

Catalytic Use of Selenium Electrophiles in Cyclizations

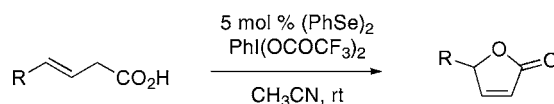
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ABSTRACT



A new and convenient one-pot method for a catalytic addition–elimination reaction using selenium electrophiles has been developed. In the presence of 5 mol % diphenyl diselenide, [bis(trifluoroacetoxy)iodo]benzene in acetonitrile converted a range of (*E*)-3-butenic acids into the corresponding butenolides in good yields.

Organic selenium compounds are frequently used as convenient reagents for introducing various functional groups to carbon–carbon double bonds and for constructing heterocyclic compounds via ring-closure processes. The mild reaction conditions usually associated with these reagents led to frequent use in organic chemistry. Some of these reactions suffer the drawback that the selenium reagent must be used in stoichiometric quantities and that the preparation of more advanced reagents requires several synthetic steps.¹

We² and other research groups have reported the use of peroxydisulfates as oxidants in addition–elimination sequences,³ but the turnover numbers are still small and the amount of catalyst is relatively high. Recently, we reported on an electrochemically induced selenenylation–deselenylation sequence.⁴ The use of hypervalent iodine compounds

as oxidants to form selenium electrophiles from diselenides has been reported previously but has not yet been applied to catalytic reaction conditions.⁵ Herein, we describe a convenient way to cyclize a range of β,γ -butenoic acids to the corresponding butenolides with catalytic amounts of selenium reagents. As butenolides are a class of biologically active compounds, different methodologies for their synthesis have been developed.⁶

Initial studies have been carried out using (*E*)-4-phenylbut-3-enoic acid **1a**, which is converted to 5-phenylfuran-2(5*H*)-one **2a**. A similar sequence has been described by Tiecco et al. using 10 mol % of diselenide and 3 equiv of peroxydisulfate as oxidant leading to the corresponding lactones in good yields.^{3b} Tiecco also found that using 2 equiv of (diacetoxyiodo)benzene with diphenyl diselenide in acetonitrile gave cleanly the corresponding lactone.⁷ The same transformation has been investigated recently by Denmark in great detail.⁸ Thus, the reaction of acid **1a** with 1.05 equiv of different hypervalent iodine reagents in the presence of 5 mol % of diphenyl diselenide in acetonitrile was performed. The results are shown in Table 1. It was found that [bis-

(1) (a) Wirth, T. *Angew. Chem.* **2000**, *112*, 3890–3900, *Angew. Chem., Int. Ed.* **2000**, *39*, 3742–3751. (b) Wirth, T., Ed. *Top. Curr. Chem.* **2000**, *208*. (c) Browne, D. M.; Wirth, T. *Curr. Org. Chem.* **2006**, *10*, 1893–1903. (d) Wirth, T. In *Comprehensive Organometallic Chemistry III*; Crabtree, R. H., Mingos, D. M. P., eds.; Elsevier: Oxford, 2006; Vol. 9, pp 457–500.

(2) Wirth, T.; Häuptli, S.; Leuenberger, M. *Tetrahedron: Asymmetry* **1998**, *9*, 547–550.

(3) (a) Iwaoka, M.; Tomoda, S. *J. Chem. Soc., Chem. Commun.* **1992**, 1165–1166. (b) Tiecco, M.; Testaferri, L.; Tingoli, M.; Bagnoli, L.; Santi, C. *Synlett* **1993**, 798–800. (c) Fujita, K.; Iwaoka, M.; Tomoda, S. *Chem. Lett.* **1994**, 923–926. (d) Fukuzawa, S.; Takahashi, K.; Kato, H.; Yamazaki, H. *J. Org. Chem.* **1997**, *62*, 7711–7716. (e) Tiecco, M.; Testaferri, L.; Santi, C. *Eur. J. Org. Chem.* **1999**, 797–803. (f) Tiecco, M.; Testaferri, L.; Santi, C.; Tomassini, C.; Marini, F.; Bagnoli, L.; Temperini, A. *Tetrahedron: Asymmetry* **2000**, *11*, 4645–4650. (g) Nishibayashi, Y.; Uemura, S. *Top. Curr. Chem.* **2000**, *208*, 201–233. (h) Tiecco, M.; Testaferri, L.; Santi, C.; Tomassini, C.; Marini, F.; Bagnoli, L.; Temperini, A. *Chem. Eur. J.* **2002**, *8*, 1118–1124.

