

A Novel Reactivity of SeO₂ with 1,3-Dienes: Formation of syn 1,2- and 1,4-Diols via a Facile C–Se Bond Oxidation

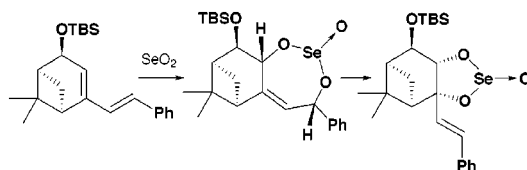
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ABSTRACT

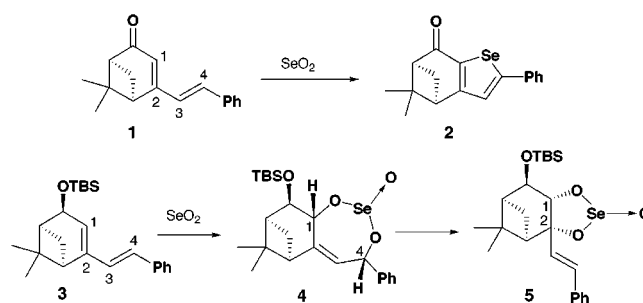


A novel reaction between 1,3-dienes and selenium dioxide to give syn 1,2- and 1,4-diol cyclic selenites was studied in detail. This study indicates that an initial concerted [4 + 2] cycloaddition followed by a stereospecific carbon–selenium bond oxidation is involved in this unprecedented syn dihydroxy addition reaction mediated by selenium dioxide.

The formation of a diol from an alkene is an important transformation in organic chemistry.¹ Usually, the syn addition of dihydroxy groups is achieved by OsO₄,² RuO₄,³ and MnO₄,⁴ whereas anti addition is brought about by other oxides such as SeO₂⁵ and WO₃.⁶ In our investigations of the reaction between SeO₂ and 1,3-dienes, a novel reactivity profile of SeO₂ was observed, affording syn 1,2- and 1,4-diols and selenophene. Treatment of diene **1**, containing a carbonyl group at the C-1 position, with SeO₂ led to the formation of selenophene **2**, whereas the analogous diene **3**,

containing a TBS-ether, yielded 1,4-diol cyclic selenite **4** and 1,2-diol cyclic selenite **5** (Scheme 1). Notably, the

Scheme 1



conversion of **3** to **4** involves an unprecedented direct oxidation of a C–Se bond to a C–O bond, a transformation known to be difficult.⁷ In this account, we elucidate the nature

(1) (a) Haines, A. H. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 7, pp 437–448. (b) Burnett, J. F. *Pure Appl. Chem.* **1981**, *53*, 305–321.

(2) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483–2547.

(3) Shing, T. K. M.; Tam, E. K. W.; Tai, V. W.-F.; Chung, I. H. F.; Jiang, Q. *Chem. Eur. J.* **1996**, *2*, 50–57.

(4) (a) Larsen, S. D.; Monti, S. A. *J. Am. Chem. Soc.* **1977**, *99*, 8015–8020. (b) Lee, D. G.; Chang, V. S. *J. Org. Chem.* **1978**, *43*, 1532–1536. (c) Wolfe, S.; Ingold, C. F.; Lemieux, R. U. *J. Am. Chem. Soc.* **1981**, *103*, 938–939.

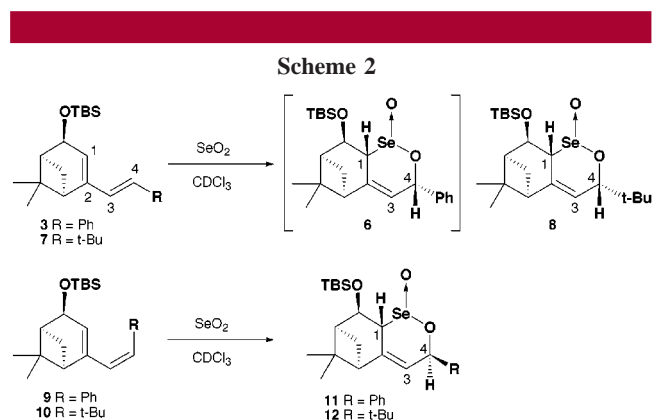
(5) (a) Knothe, G.; Glass, R. S.; Schroeder, T. B.; Bagby, M. O.; Weisleder, D. *Synthesis* **1997**, 57–60. (b) Sonoda, N.; Tsutsumi, S. *Bull. Chem. Soc. Jpn.* **1965**, *38*, 958–961. (c) Itakura, J.; Tanaka, H.; Ito, H. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 1604–1608.

(6) Mugdan, M.; Young, D. P. *J. Chem. Soc.* **1949**, 2988–3000.

