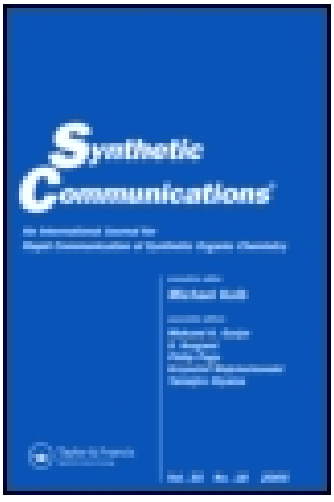

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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Published online: 14 Aug 2007.

To cite this article: Shou-Ri Sheng, Hai-Rong Luo, Zhen-Zhong Huang, Wu-Kang Sun & Xiao-Ling Liu (2007) Facile One-Pot Synthesis of Oxazolidin-2-ones from Phenyl 2-Hydroxyalkyl Selenides, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 37:16, 2693-2699, DOI: 10.1080/00397910701465420

To link to this article: http://dx.doi.org/10.1080/00397910701465420

Synthetic Communications®, 37: 2693–2699, 2007

ISSN 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910701465420

Facile One-Pot Synthesis of Oxazolidin-2-ones from Phenyl 2-Hydroxyalkyl Selenides

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Abstract: A novel, convenient, efficient, three-step, one-pot synthesis of 2-oxazolidinones from phenyl 2-hydroxyalkyl selenides was developed. Using this methodology, 2-oxazolidinones are obtained in good yields (76–85%) by reaction of phenyl 2-hydroxyalkyl selenides with benzoyl isocyanate and subsequent oxidation/cyclization, followed by hydrolysis with hydrochloric acid solution.

Keywords: one-pot synthesis, 2-oxazolidinones, phenyl 2-hydroxyalkyl selenide

Oxazolidin-2-ones are a very interesting class of compounds because of their various pharmacological effects,[1] and some molecules containing the 2-oxazolidinone moieties have shown antibacterial activity.[2] Recently, they have also found application as synthetic intermediates, mainly in synthetic organic chemistry as chiral auxiliaries.[3] A survey of the literature reveals a variety of both natural and unnatural starting points for the preparation of oxazolidinones including the reaction of diols with isocyanates, epoxide openings, amino acids, aziridines, oxetanes, 2-oxazolones, hydroxy acids or esters, and perhaps the most common, amino alcohols.[4] Tingoli et al.[5]

Received in Japan October 16, 2006
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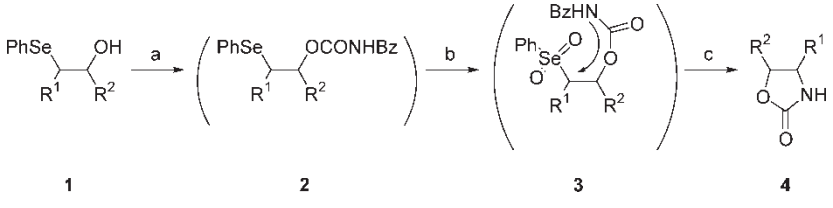
previously developed a synthetic procedure for oxazolidin-2-ones from vicinal carbamate selenides promoted by PhSeOTf. Although the synthetic routes to oxazolidinones are well documented, efforts are continuing for the development of more efficient methods with experimental simplicity. Phenyl β-hydroxyalkyl selenides are a class of valuable selenium intermediates in organic synthesis among many organoselenium reagents;[6] they can be converted to allylic alcohols, olefins, bomohydrins, vinyl selenides, epoxide, tetrahydrofuran derivatives, and some other important natural products. As part of an ongoing research program focused on the use of phenyl β-hydroxyalkyl selenides in organic synthesis,[7] we report herein a novel, convenient, efficient, three-step, one-pot preparation of 2-oxazolidinones from phenyl 2-hydroxyalkyl selenides (Scheme 1).

