Selenolactonization of Alkynoic Acids with *N*-Phenylselenophthalimide: Novel Isomerization Reaction of a Vinyl Selenide

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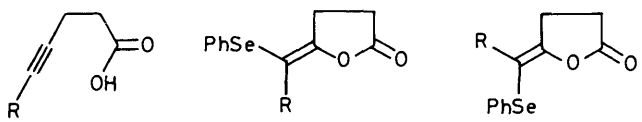
Selenolactonization is stereoselective and regiospecific for hex-4-ynoic and hept-4-ynoic acids (**1a**) and (**1b**), but pent-4-ynoic acid (**1c**) gives a mixture of stereoisomers.

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[2] in the electrophilic reaction of phenylselenenyl halide with olefins. Addition of phenylselenenyl halide to a triple bond is known[3] 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.[5] 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[6] 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_2Cl_2 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 γ-(1-phenylselenoalkylidene)-γ-butyrolactones in the yields shown in Table 1.

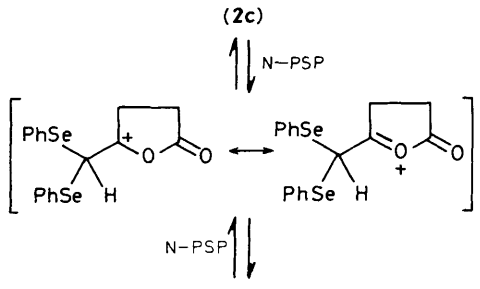
The reaction of hex-4-ynoic acid[7] (**1a**) as well as hept-4-ynoic acid[7] (**1b**) with N-PSP proceeded stereoselectively and regiospecifically to afford γ-(1-phenylselenoethylidene)- and γ-(1-phenylselenopropylidene)-γ-butyrolactones (**2a**) and (**2b**) in good yields.† On the other hand, reaction of pent-4-ynoic acid (**1c**) resulted in the formation of a significant amount of the (*Z*)-isomer (**3c**) together with the (*E*)-isomer (**2c**).‡ In order to rationalize this apparent non-stereoselective selenolactonization, a CH_2Cl_2 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



(**1**) (**2**) (**3**)

a; R = Me
b; R = Et
c; R = H



Scheme 1

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

R	Reaction time[a]/h	Product[c]/% (**2**)	(**3**)
Me	22	89	—
Me	160	75	—
Et	4	76	—
H	22	50 (79)	13 (21)
H	24[b]	67 (96)	3 (4)
H	190	39 (60)	26 (40)

[a] The reactions were performed using 1.3 equiv. of N-PSP in CH_2Cl_2 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.

† 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.

‡ *Selected spectroscopic data*, i.r. (liquid film), ^{1}H n.m.r. (CCl_4, 60 MHz): (**2a**) $\nu_{max.}$ 1800 cm^{-1}, δ 2.10 (3H, t, *J* 2 Hz), 2.41—3.40 (4H, m); (**2b**) $\nu_{max.}$ 1800 cm^{-1}, δ 1.06 (3H, t, *J* 7 Hz), 2.20—3.25 (6H, m); (**2c**) $\nu_{max.}$ 1799 cm^{-1}, δ 2.35—3.20 (4H, m), 6.04 (1H, t, *J* 1.5 Hz); (**3c**) $\nu_{max.}$ 1809 cm^{-1}, δ 2.33—3.00 (4H, m), 5.41 (1H, t, *J* 1.5 Hz). Structures of γ-butyrolactones were further confirmed by subjecting (**2a**), (**2b**), (**2c**), and (**3c**) to methanolysis (−40 °C, K_2CO_3) 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.

phenylseleno group in sharp contrast to the non-regiospecific addition of phenylselenenyl halide to alkynes.[3]

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