(7) Discussions in Supporting Information of *J. Am. Chem. Soc.* **1998**, *120*, 6844–6845.

of the intermediates involved in this novel syn dihydroxylation reaction by SeO_2 and the stereospecificity of the C–Se bond oxidation.

Despite the fact that we have not detected the selenino lactone **6** from the reaction between **3** and SeO_2 , we hypothesized the existence of **6**, which would then lead to the cyclic selenite **4**.⁸ To test this hypothesis and to probe the mechanistic aspects of the transformation from the selenino lactone to the cyclic selenite, *tert*-butyl-substituted *trans*-1,3-diene **7** and phenyl- and *tert*-butyl-substituted *cis* isomers **9** and **10**⁹ were prepared and their reactions with SeO_2 were monitored by NMR spectroscopy (Scheme 2).¹⁰

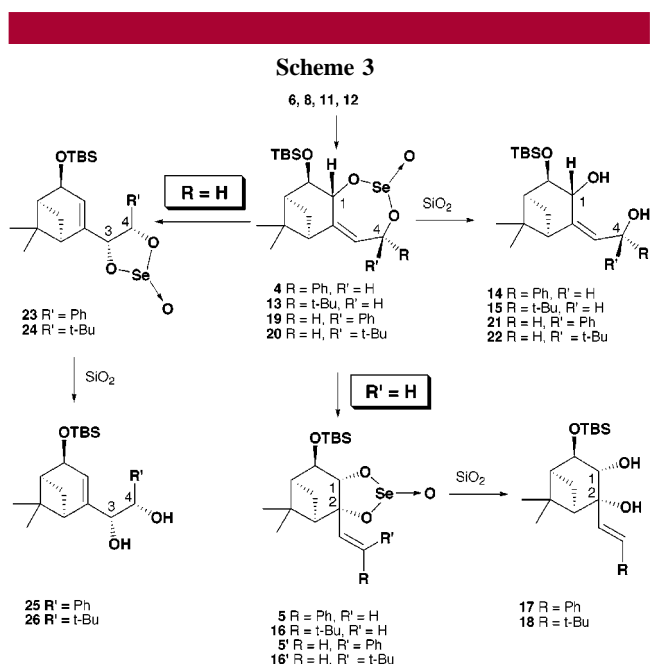


The clean conversion of the *tert*-butyl-substituted *trans* diene **7** to the corresponding selenino lactone **8** was observed within 2 h in CDCl_3 . However, the purported selenino lactone **6** was not detected by the analogous experiment involving diene **3**. The structure of selenino lactone **8** is consistent with the ^1H NMR (δ 3.61, dd, J = 8.8, 2.4 Hz, H-1; 5.94, dd, J = 5.0, 2.8 Hz, H-3; 4.11, dd, J = 4.8, 1.0 Hz, H-4) and ^{77}Se NMR (δ 1228.6, d, J = 13 Hz) resonances. This disparity indicates that the phenyl group may facilitate the conversion of **6** to **4**, whereby the accumulation of **6** to any detectable concentration was prohibited. The identity of **8** was further confirmed by the scrutiny of C–H and C–C connectivity from COSY, gradient HSQC, and carbon-observed proton-decoupled ($^{13}\text{C}\{^1\text{H}\}$) NMR experiments. The signal of the C-1 carbon was observed to be coupled to ^{77}Se (J = 93 Hz), the value of which is consistent with the coupling constant for the typical C–Se one-bond coupling ($^1J_{\text{Se-C}} > 45$ Hz).¹¹ The stereochemistry of **8** was confirmed by a NOESY

experiment showing a NOE between the H-1 and H-4 protons.

The reaction of phenyl- and *tert*-butyl-substituted *cis* dienes **9** and **10** with SeO_2 was also studied (Scheme 2). The formation of the selenino lactone **11** from **9**, with an appreciable amount of isomerization of **9** to the *trans* isomer **3**, was detected by NMR. The selenino lactone structure of **11** is supported by ^1H NMR (δ 4.12, dt, J = 4.4, 2.6 Hz, H-1; 5.80, q, J = 3.7 Hz, H-3; 5.81, t, J = 3.9 Hz, H-4), ^{77}Se NMR (δ 1218.3, dd, J = 26, 15 Hz), and $^1J_{\text{Se-C1}} = 87$ Hz. It was evident from the NMR monitoring that the *cis* isomer **9** reacts with SeO_2 faster than the *trans* isomer **3**. A quantitative conversion of diene **10** to **12** was also observed under identical conditions, albeit, at a much slower rate than the *trans* isomer **7**. The characteristic resonances of adduct **12**, ^1H NMR (δ 3.71, dt, J = 4.2, 3.1 Hz, H-1; 5.57, t, J = 3.1 Hz, H-3; 4.31, t, J = 3.2 Hz, H-4), ^{77}Se NMR (δ 1195.8, dd, J = 26, 15 Hz), and $^1J_{\text{Se-C1}} = 87$ Hz, are close to but different from those of the corresponding diastereomer **8**, which confirms the stereospecific nature of the addition reaction between dienes and SeO_2 .