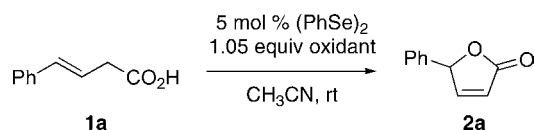
(4) Niyomura, O.; Cox, M.; Wirth, T. *Synlett* **2006**, 251–254.

(5) (a) Tingoli, M.; Tiecco, M.; Chianelli, D.; Balducci, R.; Temperini, A. *J. Org. Chem.* **1991**, *56*, 6809–6813. (b) Tingoli, M.; Tiecco, M.; Testaferri, L.; Balducci, R. *Synlett* **1993**, 211–212.

(6) (a) Knight, D. W. *Contemp. Org. Synth.* **1994**, *1*, 287–315. (b) Brückner, R. *Curr. Org. Chem.* **2001**, *5*, 679–718.

(7) Tingoli, M.; Tiecco, M.; Testaferri, L.; Temperini, A. *Synth. Commun.* **1998**, *28*, 1769–1778.

(8) Denmark, S. E.; Edwards, M. G. *J. Org. Chem.* **2006**, *71*, 7293–7306.

Table 1. Catalytic Cyclization of (*E*)-4-Phenylbut-3-enoic Acid **1a**

entry	hypervalent iodine oxidant	2a, yield (%)
1	PhI(OAc) ₂	27
2	PhI(OCOCF ₃) ₂	70
3	C ₆ F ₅ I(OCOCF ₃) ₂	59
4	IBA ^a	traces
5	FIBA ^b	50
6	IBX ^c	0

^a 1-Hydroxy-1,2-benziodoxol-3-(1*H*)-one. ^b 5,6,7,8-Tetrafluoro-1-hydroxy-1,2-benziodoxol-3-(1*H*)-one 1-oxide. ^c 1-Hydroxy-1,2-benziodoxol-3-(1*H*)-one 1-oxide.

(trifluoroacetoxy)iido]benzene produced butenolide **2a** in 70% yield, while the less reactive (diacetoxyiido)benzene only gave 27% yield. The fluorinated and more soluble reagent [bis(trifluoroacetoxy)iido]pentafluorobenzene⁹ resulted in only 59% yield, whereas the cyclic derivative IBA as well as the iodine(v) reagent IBX¹⁰ did not activate the diselenide sufficiently, and starting material was recovered. Only the more reactive cyclic FIBA¹¹ led to a 50% yield of **2a**.

The optimization of the solvent used in the catalytic reaction is summarized in Table 2. Complete conversion was

Table 2. Optimization of Solvents

entry	solvent	2a, yield (%)
1	CH ₃ CN	70
2	toluene	68
3	CH ₂ Cl ₂	66
4	Et ₂ O	64
5	MeOH	20 ^a
6	THF	15 ^a

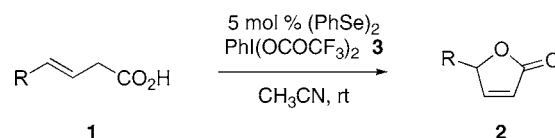
^a Conversion by ¹H NMR.

observed in acetonitrile, toluene, and dichloromethane after a reaction time of 3 h; in the other solvents, starting material **1a** remained after the same reaction time. The scope was further investigated by using different substituted β,γ -unsaturated carboxylic acids in this catalytic reaction (Table 3).

(9) (a) Moriarty, R. M.; Penmasta, R.; Prakash, I. *Tetrahedron Lett.* **1987**, 28, 877–880. (b) Harayama, Y.; Yoshida, M.; Kamimura, D.; Wada, Y.; Kita, Y. *Chem. Eur. J.* **2006**, 12, 4893–4899.

