ORGANIC
LETTERS

2004
Vol. 6, No. 5
775−777

Catalytic Allylic Oxidation with a Recyclable, Fluorous Seleninic Acid

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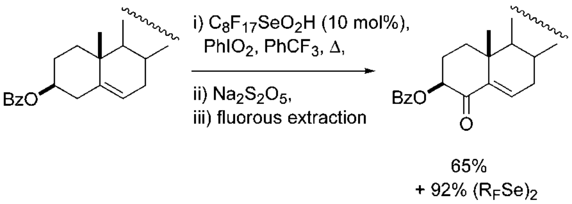
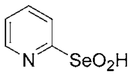
Received December 24, 2003

ABSTRACT

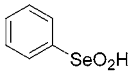


In conjunction with iodoxybenzene as reoxidant perfluorooctylseleninic acid catalyzes the allylic oxidation of alkenes to enones in trifluoromethylbenzene at reflux in moderate to good yield. After a reductive workup with sodium metabisulfite, the catalyst is recovered by fluorous extraction in the form of bis(perfluorooctyl) diselenide, which, itself, serves as a convenient catalyst precursor.

The allylic oxidation of alkenes is a reaction of fundamental importance from the research laboratory to the plant.[1] As such it is undergoing continual refinement with a view to the development of more environmentally friendly, efficient, and selective processes.[2] Selenium dioxide has long been a favorite reagent for this transformation[3] and also a target for incorporation into catalytic cycles.[4] In 1985 it was reported that 2-pyridylseleninic acid (**1**), in contrast to benzeneseleninic acid (**2**), was an effective catalyst for the allylic oxidation of alkenes to alkenones in the presence of iodoxybenzene as stoichiometric reagent.[5] Subsequently, more electron-deficient arylseleninic acids, in particular pentafluorobenzeneseleninic acid (**3**) and 2-pyridylseleninic acid *N*-oxide (**4**), were shown to be more effective allylic oxidation catalysts.[6] Unfortunately these suffered from a number of unsatisfactory characteristics, not the least of which was a tendency toward explosive decomposition. We reasoned that the attachment of a perfluoroalkyl, or fluorous, chain directly to selenium would enable the formation of a highly electron-deficient seleninic acid catalyst that would not suffer from the same problems as the aromatic variants. We report here that this is indeed the case and that perfluorooctylseleninic acid (**5**) is an effective catalyst for the oxidation of alkenes to enones when used in conjunction with a hypervalent iodine-based oxidant.



1



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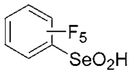

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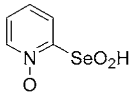

4

R_F-SeO_2H

5

$\boxed{R_F = C_8F_{17}}$

The catalyst (**5**) is readily assembled in a simple two-step protocol from perfluorooctyl iodide and dibutyl diselenide

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[1] Reviews: (a) Andrus, M. B.; Lashley, J. C. *Tetrahedron* **2002**, *58*, 845. (b) Sheldon, R. A. In *Fine Chemicals Through Heterogeneous Catalysis*; Sheldon, R. A., Van Bekkum, H., Eds.; Wiley-VCH: Weinheim, Germany, 2001; p 519. (c) Grennberg, H.; Backvall, J. E. In *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Eds.: Wiley-VCH: Weinheim, Germany, 1998; Vol. 2, p 200. (d) Schlingloff, G.; Bolm, C. In *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Eds.: Wiley-VCH: Weinheim, Germany, 1998; Vol. 2, p 193. (e) Bulman Page, P. C.; McCarthy, T. J. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.: Pergamon: Oxford, UK, 1991; Vol. 7, p 83. (f) Eames, J.; Watkinson, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 3567.

[2] Recent work: (a) Yu, J.-Q.; Corey, E. J. *J. Am. Chem. Soc.* **2003**, *125*, 3232.

[3] Hoekstra, W. J. In *EROS*; Paquette, L. A., Ed.: Wiley: Chicester, UK, 1995; Vol. 6, p 4437.