Once we confirmed the existence of the purported selenino lactones **8**, **11**, and **12**, we studied the reactivity and the fate of these intermediates by NMR, followed by the isolation of the final products (Scheme 3). To exclude the possibility



(8) Mock, W. L.; McCausland, J. H. *Tetrahedron Lett.* **1968**, 3, 391–392.

(9) A degassed benzene solution of **1** was irradiated for 3 h with a 450-W Hanovia medium-pressure mercury lamp equipped with a 0.5 M CuSO_4 filter solution. The *cis* isomer was isolated at 60% conversion in 50% yield and was converted to **9** via reduction followed by silyl protection; **10** was similarly prepared (see Supporting Information).

(10) ^{77}Se NMR spectra were referenced to external SeMe_2 in CDCl_3 ; see: Luthra, N. P.; Odom, J. D. In *The Chemistry of Organic Selenium and Tellurium Compounds*; Patai, S., Rappoport, Z. Eds.; Wiley: New York, 1986; Vol. 1, pp 189–241. A mixture of diene (**3**, **7**, **9**, **10**) and excess SeO_2 in CDCl_3 was vigorously stirred, filtered through a cotton plug to remove excess SeO_2 , and monitored by NMR spectroscopy.

(11) McFarlane, H. C. E.; McFarlane, W. In *NMR of Newly Accessible Nuclei*, Vol. 2; Laszlo, P. Ed.; Academic Press: New York, 1983; pp 275–299 and references therein.

of any acid-catalyzed processes, the selenino lactones **8**, **11**, and **12** were treated with triethylamine or pyridine. Unfortunately, under these conditions the selenino lactones underwent cycloreversion to the starting 1,3-dienes and SeO_2 .¹² In the absence of excess SeO_2 the selenino lactones **8**, **11**, and **12** are stable for several days in CDCl_3 , whereas with

(12) The addition of triethylamine to **13**, independently generated from the reaction of 1,4-diol **15** with SeO_2 , resulted in the ring opening of the cyclic selenite.

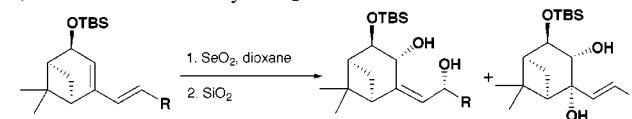
an excess amount of SeO₂ these adducts transformed to cyclic selenites **13** (⁷⁷Se NMR δ 1309.3, t, J = 9 Hz), **19** (2 diastereomers, ⁷⁷Se NMR δ 1346.5, s and δ 1341.1, t, J = 4 Hz), and **20** (⁷⁷Se NMR δ 1309.9, t, J = 9 Hz), respectively.¹³ The existence of these cyclic selenites, including **4** (⁷⁷Se NMR δ 1311.6, t, J = 9 Hz) were further confirmed by isolation of the corresponding 1,4-diols, by SiO₂ chromatography, followed by their regeneration from the reaction of the diols with SeO₂.¹⁴ Remarkably, it was observed that cyclic selenites **4** and **13** stereospecifically rearranged at ambient temperature to selenites **5** (2 diastereomers, ⁷⁷Se NMR δ 1466.0, d, J = 16 Hz and δ 1453.8, s) and **16** (2 diastereomers, δ 1463.4, d, J = 15 Hz, δ 1453.7, s), respectively. The existence of **5** and **16** was inferred from the ⁷⁷Se NMR and the isolation of 1,2-diols **17** and **18**.^{5a} The rate of formation of **5** is faster than that of **16**, presumably as a result of the thermodynamic driving force for the formation of a styrene moiety in **5**.¹⁵

Similarly, the reaction of *cis* dienes **9** and **10** with SeO₂ initially resulted in adducts **11** and **12** (Scheme 2), which smoothly transformed to the 1,4-cyclic selenites **19** and **20**, respectively (Scheme 3).¹⁶ Unlike the 1,4-cyclic selenites **4** and **13**, derived from the *trans* dienes, **19** and **20** rearranged to the regioisomeric 1,2-cyclic selenites **23** (⁷⁷Se NMR δ 1428.4, s) and **24** (⁷⁷Se NMR δ 1414.5, s), eventually affording diols **25** and **26**.^{17,18} The other regioisomers **5'** and **16'** were not detected. We assumed the generation of the *cis* double bond of **5'** and **16'** from **19** and **20** is highly unfavorable compared to the alternative rearrangement affording the endocyclic olefins **23** and **24**.