(10) (a) Wirth, T. *Angew. Chem.* **2001**, 113, 2893–2895; *Angew. Chem., Int. Ed.* **2001**, 40, 2812–2814. (b) Wirth, T. In *Organic Synthesis Highlights V*; Schmalz, H.-G., Wirth, T., Eds.; Wiley-VCH: Weinheim, 2003; pp 144–150.

(11) Richardson, R. D.; Zayed, J. M.; Altermann, S.; Smith, D.; Wirth, T., *Angew. Chem.* **2007**, 119, in press; *Angew. Chem., Int. Ed.* **2007**, 46, in press.

Table 3. Catalytic Cyclization of (*E*)- β,γ -Unsaturated Carboxylic Acids **1** to Butenolides **2**

entry	R	2, yield (%)
1	1a , Ph	70
2	1b , CH ₂ Ph	59
3	1c , 4-MeC ₆ H ₄	57
4	1d , 4-BrC ₆ H ₄	54
5	1e , 2-naphthyl	60
6	1f , 1-(2-methylnaphthyl)	65
7	1g , <i>n</i> -C ₃ H ₇	65
8	1h , <i>n</i> -C ₄ H ₉	65
9	1i , <i>n</i> -C ₅ H ₁₁	49
10	1j , <i>n</i> -C ₁₀ H ₂₁	96

The starting materials required for these reactions were obtained either from a Stille cross-coupling reaction with a stannyl ester¹² and an aryl halide or by a modified Knoevenagel condensation¹³ using a range of aldehydes and malonic acid. As highest yields have been observed using [bis(trifluoroacetoxy)iido]benzene **3** in acetonitrile, these conditions were used in all experiments.

The successful conversion of these butenoic acids into the corresponding butenolides prompted experiments to identify the active catalytic species responsible for their formation. The ¹H, ¹³C, and ¹⁹F NMR spectra of a mixture of diphenyl diselenide and [bis(trifluoroacetoxy)iido]benzene **3** (1:1, in CDCl₃) were recorded. The ¹H and ¹³C NMR indicated a clear formation of iodobenzene. The ¹⁹F NMR showed a chemical shift of $\delta = -75$ ppm, which can be assigned to phenylselenenyl trifluoroacetate **4**. Compound **4** was independently prepared from phenylselenenyl chloride and silver trifluoroacetate, and NMR experiments confirmed the results suggesting that phenylselenenyl trifluoroacetate **4** is the active catalytic selenenylating species in this reaction.

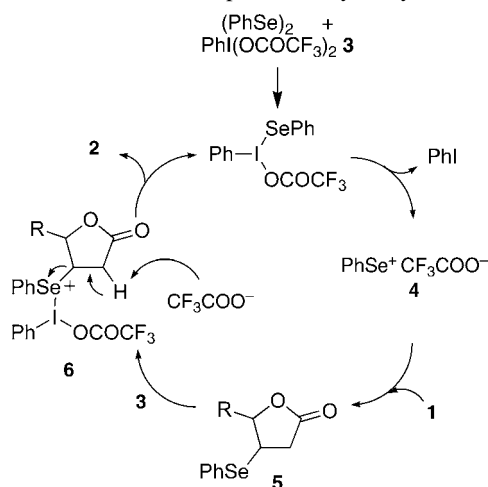
The reaction is initiated by the oxidation of diphenyl diselenide by the hypervalent iodine reagent **3** to form phenylselenenyl trifluoroacetate **4** (Scheme 1). Reagent **4** then reacts with the β,γ -unsaturated carboxylic acid **1** in a cyclization reaction to yield compound **5**. The selenide in lactone **5** can then be activated for elimination either by [bis(trifluoroacetoxy)iido]benzene **3** or by phenylselenenyl trifluoroacetate **4**. Treatment of independently synthesized **5** (R = Ph)¹⁴ with **3** and **4** revealed that a fast elimination proceeded only with [bis(trifluoroacetoxy)iido]benzene **3**, although some elimination product **2** was found also in the stoichiometric reaction of **5** and **4**. We propose that the

(12) Thibonnet, J.; Abarbri, M.; Parrain, J.-L.; Duchêne, A. *Tetrahedron* **2003**, 59, 4433–4441.

