hydrolysis of the hemisulfate has been shown to occur by cleavage of the O–S bond and therefore with retention of configuration.[17] Surprisingly, the methylene groups flanking the ether oxygen of the Mosher's esters were clearly resolved and were therefore used for the determination. The methine protons of the diastereomers, α to the ester group, were not well resolved.

CONCLUSION

Cyclic sulfate **2** is a useful and easily handled substitute for propylene oxide, provided that the associated protecting groups are, like the benzyl and TBDPS groups, sufficiently stable, or when acid catalyzed deprotection is a useful procedure, such as in the case of the *ortho* ester

group. Addition of Lewis acids or polar co-solvents is unnecessary. The reaction is also useful for the synthesis of optically pure alcohols. Extension of this work to other cyclic sulfates and acetylenes, as well as its application in total synthesis, is in hand.

EXPERIMENTAL SECTION

Flash chromatography was carried out on silica gel (230–400 mesh, Merck). Melting points were determined on a Büchi 535. NMR spectra were recorded on a Varian Gemini 2000 at 200 MHz (^{1}H) with $CDCl_3$ as the solvent and residual $CHCl_3$ or Me_4Si as the internal reference. Coupling constants are in Hz. IR spectra were recorded, neat, on a PE 1760X instrument. MS were recorded on a Finigan GCQ insturment and HRMS on a Finigan Mat 90 instrument. Optical rotation data were recorded on a Jasco P-1020 polarimeter. Propargyl alcohol derivatives were prepared by standard methods. 3,3-Diethoxypropyne and 3,3,3-triethoxypropyne were prepared by literature methods.[12,13] THF was distilled from Na/benzophenone and dichloromethane was distilled from CaH_2. All other materials were commercial and used as supplied.

Cyclic Sulfate 2[10]: Thionyl chloride (820 μL, 11.2 mmol) was added dropwise to (*S*)-propylene glycol (712 mg, 9.35 mmol) in carbon tetrachloride (10 mL) and dichloromethane (5 mL). The mixture was heated at reflux for 30 min and cooled to 0°C. Acetonitrile (10 mL), water (15 mL), ruthenium trichloride trihydrate (1.6 mg, 0.1 mol%) and sodium periodate (3.0 g, 14 mmol) were added sequentially. The reaction was stirred for 30 min at room temperature, then extracted with ether. The organic layer was washed with $NaHCO_3$ and brine, dried (Na_2SO_4) and evaporated. The residue was purified by distillation (Kugelruhr, 50°C (oven) at 1 mmHg) to give the cyclic sulfate **2** as an oil. ^{1}H NMR δ 5.15 (1H, m, $CH_3C\underline{H}$), 4.75 (1H, dd, $J = 5.3$, 9.6 Hz), 4.32 (1H, dd, $J = 8.5$, 9.6 Hz), 1.60 (3H, d, $J = 6.5$ Hz); ^{13}C NMR: δ 79.8, 74.0, 17.9; $[\alpha]_D^{31} = +16.5$ ($c = 0.16$, CH_2Cl_2).

Typical Procedure for the Synthesis of Homopropargyl Alcohols

n-BuLi in hexanes (0.97 mL of a 1.6 M solution) was added dropwise to a solution of benzyl propargyl ether **3e** (229 mg, 1.56 mmol) in THF (2 mL) at −78°C under nitrogen. The clear solution was stirred

for 30 min, then a solution of the cyclic sulfate (*S*)-**2** (180 mg, 1.3 mmol) in THF (2 mL) was added via cannula. The mixture was stirred at −78°C for 1 h, then allowed to warm to room temperature and stirred for a further 30 min. Water (24 μL) and concentrated sulfuric acid (21 μL) were added and the now opaque, cloudy mixture[18] was stirred for 15 min at room temperature. The acid was neutralized with saturated sodium bicarbonate solution. The mixture was extracted twice with ether. The combined organic layers were washed with saturated aqueous sodium chloride solution, dried ($MgSO_4$) and evaporated. The residue was purified by flash chromatography on silica gel (6 g) eluting with 20% ether/hexane, to give 1-(phenylmethoxy)-2-hexyn-5-ol **5e** (187 mg, 71%) as an oil. ^{1}H NMR δ 7.3 (5H, m), 4.48 (2H, s), 4.18 (2H, t, $J=2$ Hz), 3.96 (1H, m), 2.4 (2H, m), 2.0 (1H, brs), 1.27 (3H, d, $J=7$ Hz); ^{13}C NMR δ 137.2, 128.3, 128.0, 127.8, 83.5, 78.2, 71.5, 66.3, 57.5, 29.1, 22.2; ν/cm^{-1}: 3397, 2998, 2240, 1455; m/z (EI): 205 (5) ($M^+ + H$), 187 (58) ($M^+ - OH$), 159 (34) ($BnOC_4H_4^+$), 91(100) ($C_7H_7^+$); HRMS calcd. for $C_{13}H_{16}O_2$: 204.1150; found 204.1150; $[\alpha]_D^{31} = +4.6$ ($c=0.065$, CH_2Cl_2).