[4] (a) Umbreit, M. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 5526. (b) For a discussion of allylic oxidation with seleninic acids see: Ley, S. V. In *Organoselenium Chemistry*; Liotta, D., Ed.: Wiley: New York, 1987; p 163.

10.1021/ol036501h CCC: $27.50

with the aid of Rongalite. As expected from the recent work of Wakselman,[7] this affords perfluorooctyl butyl selenide (**6**) in good yield. Treatment with hydrogen peroxide then affords the selenoxide, which undergoes syn-elimination to give perfluorooctylseleninic acid (**7**), which then suffers further oxidation to the desired product (**5**) (Scheme 1). Although diethyl diselenide would have served admirably in place of dibutyl diselenide in this synthesis and maximized atom efficiency, dibutyl diselenide was preferred owing to its less volatile, less malodorous nature, but one that nevertheless is coupled to the formation of a single gaseous byproduct. The seleninic acid **5** generated in this manner was a stable but somewhat insoluble, amorphous white stable solid with a melting point of 135−137 °C and a high-resolution mass structure consistent with the assigned spectrum. Although **5** was insoluble in most organic solvents and fluorous hydrocarbons, it dissolved readily in hot trifluoromethylbenzene (benzotrifluoride),[8] which was selected, therefore, as the solvent of choice for the oxidation protocol. Importantly, it shows no tendency toward explosion, at least in our laboratory.

Scheme 1. Preparation of the Fluorous Selininic Acid **5**

$$R_F{-}I \;+\; 0.5\,Bu_2Se_2 \xrightarrow[\text{DMF, } N_2]{HOCH_2SO_2Na} \underset{\mathbf{6},\ 85\%}{R_F{-}SeBu}$$

$$\xrightarrow{H_2O_2} \underset{\mathbf{7}}{\left[\,R_F{-}SeOH\,\right]} \xrightarrow{H_2O_2} \underset{\mathbf{5},\ 92\%}{R_F{-}SeO_2H}$$

3*β*-Cholesteryl benzoate served as a model substrate with which to survey allylic oxidation by means of a catalytic quantity of **5** and a range of stoichiometric reoxidants. These included hydrogen peroxide, *tert*-butyl hydroperoxide, *m*-CPBA, and iodoxybenzene.[9] Of these the latter gave the cleanest overall conversion of alkenes to enones with the mimimum formation of byproducts. A protocol was therefore developed in which the olefin (1 mmol), iodoxybenzene (3 mmol), and **5** (0.1 mmol) were heated to reflux with stirring under nitrogen in benzotrofluoride (10 mL) until completion (Scheme 2). Workup involved addition of solid sodium metabisulfite (1 mmol), followed by stirring at room temperature for 3 h before dilution with ethyl acetate and washing with water.[10] After removal of the volatiles the organic phase was partitioned between dichloromethane (3.0 mL) and perfluorohexanes (10.0 mL) in a water-cooled continuous extractor[11] for 3 h. Evaporation of the fluorous phase returned the catalyst in the form of the diselenide **8**, whereas chromatography of the organic layer over silica gel yielded the enone. A number of oxidations were conducted in this manner, with the results reported in Table 1.

Scheme 2. Allylic Oxidation with Catalytic **5** and Iodoxybenzene

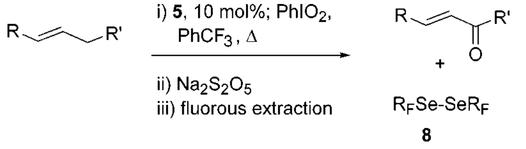
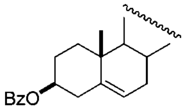
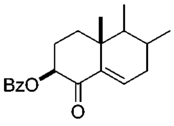
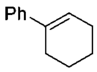
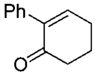
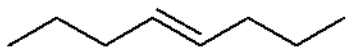
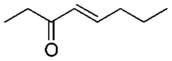
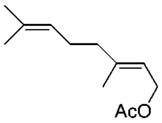
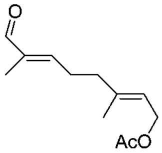
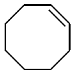
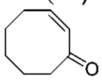
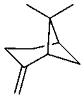
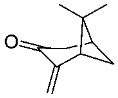
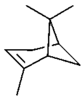
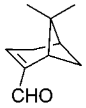