Phenyl 2-hydroxyalkyl selenides **1** could be easily obtained by the reaction of benzeneselenolate ions with the corresponding epoxides[8] in ethanol at ambient temperature in moderate to good yield. With compounds **1** in hand, we examined the synthesis of target compounds **4**. First of all, phenyl 2-hydroxy-2-phenylethyl selenide (**1a**) as starting material was reacted with benzoyl isocyanate in THF at room temperature for 16 h to give phenyl 2-[(benzoylamino)carbonyl]oxy-2-phenylethyl selenide (**2a**) in 92% yield. Reaction of benzoyl isocyanate (326 mg, 2.2 mmol) with phenyl 2-hydroxy-2-phenylethyl selenide (554 mg, 2.0 mmol) at room temperature continued until the starting alcohol was completely consumed. Then the solvent was evaporated and the crude product was purified by column chromatography on silica gel with ether/*n*-hexane (6:4) as eluent to afford phenyl 2-[(benzoylamino)carbonyl]oxy-2-phenylethyl selenide (**2a**) in 92% yield. ^{1}H NMR: δ ($CDCl_3$) = 8.12 (s, 1H, NH), 7.85–7.80 (m, 2H), 7.61–7.42 (m, 8H), 7.34–7.08 (m, 5H), 4.60 (dd, J = 8.2, 5.3 Hz, 1H), 3.22 (dd, J = 12.4, 8.2 Hz, 1H), 3.13 (dd, J = 12.4, 5.3 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ = 165.1 (CO), 147.53 (CO), 35.4. (CH2), 80.9 (CH), 117.1, 118.7, 126.6, 127.0, 127.5, 128.5, 128.9, 130.9, 132.0, 132.7, 134.4, 141.2. IR (neat): ν = 3272, 1756, 1734, 1505, 1182, 1056, 965 cm^{-1}. Anal. calcd. for $C_{22}H_{19}NO_3Se$: C, 62.27; H, 4.51; N, 3.30. Found: C, 62.33; H, 4.60; N, 3.33. Treatment of **2a** with an excess of m-chloroperbenzoic acid (MCPBA) in THF in the presence of



Scheme 1. Reaction conditions: (a) BzNCO, THF, rt, 15–17 h; (b) MCPBA, K_2HPO_4, THF, rt, 6–8 h; (c) 4 N HCl, 65°C, 4 h.

potassium hydrogenphosphate afforded the corresponding selenone intermediate **3a**; subsequently an intramolecular cyclization reaction occurred easily because of the great leaving ability of the selenonyl group. Without further isolation, 4 N HCl was added to the reaction mixture and stirred at 65°C for 4 h to afford the corresponding 5-phenyl-oxazolidin-2-one **4a** in 85% yield. After a series of experiments, we have found it most convenient to carry out the three-step reaction successively in one pot, giving almost the same yield even though selenide intermediates **2a** and cyclized product of **3a** can be isolated and purified by chromatography. With our successfull initial studies of the preparation of **4a**, extension of this method to the synthesis of other analogues in moderate to good yields was investigated (Table 1). The water-soluble potassium benzeneseleninate was obtained as a by-product, which can acidified with concd. HCl and subsequently reduced with hydrazine monohydrate to recover diphenyl diselenide in moderate yield for the preparation of starting material phenyl 2-hydroxyalkyl selenides. The alkaline aqueous solution containing potassium benzeneseleninate was neutralized with concd. HCl and then acidified by further addition of the acid. The resulting suspension was evaporated, and the residue was suspended in MeOH (20 mL). Hydrazine monohydrate (3.5 mmol, 0.16 mL) was added gradually to the suspension. Stirring continued until diphenyl diselenide was formed, as indicated by the yellow color. The mixture was then concentrated in vacuo, poured into water (30 mL), and extracted with Et_2O (320 mL). The organic layer was dried over anhydrous sodium sulfate and evaporated. Diphenyl diselenide was recovered as a pure compound in about 60% yield.

In summary, we have described a novel, convenient, three-step, one-pot ester-oxidation/cyclization-hydrolysis procedure for the conversion of phenyl 2-hydroxyalkyl selenides to oxazolidin-2-ones in moderate to good yield.

