JOC*Note*

Catalytic Oxidation Adjacent to Carbonyl Groups and at Benzylic Positions with a Fluorous Seleninic Acid in the Presence of Iodoxybenzene

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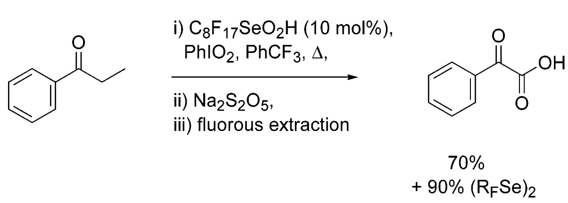
Received January 6, 2005



In conjunction with iodoxybenzene as oxidant, perfluorooctylseleninic acid serves as a catalyst for the oxidation of aryl alkyl ketones to the corresponding ketoacids. Benzylic methylene groups are also oxidized by this reagent combination to the corresponding ketones.

The development of improved oxidation reactions is an area of great current interest owing to their almost ubiquitous nature in both academic and industrial laboratories and the less than ideal nature of most classical oxidation protocols.[1] For our part we have been interested in fluorous organosulfur[2] and organoselenium[3] oxidation catalysts and reagents. Our work with fluorous organoselenium-based oxidations began,[3] as did that of other groups,[4] with the attachment of fluorous ponytails to classical arylselenium derivatives with a view to rendering them soluble in fluorous media.[5] However, the realization that the strongly electron-withdrawing fluorous ponytails ought, if attached directly to the reaction site, to enhance oxidizing power led us to the simpler fluorous seleninic acid **1**, which served as an admirable catalyst for the allylic oxidation of alkenes in the presence of stoichiometric iodoxybenzene.[6] The ability of **1** to effect allylic oxidation and its recovery from these reactions in the form of the reusable diselenide **2** make it an attractive replacement for selenium dioxide. The allylic oxidation reaction also marks the difference between **1** and classical areneseleninic acids, which do not typically bring about allylic oxidation,[7,8] and the various fluorous arylselenium-based catalysts,[4,5a] which effect epoxidation of alkenes, thereby emphasizing the profound effect of the fluorous ponytail attached directly to the reaction center. In this Note we continue the parallel between **1** and selenium dioxide and show that **1** serves as a recoverable catalyst for oxidation adjacent to carbonyl groups and of benzylic positions.

$R_F{-}SeO_2H$ **1** $(R_F{-}Se)_2$ **2** $R_F{-}SeBu$ **3**

$R_F = C_8F_{17}$

As before[6] seleninic acid **1** was accessed by treatment of butyl perfluorooctyl selenide **3**, itself obtained simply from perfluorooctyl iodide and dibutyl diselenide,[2,9] with hydrogen peroxide. Substrates for oxidation (1 mmol) were heated to reflux with stirring under nitrogen in benzotrifluoride (10 mL)[10] with **1** (0.1 mmol) and iodoxybenzene (3 mmol) until completion. The cooled reaction mixture was then treated with sodium metabisulfite, to reduce the various fluorous organoselenium products to the diselenide **2**,[11] and after washing with water, partitioned between perfluorohexanes and dichloromethane in a water-cooled continuous extractor.[12] Iodobenzene and the oxidation product were then separated by filtration of the dichloromethane layer on silica gel with any residual hypervalent iodine species remaining on the column. The results of these oxidations together with the amount of diselenide **2** recovered are presented in Table 1.

In each of the experiments presented in Table 1 the catalyst was introduced as the preformed isolated acid; however, for reasons of experimental convenience it is recovered in the reduced form as the diselenide **2**. In principle,[13] the diselenide **2** can be oxidized in situ to the acid **1** and may therefore serve as a practical catalyst

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(1) For example see: (a) *Modern Oxidation Methods*; Bäckvall, J.-E., Ed.; Wiley-VCH: Weinheim, Germany, 2004.

(2) (a) Crich, D.; Neelamkavil, S. *J. Am. Chem. Soc.* **2001**, *123*, 7449. (b) Crich, D.; Neelamkavil, S. *Tetrahedron* **2002**, *58*, 3865.

(3) (a) Crich, D.; Barba, G. R. *Org. Lett.* **2000**, *2*, 989. (b) Crich, D.; Neelamkavil, S.; Sartillo-Piscil, F. *Org. Lett.* **2000**, *2*, 4029.

