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Unexpected Remarkable Stability of Primary Ozonides Derived from Alkenyl Stannanes. One-Pot Synthesis of 1,2-Diols from Alkynes

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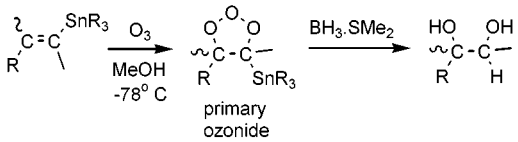
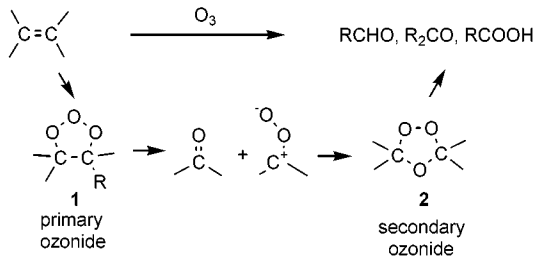
ABSTRACT



Primary ozonides derived from alkenyl stannanes display an unusual stability and can be transformed into 1,2-diols by treatment with dimethyl sulfide and borane−methyl sulfide complex. This observation has been incorporated into the development of a novel one-pot strategy for the conversion of alkynes into 1,2-diols.

The reaction of olefins with ozone is still one of the most popular methods for cleavage of alkenes and is commonly used for the preparation of aldehydes, ketones, and acids.[1] A three-step mechanism (Scheme 1) was formulated by Criegee more than 50 years ago for this process,[2] and it consists of dipolar cycloaddition to form a primary ozonide (1,2,3-trioxolane), **1**, followed by cycloreversion to carbonyl oxide and carbonyl fragments, and recombination of the carbonyl compound and the carbonyl oxide to produce the final ozonide (secondary ozonide, 1,2,4-trioxolane), **2**.[3−5]

Scheme 1. Mechanism of Ozonolysis



The primary ozonide, produced in the first step of the mechanism, is sometimes stable enough at low temperatures and has been observed by NMR and IR for a variety of alkenes.[3] It was indeed from these data as well as for the conversion of some primary ozonides into 1,2-diols[6] that the cyclic 1,2,3-trioxolane structure was inferred.[7] Although there are scarce literature reports on ozonation of heteroatom-substituted alkenes yielding products with no cleavage of the carbon chain,[8] we are not aware of any general synthetic method for the transformation of substituted olefins into diols based on the reduction of primary ozonides. In this Letter

(1) Bailey, P. S. Ozonation in Organic Chemistry. Volume I. *Olefinic Compounds*; Academic Press: New York, 1978; Vol. 39.
(2) Criegee, R. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 745.
(3) Kuczkowski, R. L. In *1,3-Dipolar Cycloadditon Chemistry*; Padwa, A.; Wiley-Interscience: New York, 1984; p 197.
(4) Kuczkowski, R. L. *Acc. Chem. Res.* **1983**, *16*, 42.
(5) Kuczkowski, R. L. Chem. Soc. Rev. **1992**, *21*, 79.
(6) Criegee, R.; Schröder, G. *Chem. Ber*. **1960**, *93*, 689. Greenwood, F. L. *J. Org. Chem.* **1964**, *29*, 1231.. Greenwood, F. L. *J. Org. Chem.* **1965**, *30*, 3108.
(7) A primary ozonide was characterized by microwave spectroscopy: Gillies, J. Z.; Gillies, C. W.; Suenram, R. D.; Lovas, F. J. *J. Am. Chem. Soc.* **1988**, *110*, 7991.

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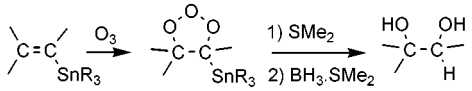
we report on (a) the, unexpected, stability of primary ozonides resulting from the treatment of alkenyl stannanes with ozone (**1a**) (Scheme 2), (b) the transformation of the