Table 1. One-pot synthesis of substituted oxazolidin-2-ones from phenyl 2-hydroxyalkyl selenides

Entry	R^1, R^2 (phenyl 2-hydroxyalkyl selenide **1**)	Product	Yield (%)[a]
1	H, C_6H_5	**4a**	85
2	H, $C_6H_5CH_2$	**4b**	82
3	H, $C_6H_5OCH_2$	**4c**	85
4	H, $C_6H_5CH_2OCH_2$	**4d**	83
5	H, 4-$CH_3C_6H_4OCH_2$	**4e**	82
6	H, CH_3	**4f**	81
7	H, C_2H_5	**4g**	81
8	(2-hydroxycyclohexyl phenyl selenide)	**4h**	76

[a]Isolated yield based on phenyl 2-hydroxyalkyl selenides **1**.

EXPERIMENTAL

Melting points were uncorrected. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker Avance (400-MHz) spectrometer, using $CDCl_3$ as the solvent and TMS as internal standard. IR spectra were taken on a Perkin-Elmer SP One FT-IR spectrophotometer. Mass spectra (EI, 70 eV) were recorded on a HP5989B mass spectrometer. Microanalyses were performed with a Perkin Elmer (PE) 2400 elemental analyzer. Styrene oxide, 3-phenylpropylene oxide, 1,2-epoxybutane, cyclohexene oxide, and propylene oxide were commercially available, and the other two epoxides were prepared according to the literature procedure.[9] Diphenyl diselenide,[10] phenyl 2-hydroxyalkyl selenides (**1a**,[11] **1c**,[8] **1d**,[8] **1e**,[7] and **1h**;[12] **1b**, **1f**, and **1g** are unknown compounds) were synthesized according to literature methods.[8] THF was distilled under N_2 from sodium/benzophenone immediately prior to use. Other reagents were obtained from commercial suppliers and used without further purification. All reactions were monitored by thin-layer chromatography (TLC).

Data

2-Hydroxy-3-phenylpropyl phenyl selenide (1b): Light yellow oil (yield: 85%); ^{1}H NMR: $\delta = 7.51–7.48$ (m, 2H), 7.32–7.21 (m, 8H), 3.96–3.94 (m, 1H), 3.30 (dd, $J = 12.4$, 7.8 Hz, 1H), 3.16 (dd, $J = 12.4$, 5.6 Hz, 1H), 3.11 (dd, $J = 14.1$, 6.0 Hz, 1H), 2.94 (dd, $J = 14.1$, 6.7 Hz, 1H), 2.87 (bs, 1H). ^{13}C NMR: $\delta = 138.2$, 135.1, 130.8, 129.3, 128.7, 128.2, 127.0, 119.7, 77.0, 40.6, 35.2. IR (neat): $\nu = 3400$, 3050, 2927, 1575, 1478, 1180, 1043, 945, 732, 690 cm^{-1}. Anal. calcd. for $C_{15}H_{16}OSe$: C, 61.86; H, 5.54. Found: C, 61.88; H, 5.58.

2-Hydroxypropyl phenyl selenide (1f): Light yellow oil (yield: 84%); ^{1}H NMR: $\delta = 7.54–7.48$ (m, 2H), 7.27–7.21 (m, 3H), 4.06–4.01 (m, 1H), 3.11 (dd, $J = 12.3$, 5.2 Hz, 1H), 3.02 (dd, $J = 12.3$, 6.6 Hz, 1H), 2.83 (br, 1H), 1.45 (d, $J = 6.3$ Hz, 3H); ^{13}C NMR: $\delta = 135.6$, 129.0, 128.2, 126.8, 77.2, 35.3, 20.8; IR (neat): $\nu = 3400$, 3052, 2927, 2875, 1580, 1478, 1375, 1180, 1043, 945, 732, 670 cm^{-1}. Anal. calcd. for $C_9H_{12}OSe$: C, 50.24; H, 5.62. Found: C, 50.27; H, 5.68.