On the basis of these results, we conclude that the initial addition of SeO₂ to form the selenino lactones (**6**, **8**, **11**, **12**) is a concerted [4 + 2] cycloaddition. These selenino lactones then undergo a stereospecific C–Se bond oxidation, leading to the 1,4-diol cyclic selenites (**4**, **13**, **19**, **20**), which undergo rearrangement to the 1,2-diol cyclic selenites (**5**, **16**, **23**, **24**). To the best of our knowledge this is the first example in which a selenino lactone undergoes a facile C–Se bond oxidation, without the involvement of the well-known [2,3] sigmatropic rearrangement, to form 1,2-diol cyclic selenite via 1,4-diol cyclic selenite as a penultimate intermediate.^{19,20}

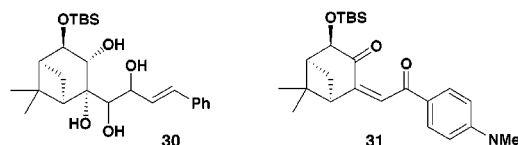
The substituent effect of this syn dihydroxylation of 1,3-dienes was examined (Table 1). The reaction of the parent *trans* phenyl-substituted diene **3** yielded diols **14** (50%) and

Table 1. Substituent Effect of syn Dihydroxylation of 1,3-Dienes Mediated by SeO₂



entry	R	temp (°C)	time (h)	yield (%)
1	Phenyl (3)	25	24	14 (50) 17 (10)
2	Phenyl (3)	80	2	17 (66)
3	2,6-Dichlorophenyl (27a)	25	96	28a (45) 29a (15)
4	2,6-Dichlorophenyl (27a)	80	6	28a (5) 29a (61)
5	Cinnamyl (27b)	25	24	29b (41) ^a
6	4-Dimethylaminophenyl (27c)	25	24	— ^b

^a 20% of products was tetraol **30**. The yield of **30** could be increased to 41% if the reaction was performed at 55 °C for 6 h. ^b 63% of products was 1,4-diketone **31**.



17 (10%) at 25 °C (entry 1). At 80 °C, only 1,2-diol **17** was isolated in 66% (entry 2). The 2,6-dichlorophenyl-substituted diene **27a** afforded diols **28a** (45%) and **29a** (15%) with comparable efficiency, although longer reaction times are required (25 °C, 96 h), presumably because of the electron-withdrawing nature of the dichloro substituents (entry 3). Similarly, 1,2-diol **29a** (61%) was obtained with minor 1,4-diol **28a** (5%) at 80 °C (entry 4). The cinnamyl derivative **27b** afforded exclusively 1,2-diol **29b** (41%) without 1,4-diol **28b**, along with tetraol **30** (20%) (entry 5). 4-Dimethylaminophenyl-substituted diene **27c** did not lead to any diols; instead, the 1,4-diketone **31** was isolated (63%) (entry 6).

In summary, we have discovered a novel syn dihydroxylation of 1,3-dienes with SeO₂, which involves a [4 + 2] cycloaddition followed by C–Se bond oxidation. The efficiency of this process is a function of the stereoelectronic nature of the substituents on the diene. Another finding is the stereospecific conversion of a 2-alkene-1,4-diol moiety to a 3-alkene-1,2-diol moiety by SeO₂ under mild conditions. The usefulness of these transformations is currently under study, and the result will be reported in due course.

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Supporting Information Available: Characterization data for all new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(13) In the conditions for the rearrangement of **13** to **16**, 1,4-diketone **32** and the corresponding hydroxyketone **33** were obtained (see Supporting Information).

(14) (a) Denney, D. B.; Denny, D. Z.; Hammond, P. J.; Hsu, Y. F. *J. Am. Chem. Soc.* **1981**, *103*, 2340–2347.

(15) The stereochemistry of the C-1 and C-2 positions of 1,2-diol **17** was confirmed by an X-ray analysis of the corresponding acetonide.

(16) The minor isomerization of *cis*-diene **9** induced by SeO₂ to *trans*-dienes **3** resulted in the formations of diols **14**, **17**, **21**, and **25**.

(17) Interestingly, the reaction of **21** with excess SeO₂ at 40 °C did not lead to any expected 1,2-diol **25**, and instead 1,2-diol **17** was isolated. It is believed that under the reaction conditions **19** rearranged to **5** via a benzylic cation.

(18) Diol **26** was independently generated by reaction of *cis* diene **10** with OsO₄/NMO at 50 °C.

(19) Sharpless, K. B.; Singer, S. P. *J. Org. Chem.* **1976**, *41*, 2504–2506.

(20) The reaction of a purified selenino lactone **12** with mCPBA in CDCl₃ directly produced 1,2-cyclic selenite **24**. The 1,4-cyclic selenite **20** was not observed.