Scheme 2. Ozonation of Alkenyl Stannanes Leading to 1,2-Diols



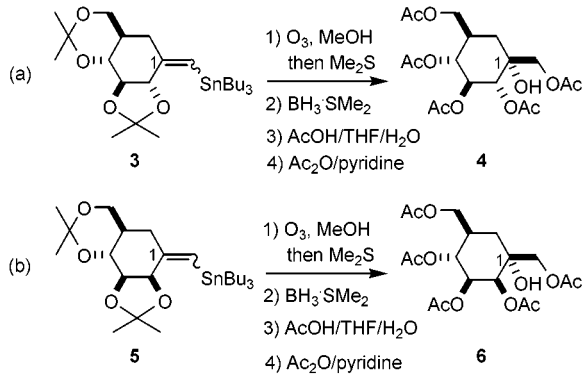
1a R=SnBu$_3$

primary ozonide

above-mentioned 1,2,3-trioxolanes into 1,2-diols, and (c) a novel one-pot procedure for the transformation of alkynes into 1,2-diols.

This study originated from the observation, during the course of some unrelated work underway in our laboratory,[9] of the transformation outlined in Scheme 3a. Ozonolysis of

Scheme 3. Ozonolysis of Alkenyl Stannanes



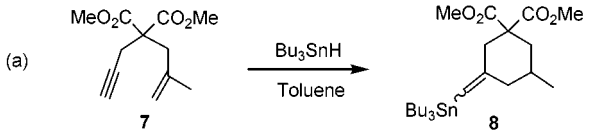
compound **3**, followed by reductive treatment with borane−methyl sulfide complex, acid hydrolysis, and acetylation, resulted in the obtention of acetate **4** with no sign of the expected methyl cyclohexanol. A similar result was obtained when alkenyl stannane **5** (Scheme 3b) was treated with ozone, followed by standard reductive treatment, hydrolysis, and acetylation, thus leading to carbasugar derivative **6**.

To study the scope and generality of this process we prepared alkenyl stannanes **8**, **10a**−**d** and submitted them to ozonation (ozone, MeOH, −78 °C, 15 min) followed by reductive treatment as above. Compound **8** was prepared by radical cyclization, from an enyne precursor (**7**), according to Stork and Mook (Scheme 4a),[10] and alkenyl stannanes **10**

(8) Vinyl sulfides: Chaussin, R.; Leriferend, P.; Paquer, D. *J. Chem. Soc., Chem. Commun.* **1978**, 1032. Strobel, M.-P.; Morin, L.; Paquer, D. *Tetrahedron Lett.* **1980**, *21*, 523. Vinyl silanes: Renaud, P.; Gerster, M.; Ribezzo, M. *Chimia* **1994**, *48*, 366. Silyloxyalkenes: Clark, R. D.; Heathcock, C. H. *Tetrahedron Lett.* **1974**, 523.

(9) Gómez, A. M.; Danelón, G. O.; Valverde, S.; López, J. C. *J. Org. Chem.* **1998**, *63*, 9626.

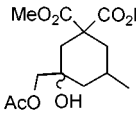
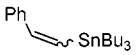
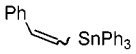
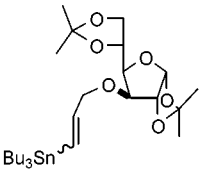
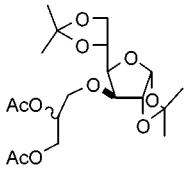
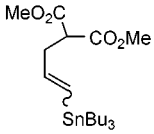
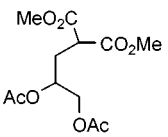
Scheme 4. Preparation of Alkenyl Stannanes



were obtained by triethylborane-mediated addition of R_3SnH to the corresponding alkynes (**9**) following a protocol described by Oshima and co-workers (Scheme 4b).[11]

The results obtained are outlined in Table 1. In most of the cases the corresponding 1,2-diol was obtained as the sole reaction product, and only in two instances (entries ii and iii) were compounds resulting from cleavage of the carbon−carbon bond observed, although in a small percentage. These results provide good evidence for the stability of stannyl-substituted primary ozonides at −78 °C and also seemed to

Table 1. Ozonation of Alkenyl Stannanes **8** and **10a**−**d** Leading to 1,2-Diols