2-Hydroxybutyl phenyl selenide (1g): Light yellow oil (yield: 86%); ^{1}H NMR: $\delta = 7.55–7.47$ (m, 2H), 7.29–7.22 (m, 3H), 4.05–3.99 (m, 1H), 3.13 (dd, $J = 12.4$, 5.5 Hz, 1H), 3.05 (dd, $J = 12.4$, 6.8 Hz, 1H), 2.86 (br, 1H), 1.87–1.65 (m, 2H), 1.02 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR: $\delta = 135.7$, 129.2, 128.2, 126.5, 77.1, 35.3, 27.8, 8.8; IR (neat): $\nu = 3400$, 3053, 2927, 2872, 1580, 1478, 1378, 1182, 1045, 943, 736, 669 cm^{-1}. Anal. calcd. for $C_{10}H_{14}OSe$: C, 52.41; H, 6.16. Found: C, 52.46; H, 6.21.

General Procedure for the Preparation of Oxazolidin-2-ones 4a–4h

Under a nitrogen atmosphere, benzoyl isocyanate (326 mg, 2.2 mmol) was added to a solution of phenyl 2-hydroxyalkyl selenide (2.0 mmol) in anhydrous THF (20 mL), and the reaction mixture was stirred at room temperature until TLC analysis indicated that the starting alcohol was completely consumed (15–17 h). Then the reaction mixture was treated with *meta*-chloroperoxybenzoic acid (1.38 g, 8.0 mol) and potassium hydrogenphosphate (1.69 g, 10.0 mmol) and stirred for 6–8 h (monitored by TLC). Without isolation, 4 N HCl (6.5 mL) was added to the reaction mixture and stirred for 4 h at 65°C. After cooling, the mixture was quenched slowly with saturated $KHCO_3$ solution, followed by extraction with CH_2Cl_2 (20×3 mL). The combined organic layer was washed with water (the potassium benzeneseleninate in alkaline aqueous phase could be converted to diphenyl diselenide for reuse and dried over magnesium sulfate. Then the solvent was removed in vacuo, and the residue was purified by flash silica-gel column chromatography (CH_2Cl_2/AcOEt, 80:20–65:35) to give pure product.

Data

5-Phenyl-oxazolidin-2-one (4a): White solid; mp. 91–92°C (lit.[4b] mp. 90–91°C); ^{1}H NMR: $\delta = 3.55$ (ddd, $J = 0.8$, 7.6, 8.6 Hz, 1H), 3.98 (ddd, $J = 0.8$, 8.6, 8.6 Hz, 1H), 5.50 (bs, 1H, NH), 5.63 (t, $J = 8.6$ Hz, 1H), 7.34–7.36 (m, 3H), 7.41–7.44 (m, 2H); IR (KBr): $\nu = 3278$, 1721 cm^{-1}.

5-Benzyl-oxazolidin-2-one (4b): White solid; mp. 108–109°C (lit.[4c] mp. 107–109°C); ^{1}H NMR: $\delta = 2.94$ (dd, $J = 6.8$, 14.0 Hz, 1H), 3.15 (dd, $J = 6.0$, 14.0 Hz, 1H), 3.33 (ddd, $J = 0.8$, 7.2, 8.4 Hz, 1H), 3.58 (ddd, $J = 0.8$, 8.4, 8.4 Hz, 1H), 4.83–4.90 (m, 1H), 5.59 (bs, 1H, NH), 7.19–7.23 (m, 3H), 7.32–7.36 (m, 2H); IR (KBr): $\nu = 3286$, 1730 cm^{-1}.