Table 1. Allylic Oxidation with Catalytic **5** and Iodoxybenzene

substrate	product (% yield)	% recovered R_FSeSeR_F (**8**)
 **9**	 **10** (65)	92
 **11**	 **12** (63)	88
 **13**	 **14** (64)	88
 **15**	 **16** (50)	90
 **17**	 **18** (58)	90
 **19**	 **20** (41)	90
 **21**	 **22** (62)	86

It is noteworthy that none of the oxidations reported in Table 1 are complicated by the issue of allylic transposition. The chemistry therefore closely parallels that of selenium

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(5) Barton, D. H. R.; Crich, D. *Tetrahedron* **1985**, *41*, 4359.

(6) Barton, D. H. R.; Wang, T.-L. *Tetrahedron Lett.* **1994**, *35*, 5149

(7) Magnier, E.; Vit, E.; Wakselman, C. *Synlett* **2001**, 1260.

(8) (a) Ogawa, A.; Curran, D. P. *J. Org. Chem.* **1997**, *62*, 450. (b) Maul, J. J.; Ostrowski, P. J.; Ublacker, G. A.; Linclau, B.; Curran, D. P. *Top. Curr. Chem.* **1999**, *206*, 79.

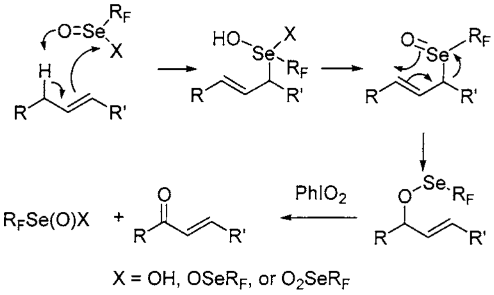
(9) For the first use of iodoxybenzene as stoichiometric oxidant in conjunction with an organoselenium catalyst see: Barton, D. H. R.; Morzycki, J. W.; Motherwell, W. B.; Ley, S. V. *J. Chem. Soc., Chem. Commun.* **1981**, 1044.

(10) The insertion of a reduction into the workup is to facilitate recovery of the fluorous reagent—diselenide **8** dissolves readily in organic and fluorous solvents whereas the amorphous seleninic acid is poorly soluble and so not accessible to an extractive workup and separation.

(11) Crich, D.; Hao, X.; Lucas, M. *Tetrahedron* **1999**, *55*, 14261.

dioxide and accordingly, in line with current mechanistic thinking,[12] we postulate a mechanism involving an initial ene reaction followed by a 2,3-sigmatropic rearrangement (Scheme 3). At this stage it is not possible to determine the mode of oxidation of the rearranged selenous ester to the final product: both direct oxidation and oxidation of the liberated allylic alcohol can be envisaged. Similarly, it is not possible at the present time to determine whether the oxidation is occurring via the acid **5**, its anhydride, or a mixed anhydride of **5** and the corresponding seleninic acid.

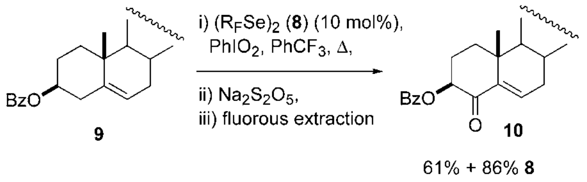
Scheme 3. Probable Mechanism for Oxidation by **5** and $PhIO_2$