(13) Kumar, H. M. S.; Reddy, B. V. S.; Reddy, E. J.; Yadav, J. S. *Tetrahedron Lett.* **1999**, 40, 2401–2404.

(14) Tiecco, M.; Testaferri, L.; Temperini, A.; Bagnoli, L.; Marini, F.; Santi, C. *Synlett* **2001**, 1767–1771.

Scheme 1. Proposed Catalytic Cycle



catalytic cycle proceeds mainly via the intermediate **6** to the butenolide **2** in an elimination process while regenerating the selenium electrophile **4**.

When only 2 mol % of the catalyst was used in this reaction, the yield of **2a** was reduced to 32% together with a side product **7** (Figure 1). The formation of **7** was increased

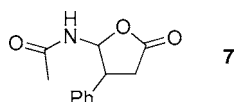


Figure 1. Side product **7** obtained without catalyst.

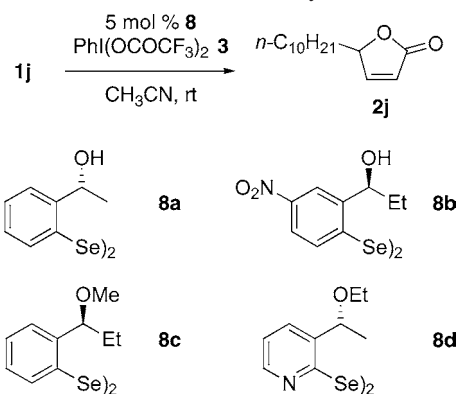
to 43% when the reaction was performed without diphenyl diselenide as catalyst. It seems that the hypervalent iodine compound reacted as an electrophile, and after cyclization, a phenyl migration took place and the resulting carbocation was captured by acetonitrile. Such phenyl migrations in cyclization reactions of substituted styrene derivatives with hypervalent iodine reagents have already been observed.¹⁵

The development of organoselenium reagents for asymmetric synthesis has produced a range of chiral diselenides, which are efficient in the transfer of chiral information.^{1a,c}

Catalytic quantities of several enantiomerically pure diselenides were used in place of diphenyl diselenide with identical reaction conditions (Scheme 2). Substrate **1j** was chosen as it gave the highest yields in the range of examples.

(15) Boye, A. C.; Meyer, D.; Ingison, C. K.; French, A. N.; Wirth, T. *Org. Lett.* **2003**, *5*, 2157–2159.

Scheme 2. Use of Enantiomerically Pure Diselenides **8**



It was found that longer reaction times were required, lower yields were observed, and the enantioselectivity was low. The use of diselenides **8b** and **8c** resulted in almost racemic product **2j**, whereas with **8a** the butenolide **2j** was obtained with an enantiomeric ratio (er) of 57:43 (84% yield). Diselenide **8d** led to 61:39 er (46% yield) of **2j** in the catalytic reaction.¹⁶ In a stoichiometric reaction, performed at $-100\text{ }^{\circ}\text{C}$, the lactone **2a** was obtained in a enantiomeric ratio of 86:14,¹⁷ this ratio changed to 63:37 when the reaction was performed at room temperature. Further work is required to scan a broader range of diselenides and substrates for the asymmetric catalytic reaction. Sulfur-containing diselenides^{3h} and a camphor-based compound¹⁸ have been used for the peroxydisulfate-promoted reaction to butenolides and up to 78:22 er have been obtained.

We have developed a novel method for the synthesis of butenolides **2** from butenoic acids **1** using catalytic amounts of diphenyl diselenide. [Bis(trifluoroacetoxy)iodo]benzene **3** as stoichiometric oxidant in acetonitrile gave the highest yields. Using 5 mol % of the catalyst is critical since lower catalytic loadings resulted in a side product. Further work is required to achieve higher enantioselectivities in this reaction.

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

OL071223Y

(16) Slow racemization was observed under the reaction conditions.

(17) Fragale, G.; Wirth, T. *Eur. J. Org. Chem.* **1998**, 1361–1369.

(18) Tiecco, M.; Testaferri, L.; Marini, F.; Santi, C.; Bagnoli, L.; Temperini, A. *Tetrahedron: Asymmetry* **1999**, *10*, 747–757.