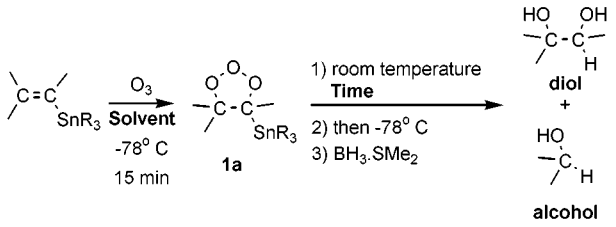
entry	substrate	product	yield (%)
i	**8**	 **11**	67[a]
ii	 **10a**	 **12**	61[b]
iii	 **10b**	**12**	63[b]
iv	 **10c**	 **13**	65[a]
v	 **10d**	 **14**	60[a]

[a] The crude reaction mixture was evaporated and the residue submitted to acetylation (Ac_2O/pyridine). [b] Benzyl alcohol (≈10%) was also obtained.

indicate that the cycloreversion step in the ozonation mechanism is favored for aryl-substituted olefins.

In an effort to evaluate the stability of stannyl-substituted primary ozonides in different solvents, we carried out the following experiment: Ozone was bubbled through a solution of the corresponding olefin, at −78 °C, in the solvent indicated in Table 2, after 15 min the reaction was warmed to room temperature and kept at this temperature for the time shown in the table. After reductive workup, a mixture of the corresponding diol and alcohol (where carbon−carbon bond cleavage had taken place) was obtained and their ratio determined by ^{1}H NMR.

Table 2. Ozonation of Alkenyl Stannanes **8** and **10a**, in Different Solvents, Followed by Warming to Room Temperature (time), Cooling at −78 °C, and Reductive Workup, Leading to 1,2-Diols and Monohydroxy Compounds

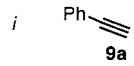
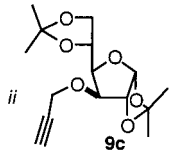
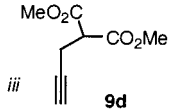
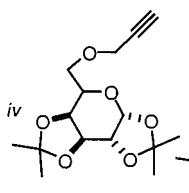
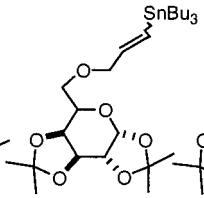
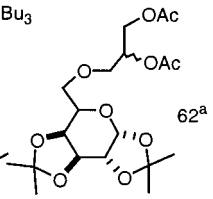
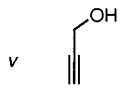
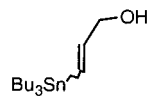
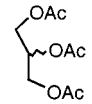
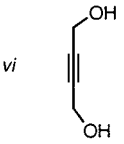
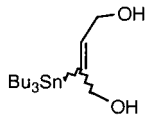
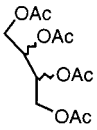


entry	substrate	solvent	time (h)	ratio diol:alcohol	yield (%)
i	**8**	MeOH	0[a]	1:0	67
ii	**8**	MeOH	0.5	1:2	62
iii	**8**	MeOH	2	1:8	63
iv	**8**	MeOH	4	0:1	65
v	**8**	EtOAc	0[a]	1:0	59
vi	**8**	EtOAc	2	1:1	63
vii	**8**	CH_2Cl_2	0[a]	1:0	65
viii	**8**	CH_2Cl_2	2	1:2	61
ix	**10a**	MeOH	0[a]	5:1	71
x	**10a**	MeOH	2	1:3	68
xi	**10a**	EtOAc	0[a]	2:1	69
xii	**10a**	EtOAc	2	1:5	66
xiii	**10a**	CH_2Cl_2	0[a]	4:1	62
xiv	**10a**	CH_2Cl_2	2	1:7	58
xv	**10a**	toluene	0[a]	1:1.5	59

[a] The reactions were not warmed to room temperature.

From the results outlined in Table 2, some conclusions can be drawn: (a) the nature of the solvent influences considerably the rate of cycloreversion of the primary ozonide (compare entries i, v, ix, xi, xii, and xv), (b) ozonolytic cleavage of the double bond in alkenyl stannanes becomes a favored reaction pathway in certain solvents (compare entries i and xv), and (c) the cycloreversion step is accelerated with the temperature, and compounds resulting from carbon−carbon bond cleavage can become the sole reaction products after warming of the reaction mixture (compare entries i, ii, iii, iv). By corollary, ozonation of alkenyl stannanes can be driven either to the preparation of diols or to the synthesis of compounds resulting from ozonolytic cleavage, by changes in solvent and/or temperature.