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

(5) Reviews on fluorous supported oxidations: (a) Crich, D.; Zou, Y. In *Handbook of Fluorous Chemistry*; Gladysz, J. A., Curran, D. P., Horváth, I. T., Eds.; Wiley-VCH: Weinheim, Germany, 2004; p 202. (b) Pozzi, G.; Quici, S. In *Handbook of Fluorous Chemistry*; Gladysz, J. A., Curran, D. P., Horváth, I. T., Eds.; Wiley-VCH: Weinheim, Germany, 2004; p 290. (c) Vincent, J.-M.; Lastécouères, D.; Contel, M.; Laguna, M.; Fish, R. H. In *Handbook of Fluorous Chemistry*; Gladysz, J. A., Curran, D. P., Horváth, I. T., Eds.; Wiley-VCH: Weinheim, Germany, 2004; p 298. (d) Bégué, J.-P.; Bonnet-Delpon, D.; Crousse, B. In *Handbook of Fluorous Chemistry*; Gladysz, J. A., Curran, D. P., Horváth, I. T., Eds.; Wiley-VCH: Weinheim, Germany, 2004; p 341.

(6) Crich, D.; Zou, Y. *Org. Lett.* **2004**, *6*, 775.

(7) 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.

(8) The exceptions here are 2-pyridineseleninic acid, the unstable 2-pyridineseleninic acid *N*-oxide, and pentafluorobenzeneseleninic acid, each of which effect allylic oxidation: (a) Barton, D. H. R.; Crich, D. *Tetrahedron* **1985**, *41*, 4359. (b) Barton, D. H. R.; Wang, T.-L. *Tetrahedron Lett.* **1994**, *35*, 5149.

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

(10) (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. (c) Gladysz, J. A.; Emnet, C. In *Handbook of Fluorous Chemistry*; Gladysz, J. A., Curran, D. P., Horváth, I. T., Eds.; Wiley-VCH: Weinheim, Germany, 2004; p 11.

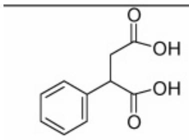
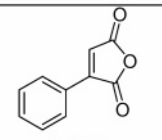
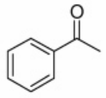
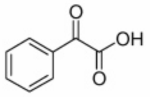
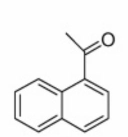
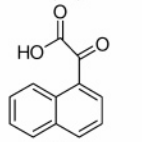
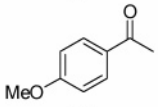
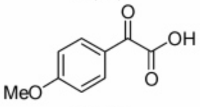
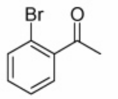
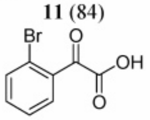
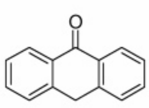
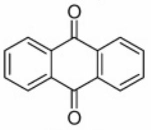
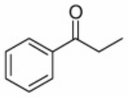
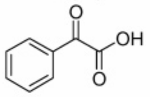
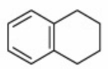
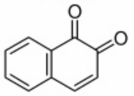
(11) The reduction step is to facilitate recovery of the fluorous reagent: diselenide **2** dissolves readily in organic and fluorous solvents whereas the amorphous seleninic acid is poorly soluble and so is not accessible to an extractive workup and separation.

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

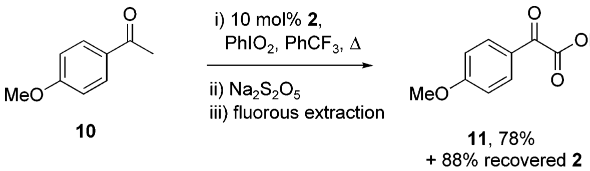
(13) Barton, D. H. R.; Morzycki, J. W.; Motherwell, W. B.; Ley, S. V. *J. Chem. Soc., Chem. Commun.* **1981**, 1044.

10.1021/jo0500333 CCC: $30.25

TABLE 1. Oxidations with Iodoxybenzene and Catalytic 1

Substrate	Product (% yield)	Recovered 2 (%)
 **4**	 **5** (70)	90
 **6**	 **7** (80)	89
 **8**	 **9** (72)	92
 **10**	 **11** (84)	90
 **12**	 **13** (82)	92
 **14**	 **15** (72)	90
 **16**	 **7** (70)	90
 **17**	 **18** (50)	90

SCHEME 1. Use of Diselenide 2 as a Catalyst Precursor



precursor. We had previously established this to be the case for the allylic oxidation sequence and now show through the example of Scheme 1 that this maxim also holds for the present oxidations.