5-(Phenoxymethyl)-oxazolidin-2-one (4c): Colorless oil; ^{1}H NMR: $\delta = 3.35$ (ddd, $J = 0.8$, 7.0, 8.5 Hz, 1H), 3.62 (ddd, $J = 0.8$, 8.5, 8.4 Hz, 1H), 3.90 (dd, $J = 9.6$, 4.8 Hz, 1H), 3.95 (dd, $J = 9.6$, 5.2 Hz, 1H), 4.83–4.90 (m, 1H), 5.45 (bs, 1H, NH), 6.96–7.01 (m, 2H), 7.26–7.29 (m, 3H); ^{13}C NMR: $\delta = 46.4$, 75.0, 76.1, 115.2, 121.7, 129.4, 135.1, 160.1; IR (KBr): $\nu = 3283$, 1736 cm^{-1}; EIMS: m/z (%) = 193 (M^+). Anal. calcd. for $C_{10}H_{11}NO_3$: C, 62.17; H, 5.74; N, 7.25. Found: C, 62.23; H, 5.80; N, 7.31.

5-(Benzyloxymethyl)-oxazolidin-2-one (4d): Colorless oil; ^{1}H NMR: $\delta = 3.33$ (ddd, $J = 0.8$, 7.0, 8.4 Hz, 1H), 3.61 (ddd, $J = 0.8$, 8.3, 8.1 Hz, 1H), 3.89 (dd, $J = 4.8$, 9.6 Hz, 1H), 3.93 (dd, $J = 5.2$, 9.6 Hz, 1H), 4.56 (d, $J = 12.1$ Hz, 1H), 4.61 (d, $J = 12.2$ Hz, 1H), 4.85–4.89 (m, 1H), 5.53

(bs, 1H, NH), 7.02–7.08 (m, 2H), 7.31–7.35 (m, 3H); ^{13}C NMR: $\delta = 41.7$, 46.3, 75.1, 78.5, 155.6, 126.7, 128.3, 129.1, 159.5. IR (KBr): $\nu = 3286$, 1738 cm^{-1}; EIMS: m/z (%) = 207 (M^+). Anal. calcd. for $C_{11}H_{13}NO_3$: C, 63.76; H, 6.32; N, 6.76. Found: C, 63.79; H, 6.38; N, 6.80.

5-(4-Methylphenoxymethyl)-oxazolidin-2-one (4e): Colorless oil; ^{1}H NMR: $\delta = 2.31$ (s, 3H), 3.34 (ddd, $J = 0.8$, 7.1, 8.6 Hz, 1H), 3.62 (ddd, $J = 0.8$, 8.2, 8.5 Hz, 1H), 3.90 (dd, $J = 5.1$, 9.7 Hz, 1H), 3.95 (dd, $J = 5.2$, 9.7 Hz, 1H), 4.85–4.93 (m, 1H), 5.52 (bs, 1H, NH), 7.52 (d, $J = 8.5$ Hz, 2H), 6.77 (d, $J = 8.5$ Hz, 2H); ^{13}C NMR: $\delta = 20.4$, 46.5, 76.8, 76.1, 114.5, 121.2, 129.2, 133.6, 160.2; IR (KBr): $\nu = 3284$, 1740 cm^{-1}; EIMS: m/z (%) = 207 (M^+). Anal. calcd. for $C_{11}H_{13}NO_3$: C, 63.76; H, 6.32; N, 6.76. Found: C, 63.78; H, 6.38; N, 6.81.

5-Methyloxazolidin-2-one (4f): Colorless oil (lit.[4b] oil); ^{1}H NMR: $\delta = 1.46$ (d, $J = 6.2$ Hz, 3H), 3.21 (ddd, $J = 0.8$, 7.2, 8.4 Hz, 1H), 3.69 (ddd, $J = 0.8$, 8.4, 8.4 Hz, 1H), 4.74–4.82 (m, 1H), 5.57 (bs, 1H, NH); IR (neat): $\nu = 3298$, 1739 cm^{-1}.

5-Ethyl-oxazolidin-2-one (4g): White solid; mp. 51–52°C (lit.[4c] mp. 51–53°C); ^{1}H NMR: $\delta = 1.02$ (t, $J = 7.5$ Hz, 3H), 1.66–1.85 (m, 2H), 3.24 (ddd, $J = 1.2$, 7.2, 8.4 Hz, 1H), 3.66 (ddd, $J = 1.2$, 8.4, 8.4 Hz, 1H), 4.56–4.62 (m, 1H), 5.32 (bs, 1H, NH); IR (KBr): $\nu = 3299$, 1740 cm^{-1}.