Other homopropargyl alcohols were prepared similarly.

1-Phenyl-1-pentyn-4-ol 5a: ^{1}H NMR δ 7.3 (5H, m,), 4.05 (1H, m), 2.63 (1H, dd, $J=17$, 5), 2.51 (1H, dd, $J=17$, 7), 2.3 (1H, brs), 1.30 (3H, d, $J=6$); ^{13}C NMR δ 131.5, 128.1, 127.7, 123.3, 86.2, 82.7, 66.4, 29.7, 22.2; ν/cm^{-1}: 3372, 2978, 2928, 2233, 1600, 1489, 1122; m/z (EI): 161 (2) ($M^+ + H$), 143 (5) ($M^+ - OH$), 115 (100) ($PhC_3H_2^+$), HRMS calcd. for $C_{11}H_{12}O$ 160.0888, found 160.0891.

1-Trimethylsilyl-1-pentyn-4-ol 5b: ^{1}H NMR δ 3.92 (1H, sextet, $J=6$), 2.42 (1H, dd, $J=17,5$), 2.31 (1H, dd, $J=17$, 6), 2.0 (1H, brs), 1.22 (3H, d, $J=6$), 0.10 (9H, s); ^{13}C NMR δ 103.4, 86.9, 66.1, 30.1, 22.0, −3.1; ν/cm^{-1}: 3361, 2961, 2178, 1256.

1,1-Diethoxy-2-hexyn-5-ol 5c: ^{1}H NMR δ 5.25 (1H, m), 3.94 (1H, sextet, $J=6$), 3.6 (4H, m), 2.39 (2H, m), 2.20 (1H, brs), 1.23 (3H, d, $J=6$), 1.19 (6H, t, $J=7$); ^{13}C NMR δ 91.1, 82.8, 77.4, 65.8, 60.4, 28.8, 22.1, 14.8; ν/cm^{-1}: 3428, 2978, 2239, 1361, 1056; m/z (EI): 185 (3) ($M^+ + H$), 141 (100) ($M^+ - OEt$); HRMS calcd. for $C_8H_{13}O_2$ ($M^+ - OEt$): 141.0916, found 141.0918.

1-(*t*-Butyldimethylsiloxy)-2-hexyn-5-ol 5g: ^{1}H NMR δ 4.28 (2H, t, $J=2$), 3.91 (1H, sextet, $J=5$), 2.33 (2H, m), 2.0 (1H, brs), 1.22 (3H, d, $J=6$), 0.86 (9H, s), 0.09 (6H, s); ^{13}C NMR δ 82.6, 80.9, 66.3, 51.0, 29.1, 25.6, 22.3, 17.6, −3.6.

1-(*t*-Butyldiphenylsiloxy)-2-hexyn-5-ol 5h: ^{1}H NMR δ 7.72 (4H, m), 7.40 (6H, m), 4.33 (2H, d, $J=2$), 3.82 (1H, sextet, $J=6$), 2.28 (2H, m), 2.20 (1H, brs), 1.20 (3H, d, $J=6$), 1.05 (9H, s); ^{13}C NMR δ 135.5, 134.7, 129.7, 127.6, 81.8, 80.9, 66.3, 52.8, 29.2, 26.6, 22.3, 19.1; ν/cm^{-1}: 3394,

2928, 2856, 2239, 1433, 1122; *m/z* (EI) 295 (54), 217 (100), 199 (71); HRMS calcd. for $C_{22}H_{28}O_2Si$ 352.1859, found 352.1860.

Ethyl 5-hydroxy-2-hexynoate 5i[14]: ^{1}H NMR δ 4.19 (2H, q, $J = 7$ Hz), 4.02 (1H, sept, $J = 5$), 2.47 (2H, m), 2.32 (1H, brd, $J = 4$ Hz), 1.27 (3H, t, $J = 7$ Hz), 1.26 (3H, t, $J = 6$ Hz); ^{13}C NMR δ; ν/cm^{-1}: 3394, 2978, 2239, 1717, 1261.

2-Hexyn-1,5-diol 5j[15]: ^{1}H NMR δ 4.26 (2H, t, $J = 2$), 3.98 (1H, dquin, $J = 5$, 6.5), 3.0 (2H, brs), 2.46 (1H, ddt, $J = 17$, 4, 2), 2.32 (1H, ddt, $J = 17$, 7, 2), 1.22 (3H, d, $J = 6$).