Experimental Section

Dibutyl Diselenide. To a mixture of selenium powder (2.0 g, 25 mmol) and sodium hydroxide (1.0 g, 25 mmol) was added 85% hydrazine hydrate (0.5 mL, 8.5 mmol) under nitrogen. The mixture was heated to 70 °C with stirring until all the selenium powder was consumed (3 h). Tetrabutylammonium bromide (0.15 g, 88 mmol) and butyl bromide (3.4 g, 25 mmol) were then added leading to the separation of a heavy oil. The reaction mixture was allowed to cool to room temperature, the organic layer was separated, and the aqueous layer was extracted with petroleum ether (2 × 5 mL). The combined organic layer was washed with water (2 × 10 mL), then brine (2 × 10 mL) and dried over anhydrous sodium sulfate. After concentration of the crude mixture, the residue was distilled (80 °C, 1 mmHg) to afford dibutyl diselenide[14] (2.72 g, 80%) as an oil. ^{1}H NMR (CDCl$_3$) δ 0.92 (t, J = 7.5 Hz, 6H), 1.39 (sextet, J = 7.5 Hz, 4H), 1.71 (quintet, J = 7.5 Hz, 4H), 2.93 (t, J = 7.5 Hz 4H); ^{13}C NMR δ 13.6, 22.6, 30.0, 33.1.

Butyl Perfluorooctyl Selenide (3). Dibutyl diselenide (1.20 g, 4.41 mmol) was dissolved in DMF (15.0 mL) under nitrogen. Perfluorooctyl iodide (2.36 mL, 8.80 mmol), prewashed with a 10% aqueous solution of Na$_2$S$_2$O$_5$, was added followed by water (0.5 mL). Last, sodium hydroxymethanesulfinate (2.04 g, 13.2 mmol) was added in portions over 3 h. The solution was stirred at room temperature for 20 h, then the mixture was extracted with Et$_2$O and the organic layer washed with 5% aqueous NaHCO$_3$ and water, then dried over Na$_2$SO$_4$ and concentrated under reduced pressure. The product was purified by flash chromatography on silica gel with hexane as eluent to afford butyl perfluorooctyl selenide (4.15 g, 85% based on C$_8$F$_{17}$I) in the form of an oil. ^{1}H NMR (CDCl$_3$) δ 0.94 (t, J = 7.5 Hz, 3H), 1.43 (sextet, J = 7.5 Hz, 2H), 1.76 (quintet, J = 7.5 Hz, 2H), 3.03 (t, J = 7.5 Hz, 2H); ^{19}F NMR δ 8.4, −14.4, −45.9, −48.9, −49.5, −50.4, −53.8; HRMS [M$^{\bullet+}$] 555.9598, found 555.9559.

Perfluorooctylseleninic Acid (1). Hydrogen peroxide (30%, 10.00 mmol, 1.00 mL) was added to a stirred solution of butyl perfluorooctyl selenide (0.56 g, 1.00 mmol) in hexafluoro-2-propanol (8.00 mL) in a closed flask at 0 °C, and then the reaction mixture was warmed to room temperature and stirred for 20 h. Perfluorooctylseleninic acid (0.49 g, 92%) was obtained as an insoluble, amorphous white solid after evaporation of the solvent. Mp 135−137 °C; HRMS [M − H]$^-$ 530.8799, found 530.8792.

General Procedure for Oxidation. The substrate (1.0 mmol), iodoxybenzene (3.0 mmol), and perfluorooctyl seleninic acid (0.1 mmol) were stirred in anhydrous α,α,α-trifluorotoluene (10.0 mL) at reflux under nitrogen. After complete conversion (TLC) of the substrate, the mixture was allowed to cool to room temperature. Sodium metabisulfite (1.0 mmol) was then added and the mixture stirred for 3 h. The reaction mixture was then diluted with ethyl acetate (8.0 mL), and the organic phase was washed with water and brine and concentrated in vacuo to give a residue that was portioned between CH$_2$Cl$_2$ (3.0 mL) and FC-72 (20.0 mL) in the water-cooled continuous extractor[12] for 3 h. Evaporation of the FC-72 phase provided the recovered diselenide whereas elution of the organic phase from silica gel with hexane/dichloromethane mixtures gave first iodobenzene and then the oxidation product.

