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A Novel Reactivity of SeO_2 with 1,3-Dienes: Formation of syn 1,2- and 1,4-Diols via a Facile C–Se Bond Oxidation

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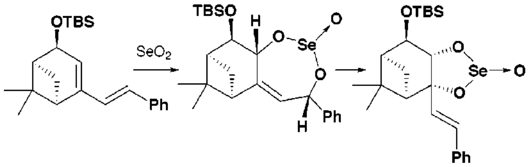
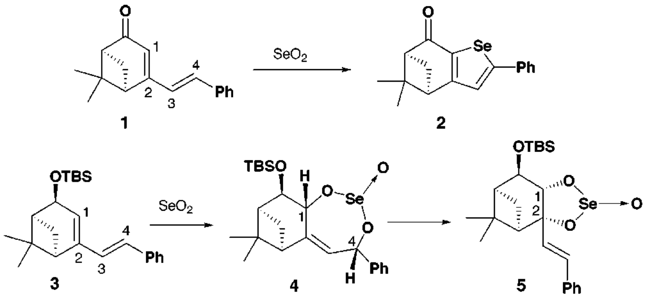
ABSTRACT



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 OsO_4,[2] RuO_4,[3] and MnO_4,[4] whereas anti addition is brought about by other oxides such as SeO_2[5] and WO_3.[6] In our investigations of the reaction between SeO_2 and 1,3-dienes, a novel reactivity profile of SeO_2 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 SeO_2 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 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

Scheme 1



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(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.

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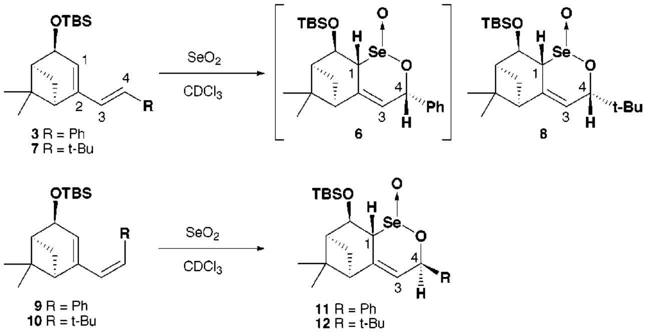
of the intermediates involved in this novel syn dihydroxylation reaction by SeO_2 and the stereospecificity of the C−Se bond oxidation.

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 monitered by NMR spectroscopy (Scheme 2).[10]

Scheme 2

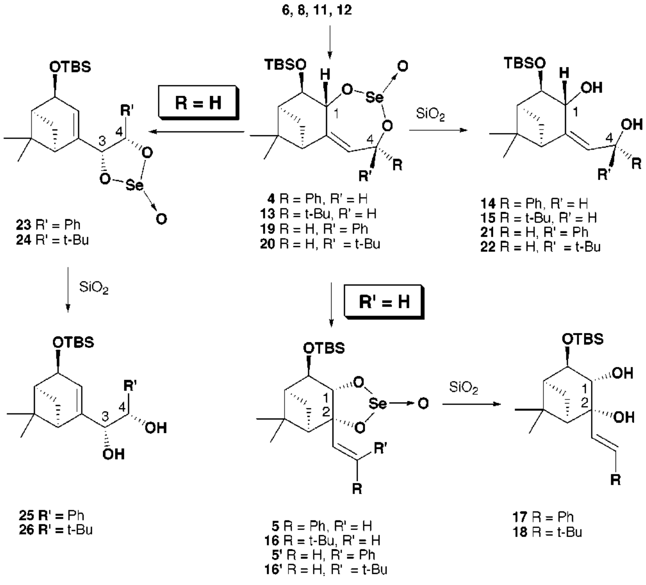


The clean conversion of the *tert*-butyl-substituted *trans* diene **7** to the corresponding selenino lactone **8** was observed within 2 h in $CDCl_3$. However, the purported selenino lactone **6** was not detected by the analogous experiment involving diene **3**. The structure of selenino lactone **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 ($^{13}C\{^1H\}$) 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 ($^1J_{Se-C} > 45$ 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 $^1J_{Se-C1} = 87$ 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 $^1J_{Se-C1} = 87$ 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 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

Scheme 3



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(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.

(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.

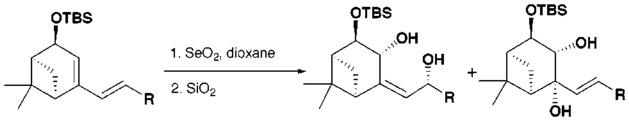
an excess amount of SeO_2 these adducts transformed to cyclic selenites **13** (^{77}Se NMR δ 1309.3, t, $J = 9$ Hz), **19** (2 diastereomers, ^{77}Se NMR δ 1346.5, s and δ 1341.1, t, $J = 4$ Hz), and **20** (^{77}Se NMR δ 1309.9, t, $J = 9$ Hz), respectively.[13] The existence of these cyclic selenites, including **4** (^{77}Se NMR δ 1311.6, t, $J = 9$ Hz) were further confirmed by isolation of the corresponding 1,4-diols, by SiO_2 chromatography, followed by their regeneration from the reaction of the diols with SeO_2.[14] Remarkably, it was observed that cyclic selenites **4** and **13** stereospecifically rearranged at ambient temperature to selenites **5** (2 diastereomers, ^{77}Se 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 ^{77}Se 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 SeO_2 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** (^{77}Se NMR δ 1428.4, s) and **24** (^{77}Se 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 SeO_2 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]

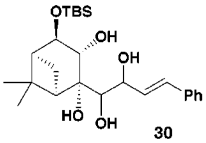
The substituent effect of this syn dihydroxylation of 1,3-dienes was examined (Table 1). The reaction of the parent *trans* phenyl-substituted diene **3** yielded diols **14** (50%) and **17** (10%) at 25 °C (entry 1). At 80 °C, only 1,2-diol **17** was isolated in 66% (entry 2). The 2,6-dichlorophenyl-substituted 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).

Table 1. Substituent Effect of syn Dihydroxylation of 1,3-Dienes Mediated by SeO_2



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**.



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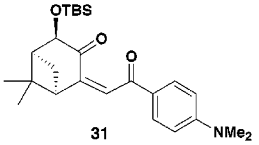

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In summary, we have discovered a novel syn dihydroxylation of 1,3-dienes with SeO_2, which involves a [4 + 2] cycloaddition followed by C−Se bond oxidation. The efficiency of this process is a function of the stereoelectronic nature of the substituents on the diene. Another finding is the sterospecific conversion of a 2-alkene-1,4-diol moiety to a 3-alkene-1,2-diol moiety by SeO_2 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 SeO_2 to *trans*-dienes **3** resulted in the formations of diols **14**, **17**, **21**, and **25**.

[17] Interestingly, the reaction of **21** with excess SeO_2 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 OsO_4/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 $CDCl_3$ directly produced 1,2-cyclic selenite **24**. The 1,4-cyclic selenite **20** was not observed.