## J. CHEM. SOC., CHEM. COMMUN., 1985 Selenolactonization of Alkynoic Acids with N-Phenylselenophthalimide: Novel

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Isomerization Reaction of a Vinyl Selenide

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Selenolactonization is stereoselective and regiospecific for hex-4-ynoic and hept-4-ynoic acids (1a) and (1b), but pent-4-ynoic acid (1c) gives a mixture of stereoisomers.

N-Phenylselenophthalimide (N-PSP)1 is an excellent reagent for the selenolactonization of alkenoic acids. This reaction affords without exception the anti-addition product possibly via a seleniranium ion which is an intermediate<sup>2</sup> in the electrophilic reaction of phenylselenenyl halide with olefins. Addition of phenylselenenyl halide to a triple bond is known<sup>3</sup> to be anti presumably via the same intermediate. Furthermore, treatment of alkynols with phenylselenenyl chloride gives rise to the anti-1,2-addition products instead of the expected cyclized enol ethers. 4 This result presents a contrast to the successful selenocyclization of alkenols.<sup>5</sup> In the course of our studies on the development of a new method for the synthesis of γ-alkylidene-γ-butyrolactones, which are interesting compounds owing to their demonstrated biological activities<sup>6</sup> and synthetic utility, we examined the cyclization reaction of alkynoic acids with N-PSP. We report here a successful selenolactonization of alkynoic acids involving an unexpected formation of the (Z)-isomer besides the (E)isomer in the reaction of pent-4-ynoic acid.

To N-PSP (1.3 equiv.) was added a solution of alkynoic acid in CH<sub>2</sub>Cl<sub>2</sub> which was then stirred at room temperature. After completion of the reaction, n-hexane was added to the reaction mixture and the resultant precipitate was filtered. Evaporation of the solvent and flash chromatography over silica gel with an n-hexane-ethyl acetate mixture gave  $\gamma$ -(1-phenylselenoalkylidene)- $\gamma$ -butyrolactones in the yields shown in Table 1.

The reaction of hex-4-ynoic acid<sup>7</sup> (1a) as well as hept-4ynoic acid<sup>7</sup> (1b) with N-PSP proceeded stereoselectively and regiospecifically to afford γ-(1-phenylselenoethylidene)- and γ-(1-phenylselenopropylidene)-γ-butyrolactones (2a) and (2b) in good yields.† On the other hand, reaction of pent-4-ynoic acid (1c) resulted in the formation of a significant amount of the (Z)-isomer (3c) together with the (E)-isomer

**Table 1.** Selenolactonization of alkynoic acids (1) with N-PSP.

	Reaction	Product <sup>c</sup> /%	
R	time <sup>a</sup> /h	<b>(2)</b>	(3)
Me	22	89	_
Me	160	75	_
Et	4	76	_
Н	22	50 (79)	13 (21)
H	24ь	67 (96)	3 (4)
Н	190	39 (60)	26 (40)

<sup>a</sup> The reactions were performed using 1.3 equiv. of N-PSP in CH<sub>2</sub>Cl<sub>2</sub> at room temperature. b The reaction was performed with 1.1 equiv. of N-PSP. c Yields refer to isolated products of analytical purity; the ratios (2): (3) are shown in parentheses.

(2c).‡ In order to rationalize this apparent non-stereoselective selenolactonization, a CH<sub>2</sub>Cl<sub>2</sub> solution of (2c) was treated with 0.1 equiv. of phthalimide, apparently formed during the selenolactonization reaction, but no formation of (3c) was observed after 2 days stirring either at room temperature or at reflux. Compound (2c) was isomerized to (3c) smoothly at room temperature by the action of N-PSP (0.1 equiv.), and the reaction reached equilibrium after 190 h [(2c):(3c) 83:17, 22 h; 60:40, 190; h h.p.l.c., silica gel, n-hexane-ethyl acetate 99:1]. The equilibrium was reached much faster in the isomerization of (3c) than in that of (2c) [(2c): (3c) 49: 51, 3 h; 60:40, 24 h].† Thus, the isomerization pathway proceeds via the electrophilic addition of the phenylselenenium ion to the exo-olefin of the lactones followed by its elimination (Scheme 1).§ A similar olefin isomerization was observed in the mercury-catalysed lactonization of alkynoic acids.8

Finally, the exo-ring closure of the selenolactonization of alkynoic acids led to the regiospecific introduction of the

‡ Selected spectroscopic data, i.r. (liquid film), <sup>1</sup>H n.m.r. (CCl<sub>4</sub>, 60 MHz): (2a)  $v_{\text{max}}$ . 1800 cm<sup>-1</sup>,  $\delta$  2.10 (3H, t, J 2 Hz), 2.41—3.40 (4H, m); (2b)  $v_{\text{max}}$ , 1800 cm<sup>-1</sup>,  $\delta$  1.06 (3H, t, J 7 Hz), 2.20—3.25 (6H, m); (2c)  $v_{\text{max}}$  1799 cm<sup>-1</sup>,  $\delta$  2.35—3.20 (4H, m),  $\delta$ .04 (1H, t, J 1.5 Hz); (3c)  $v_{\text{max}}$  1809 cm<sup>-1</sup>,  $\delta$  2.33—3.00 (4H, m), 5.41 (1H, t, J 1.5 Hz). Structures of y-butyrolactones were further confirmed by subjecting (2a), (2b), (2c), and (3c) to methanolysis (-40 °C, K<sub>2</sub>CO<sub>3</sub>) giving 4-keto-5-phenylselenocarboxy esters.

§ The failure to observe (3a) and (3b) is consistent in that (2) is clearly favoured for R = H over R = Me and Et on steric grounds, and the equilibrium could well lie to one side.

<sup>†</sup> The stereochemical assignments are not concretely defined, but the lactones (2a) and (2b) probably have the (E)-configuration based on mechanistic grounds as well as on the fact that we observed the stereoselective formation of (2) in the reaction of alkynoic acids with phenylselenenyl chloride.

phenylseleno group in sharp contrast to the non-regiospecific addition of phenylselenenyl halide to alkynes.<sup>3</sup>

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