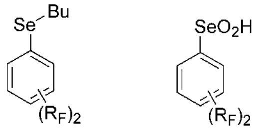
Where regiochemistry is an issue Guillemonat's rules[13] for allylic oxidation by selenium dioxide are shadowed. For example, 1-phenylcyclohexene (**11**) undergoes oxidation at the more hindered end of the alkene; geranyl acetate (**15**) selectively gave the 8*E*-aldehyde (**16**), again in line with precedent.[5] Interestingly, oxidation of the 3β-cholesteryl benzoate (**9**) yielded only the 4-one (**10**) whereas oxidation of the same substrate by **1** resulted in a 3.7:1 mixture of the 4-one and the corresponding 7-one. The oxidation of 3β-cholesteryl benzoate by selenium dioxide is not a clean reaction and affords 4β-hydroxy-3β-cholesteryl benzoate in approximately 30% yield.[14]

The workup protocol devised involves a reduction step. This is necessary because of the somewhat insoluble nature of **5** in typical organic and fluorous solvents, which hampers direct recovery of the catalyst. As this protocol returns the catalyst in the form of the diselenide, it was necessary for the purposes of recycling to demonstrate the ability of this substance to serve as catalyst precursor. In the event, replacement of **5** by the diselenide in a typical oxidation proceeded according to the established pattern (Scheme 4).

Scheme 4. Oxidation of Cholesteryl Benzoate by the Diselenide and $PhIO_2$



It is of some interest to note the difference between catalyst **5** and the related fluorous seleninic acids **25** and **26**, generated in situ from the butyl selenides **23** and **24**, which are reported to catalyze the epoxidation of alkenes when used in conjunction with 60% hydrogen peroxide.[15,16] This difference in reactivity, allylic oxidation vs epoxidation, may be a function of the more electron-deficient selenium in **5**, or may arise from the different reoxidants employed. The formation of perseleninic acids with hydrogen peroxide as oxidant, which presumably accounts for the epoxidation reaction, is obviously not possible when iodoxybenzene is employed as reoxidant. Unfortunately, when hydrogen peroxide was employed as oxidant in conjunction with **5** complex reaction mixtures were obtained: similar results were observed with **5** and *tert*-butyl hydroperoxide.



23: 2,4-$(C_8F_{17})_2$ **25:** 2,4-$(C_8F_{17})_2$
24: 3,5-$(C_8F_{17})_2$ **26:** 3,5-$(C_8F_{17})_2$

In closing we stress that the chemistry described herein differs significantly from that of most fluorous reagents developed to date[17] insofar as it takes direct advantage of the powerfully electron-drawing nature of the fluorous chain, rather than interposing a spacer group. We anticipate the development of further useful reagents based on this concept.[18]

Acknowledgment. We thank the NSF (CHE 9986200) for support of this work.

Supporting Information Available: Experimental details for the preparation of **5** and for the allylic oxidation protocol. This material is available free of charge via the Internet at http://pubs.acs.org.

OL036501H

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[12] (a) Singleton, D. A.; Hang, C. *J. Org. Chem*. **2000**, *65*, 7554. (b) Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc*, **1972**, *94*, 7154.

[13] (a) Guillemonat, A. *Ann. Chim*. **1939**, *11*, 143. (b) Fieser, L. F.; Fieser, M. In *Reagents for Organic Synthesis*; Wiley: New York, 1967; Vol. 1, p 992.

[14] Vigier, A.; Marquet, A.; Barton, D. H. R.; Motherwell, W. B.; Zard, S. Z. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1937.

[15] (a) Betzemeier, B.; Lhermitte, F.; Knochel, P. *Synlett* **1999**, 489. (b) ten Brink, G.-J.; Vis, M.; Arends, I. W. C. E.; Sheldon, R. A. *Tetrahedron* **2002**, *58*, 3977.

[16] The 3,5-disubstituted system also catalyzes the Baeyer−Villiger oxidation of cyclobutanone.[15b]

[17] For a collection of articles on fluorous reagents and catalysts see: Curran, D. P.; Gladysz, J. A., Eds. *Tetrahedron* **2002**, *58*, 3823.

[18] In a similar vein we have also reported the development of a fluorous version of borane dimethyl sulfide in which the fluorous chain serves the dual purposes of facilitating purification/recycling and of rendering the borane air stable: Crich, D.; Neelamkavil, S. *Org. Lett.* **2002**, *4*, 4175.