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REFERENCES

1. (a) Gorzynski Smith, J. Synthesis **1984**, 629; (b) Garratt, P.J. *Comprehensive Organic Synthesis*; Trost, B.M., Ed.; Pergamon: Oxford, 1991; Vol. 3, 277.
2. Brandsma, L. *Preparative Acetylenic Chemistry*; Elsevier: Amsterdam, 1988; 40.
3. Yamaguchi, M.; Hirao, I. Tetrahedron Lett. **1983**, *24*, 391; see also: Eis, M.J.; Wrobel, J.E.; Ganem, B. J. Am. Chem. Soc. **1984**, *106*, 3693; Cink, R.D.; Forsyth, C.J. J. Org. Chem. **1995**, *60*, 8122; Ooi, T.; Kagashima, N.; Ichikawa, I.; Maruoka, K. J. Am. Chem. Soc. **1999**, *121*, 3328.
4. Fried, J.; Lin, C.H.; Ford, S.H. Tetrahedron Lett. **1969**, 1379.
5. For examples of reactions of propylene oxide with acetylides, see: (a) Seebach, D.; Seidel, W. Tetrahedron Lett. **1982**, *23*, 159; (b) Hillis, L.R.; Ronald, R.C. J. Org. Chem. **1985**, *50*, 470; (c) Nokamai, J.; Taniguchi, T.; Ogawa, Y. Chem. Lett. **1995**, 43.
6. Ellis, M.K.; Golding, B.T. Org. Syn. Coll. **1990**, *7*, 356; Mori, K.; Senda, S. Tetrahedron **1985**, *41*, 541.
7. For reviews, see Lohray, B.B. Synthesis **1992**, 1035; Lohray, B.B.; Bhusan, V. Adv. Het. Chem. **1997**, *68*, 90; Byun, H.-S.; He, L.; Bittman, R. Tetrahedron **2000**, *56*, 7051. For recent examples of C–C bond formation, see Hoye, T.R.; Crawford, K.B. J. Org. Chem. **1994**, *59*, 520; Baldwin, J.E.; Adlington, R.M.; Gollins, D.W.;

Godfrey, C.R.A. Tetrahedron **1995**, *51*, 5169; Stiasny, H.C. Synthesis **1996**, 259.

8. Gao, Y.; Sharpless, K.B. J. Am. Chem. Soc. **1988**, *110*, 7538.
9. Tomalia, D.A.; Falk, J.C. J. Heterocycl. Chem. **1972**, *9*, 891; Bates, R.W.; Fernandez-Moro, R.; Ley, S.V. Tetrahedron **1991**, *47*, 9929; Pais, G.C.G.; Byun, H.-S.; Sadlofsky, J.A.; Bittman, R. J. Org.Chem. **1998**, *63*, 2560; Fernandes, R.A.; Kumar, P. Tetrahedron **1999**, *55*, 13445; Gourlain, T.; Wadouachi, A.; Beauére, D. Synthesis **1999**, *2*, 290. A Payne rearrangement of a hydroxymethyl cyclic sulfate, followed by acetylide attack on the resulting epoxide has been reported: Ko, S.Y. Tetrahedron Lett. **1994**, *35*, 3601.
10. Berridge, M.S.; Franceschini, M.P.; Rosenfield, E.; Tewson, T.J. J. Org. Chem. **1990**, *55*, 1211. Preparation by the method of Gao and Sharpless[8] is higher yielding and more convenient. Propylene glycol is appreciably hygroscopic, but it may be conveniently dried by azeotropic removal of water with toluene.
11. Kim, B.M.; Sharpless, K.B. Tetrahedron Lett. **1989**, *30*, 655.
12. Le Coq, A.; Gorgues, A. Org. Syn. Coll. **1988**, *6*, 954.
13. Prepared by bromination of triethyl orthopropionate (Beyerstedt, F.; McElvain, S.M. J. Am. Chem. Soc. **1937**, *59*, 1273; Walters, P.M.; McElvain, S.M. J. Am. Chem. Soc. **1940**, *62*, 1482), then elimination, bromination and elimination again (Stetter, H.; Uerdingen, W.; Synthesis **1973**, 207; Gassman, P.G.; Chavan, S.P. Tetrahedron Lett. **1988**, *29*, 3407). For both elimination reactions, powdered KOH in DMSO was used in place of KO*t*-Bu. An alternative method has been described.[14]
14. For the corresponding epoxide reaction, see Boche, G.; Bigalke, J. Tetrahedron Lett. **1984**, *25*, 955.
15. Trost, B.M.; Krause, L.; Portnoy, M. J. Am. Chem. Soc. **1997**, *119*, 11319.
16. Dale, D.E.; Rhee, C.K. Tetrahedron Lett. **1991**, *32*, 7165.
17. For numerous examples, see Ref.[7]
18. The rapid formation of a cloudy precipitate indicates that sufficient acid has been added. If the mixture is not opaque, hydrolysis of the hemisulfate does not occur and more acid is required.

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