Di(perfluorooctyl) Diselenide (2). As recovered from the above experiments **2** was a white solid. Mp 58−60 °C; ^{19}F NMR (C$_6$D$_6$/hexane) δ −9.3, −13.4, −45.3, −49.3, −49.9, −50.8, −54.4. FAB-HRMS, calcd for C$_{16}$F$_{34}$Se$_2$ 997.7787, found 997.7872 (M$^{+\bullet}$)

Phenylmaleic Anhydride (5). Oxidation of phenylsuccinic acid (194 mg, 1.0 mmol) provided phenylmaleic anhydride (125 mg, 70%). Mp 119−120 °C (lit.[15] mp 119−120.5 °C). ^{1}H NMR (CDCl$_3$) δ7.95−7.99 (m, 2H), 7.51−7.55 (m, 3H), 7.00 (s, 1H). Diperfluorooctyl diselenide (45 mg, 90%) was recovered from this experiment.

Phenylglyoxylic Acid (7). Following the general procedure, acetophenone (120 mg, 1.0 mmol) afforded phenylglyoxylic acid (123 mg, 80%). Mp 62−64 °C (lit.[16] mp 62−64 °C). ^{1}H NMR (CDCl$_3$) δ 12.47 (s, 1H), 8.14 (d, J = 7.8, 2H), 7.65 (t, J =

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7.8 Hz, 1H), 7.51 (t, $J = 7.8$ Hz, 2H). Diperfluorooctyl diselenide (44.5 mg, 89%) was recovered from this experiment. Phenylglyoxylic acid was also obtained in 70% yield on subjection of propiophenone to the standard oxidation conditions.

1-Naphthylglyoxylic Acid (9). Oxidation of 1-(1-naphthyl)-ethanone (170 mg, 1.0 mmol) gave 1 naphthylglyoxylic acid (145 mg, 72%). Mp 112−114 °C (lit.[17] mp 111−114 °C). ^{1}H NMR (CDCl$_3$) δ 9.08 (d, 1H), 8.41 (d, 1H), 8.10 (d, 1H), 7.93 (d, 1H), 7.67(t, 1H), 7.53−7.59 (m, 2H). Diperfluorooctyl diselenide (46 mg, 92%) was recovered from this experiment.

(4-Methoxyphenyl)glyoxylic Acid (11). Oxidation of *p*-methoxyacetophenone (150 mg, 1.0 mmol) provided (4-methoxyphenyl)glyoxylic acid (158 mg, 84%). Mp 92−94 °C (lit.[18] mp 91−93 °C). ^{1}H NMR (CDCl$_3$) δ 8.07 (d, $J = 9.0$ Hz, 2H), 6.95 (d, $J = 9.0$ Hz, 2H), 3.88 (s, 3H). Diperfluorooctyl diselenide (45 mg, 90%) was recovered from this experiment.

(2-Bromophenyl)glyoxylic Acid (13). Oxidation of *o*-bromoacetophenone (198 mg, 1.0 mmol) provided 2-bromophenylglyoxylic acid (188 mg, 82%). Mp 102−104 °C (lit.[19] mp 93−103 °C). ^{1}H NMR (CDCl$_3$) δ 8.01 (d, 1H), 7.72 (d, 2H), 7.40 (m, 2H). Diperfluorooctyl diselenide (46 mg, 92%) was recovered from this experiment.

Anthraquinone (15). Oxidation of anthrone (194 mg, 1.0 mmol) afforded anthraquinone (150 mg, 72%). Mp 280−282 °C (lit.[20] mp 280−282 °C). ^{1}H NMR (CDCl$_3$) δ 8.32 (m, 4H), 7.81 (m, 4H). Diperfluorooctyl diselenide (45 mg, 90%) was recovered from this experiment.

1,2-Naphthoquinone (18). Oxidation of tetralin (132 mg, 1.0 mmol) provided **18** (80 mg, 50%). Mp 144−146 °C (lit.[21] mp 145−146 °C). ^{1}H NMR (CDCl$_3$) δ 8.12 (d, $J = 7.8$ Hz, 1H), 7.65 (t, $J = 7.8$ Hz, 1H), 7.52 (t, $J = 7.8$ Hz, 1H), 7.44 (d, $J = 10.2$ Hz, 1H), 7.36 (d, $J = 7.8$ Hz, 1H), 6.40 (d, $J = 10.2$ Hz, 1H). Diperfluorooctyl diselenide (45 mg, 90%) was recovered from this experiment.

Acknowledgment. The University of Illinois at Chicago is acknowledged for partial support.

Supporting Information Available: Copies of ^{1}H or ^{19}F NMR spectra of all products. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0500333

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