***Cis*-Cyclohexano[b]-2-oxazolidone (4h):** White solid; mp. 55–56°C (lit.[13] mp. 55°C); ^{1}H NMR: $\delta = 1.15$–1.46 (m, 4H), 1.60–1.84 (m, 2H), 2.10–2.20 (m, 2H), 3.47 (ddt, $J = 0.8$, 7.5, 8.2 Hz, 1H), 4.72–4.80 (m, 1H), 5.37 (bs, 1H, NH); IR (KBr): $\nu = 3281$, 1740 cm^{-1}.

ACKNOWLEDGMENTS

We gratefully acknowledge financial support from the National Natural Science Foundation of China (No. 20562005) and NSF of Jiangxi Province (No. 0620021).

REFERENCES

1. Danielmeier, K.; Steckhan, E. *Tetrahedron: Asymmetry* **1995**, *6*, 1181.
2. Some molecules containing the oxazolidin-2-one moiety have shown interesting pharmaceutical activity. For recent leading references, see (a) Mai, A.; Artico, M.; Esposito, M.; Sbardella, G.; Massa, S.; Befani, O.; Turini, P.; Giovannini, V.; Mondovi, B. *J. Med. Chem.* **2002**, *45*, 1180; (c) Seki, M.; Mori, K. *Eur. J. Org. Chem.* **1999**, *64*, 2965.

3. For some recent selected examples of the use of oxazolidin-2-ones as chiral auxiliary, see (a) Wu, Y. K.; Shen, X.; Tang, C. J.; Chen, Z. L.; Hu, Q.; Shi, W. J. *Org. Chem.* **2002**, *67*, 3802; (b) Faita, G.; Paio, A.; Quadrelli, P.; Rancati, F.; Senesi, P. *Tetrahedron* **2001**, *57*, 8313; (c) Gaul, C.; Scharer, K.; Seebach, D. *J. Org. Chem.* **2001**, *66*, 3059; (d) Yamamoto, H.; Watanabe, S.; Kadotani, K.; Hasegawa, M.; Noguchi, M.; Kanemasa, S. *Tetrahedron Lett.* **2000**, *41*, 3131.
4. For some recent developments in 2-oxazolidinone synthesis, see (a) Ager, D. J.; Prakash, I.; Schaad, D. R. *Chem. Rev.* **1996**, *96*, 835; (b) Bergmeier, S. C.; Katz, S. J. *J. Comb. Chem.* **2002**, *4*, 162; (c) Gabriele, B.; Mancuso, R.; Salerno, G.; Costa, M. *J. Org. Chem.* **2003**, *68*, 601; (d) Bartoli, G.; Bosco, M.; Carlone, A.; Locatelli, M.; Melchiorre, P.; Sambri, L. *Org. Lett.* **2005**, *7*, 1983.
5. Tingoli, M.; Testaferri, L.; Temperini, A.; Tiecco, M. *J. Org. Chem.* **1996**, *61*, 7085.
6. Krief, A. *Tetrahedron* **1980**, *36*, 2531.
7. Sheng, S.-R.; Luo, H.-R.; Sun, W.-K.; Liu, X.-L.; Xin, Q.; Wang, Q.-Y. *Synth. Commun.* **2005**, *35*, 2839.
8. Engman, L.; Gupta, V. *J. Org. Chem.* **1997**, *62*, 157.
9. Mouzin, G.; Cousse, H.; Rieu, J.-P.; Duflos, A. *Synthesis* **1983**, 117.
10. Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434.
11. Sakakibara, M.; Katsumata, K.; Watanabe, Y.; Toru, T.; Ueno, Y. *Synthesis* **1992**, 377.
12. Bagul, T. D.; Lakshmaiah, G.; Kawabata, T.; Fuji, K. *Org. Lett.* **2002**, *4*, 249.
13. Hassner, A.; Lorber, M. E.; Heathcock, C. *J. Org. Chem.* **1967**, *32*, 540.