Table 3. One-Pot Syntheses of 1,2-Diols from Alkynes by BEt_3-Mediated Addition of Bu_3SnH Followed by Ozonation and Reductive Workup

entry	substrate	alkenyl stannane	product	yield (%)
i	 **9a**	**10a**	**12**	61
ii	 **9c**	**10c**	**13**	69[a]
iii	 **9d**	**10d**	**14**	63[a]
iv	 **9e**	 **10e**	 **15**	62[a]
v	 **9f**	 **10f**	 **16**	60[a]
vi	 **9g**	 **10g**	 **17**	63[a]

[a] The crude reaction mixture was evaporated and the residue submitted to acetylation (Ac_2O/pyridine).

We next turned our attention to the reactions shown in Schemes 4b and 2 (radical-mediated tin addition to an alkyne, and ozonation of alkenyl stannanes, respectively). We envisaged that both processes could be carried out as one-pot operations without the need for isolation of the intermediate alkenyl stannane. The only factor to be adjusted was the solvent since toluene, which had been the solvent currently used in triethylborane-catalyzed addition of Bu_3SnH to alkynes, would facilitate the unwanted cycloreversion step (see Table 2, entry xv). After some experimentation we

(10) Stork, G.; Baine, N. H. *J. Am. Chem. Soc.* **1982**, *104*, 2321. Stork, G.; Mook, R., Jr. *J. Am. Chem. Soc.* **1983**, *105*, 3720. Stork, G.; Mook, R., Jr. *J. Am. Chem. Soc.* **1987**, *109*, 2829.

(11) Nozaki, K.; Oshima, K.; Utimoto, K. *J. Am. Chem. Soc.* **1987**, *109*, 2547. Nozaki, K.; Oshima, K.; Utimoto, K. *Tetrahedron* **1989**, *45*, 923.

chose methanol as solvent for the radical addition and ozonation. The results in Table 3 show how alkynes can be transformed into 1,2-diols in a one-pot tandem process.[12]

Terminal alkynes uderwent smooth tin addition in methanol and give moderate yields of the corresponding 1,2-diols upon ozonation. One example of a disubstituted alkyne (entry vi) is also included.

In summary, we have reported the remarkable stability of primary ozonides (**1a**) derived from alkenyl stannanes. This stability allows the preparation of 1,2-diols from alkenyl stannanes by ozonation followed by reductive treatment of the primary ozonides. The procedure disclosed in this Letter extends the scope of the vinyl radical cyclization mediated by the addition of stannyl radicals to triple bonds,[10] since it provides a method for simple functionalization of the resulting alkenyl stannane. Furthermore this transformation has been incorporated, together with the radical addition of Bu_3SnH to alkynes, in a highly useful one-pot method for the transformation of alkynes into 1,2-diols.

(12) **Representative experimental procedure:** The alkyne is dissolved in MeOH and treated with Bu_3SnH in the presence of BEt_3 (−78 °C); once the starting material has dissappeared (TLC) ozone is bubbled through the solution (15 min). Oxygen is then bubbled, to eliminate ozone from the reaction mixture, and then $BH_3{\cdot}SMe_2$ is added. Evaporation of the solvent and flash chromatography afforded the corresponding 1,2-diol.

Moreover, ozonation of alkenyl stannanes might then be driven to the formation of diols or products resulting from carbon−carbon bond breaking by changes in the temperature and solvent. The influence of the temperature in this process has already been well documented.[3] On the other hand, the role of the solvent in the above-mentioned process is noteworthy. Cycloreversion of the primary ozonide is, thus, favored in certain solvents, and this could be related with the concerted, or not, nature of the process.[5]

Additional work with primary ozonides derived from alkenyl stannanes, as well as their detailed NMR study, is under consideration in our laboratory and will be reported in due course.

Acknowledgment. This work was supported by grants from the Dirección General de Enseñanza (Grants PB97-1244, PPQ2000-1330, and BQU2001-0582). M.D.C. thanks the Comunidad Autónoma de Madrid for a fellowship.

Supporting Information Available: Complete experimental procedures and spectroscopic and analytical data for new compounds This material is available free of charge via Internet at http://pubs.acs.org

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