2-(Phenylseleno)prop-2-enenitrile: a Three-carbon Unit for Radical Cyclization

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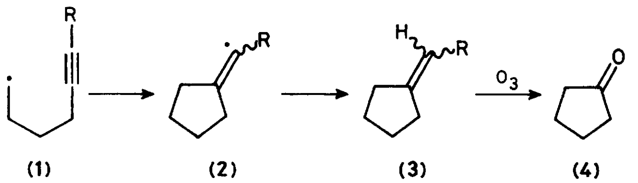
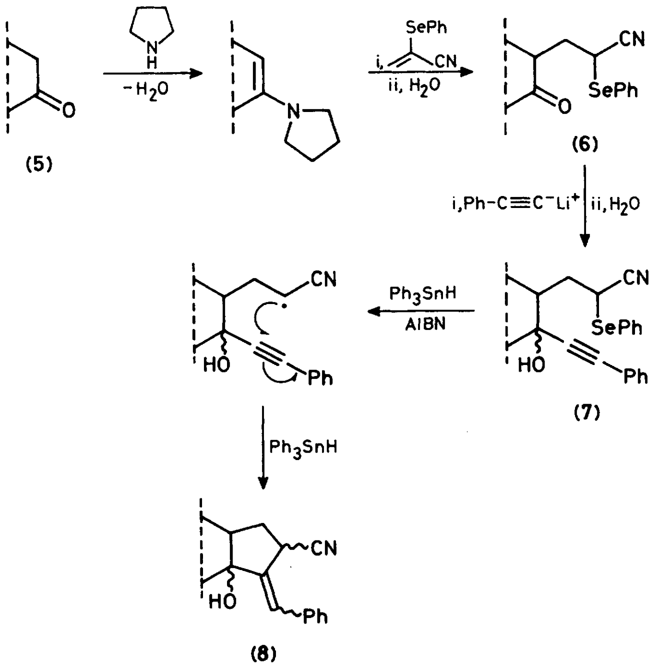
Successive reaction of enamines with 2-(phenylseleno)prop-2-enenitrile, lithium phenylacetylide, and triphenyltin hydride serves to generate carbocycles by a process of radical ring closure.

Cyclization of δ-acetylenic radicals [(**1**)→(**2**)→(**3**)] could be a very useful method for synthesis of carbocycles that incorporate a ketone group [*cf.* (**3**)→(**4**)].[1] However, implementation of this approach depends on the methods of access to appropriate acetylenic radicals.[2] We report a new and efficient procedure (see Scheme 1) for generating such species and have observed that they undergo cyclization in the required manner.

Ketones (**5a**—**d**) (see Table 1) were converted into the corresponding enamines using pyrrolidine for (**5a**—**c**) and morpholine for (**5d**). Reaction of the enamines with 2-(phenylseleno)prop-2-enenitrile[7] proceeds easily at room temperature in tetrahydrofuran (THF) (3 h) in the manner summarized by Scheme 1 [(**5**)→(**6**)].† When performed under these conditions, the reaction is efficient and, evidently, it is free from serious complications such as dialkylation of the enamine, or formation of cyclobutanes or quaternary ammonium salts, the last two being the main processes with 2-chloroprop-2-enenitrile.[8]‡ As shown in Table 1, the required ketones (**6a**—**d**) are obtained in good yield. These ketones react (THF; −78 °C; 1 h) with lithium phenylacety-





Scheme 1

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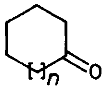
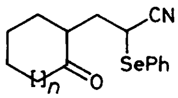
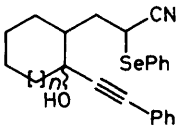
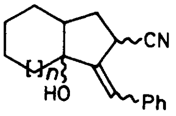
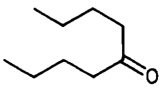
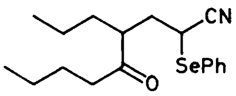
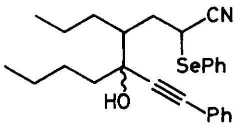
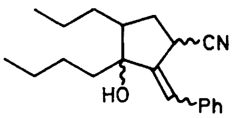
† At the end of the specified period the reaction mixture is diluted with water and stirred for 30 min before isolation of the keto-nitrile.

‡ In principle, this compound could also be used in the sense of Scheme 1, but has not been examined for the reason stated.

Table 1. Preparation of the keto-nitriles (**6**) and cyclization of the derived acetylenic alcohols (**7**) to give (**8**).

Starting ketone[a]	Keto-nitrile (yield %)[b,c]	Acetylenic alcohol (yield %)[c]	Cyclization product (yield %)[c]
 (5a) $n = 0$ (5b) $n = 1$ (5c) $n = 2$	 (6a) (94)[d] (6b) (91) (6c) (75)	 (7a) (68)[e] (7b) (93) (7c) (94)	 (8a) (89) (8b) (94) (8c) (91)
 (5d)	 (6d) (77)	 (7d) (80)	 (8d) (79)

[a] Pyrrolidine enamine was used except for (**5d**), for which the morpholine enamine was employed. For preparation of the enamines derived from (**5a**—**d**) see refs. 3—6. [b] Yields based on enamine. [c] Mixture of stereoisomers. [d] Contained trace impurities. [e] Yield from enamine.

lide (1.5 equiv.) to produce the corresponding alcohols (**7a**—**d**) as mixtures of stereoisomers.

The cyclizations, which proceed without protection of hydroxy groups [see Scheme 1, (**7**)→(**8**)], were carried out under argon by the following general procedure. Benzene solutions of triphenyltin hydride (1.15 equiv.; 0.064—0.088 M) and of azobisisobutyronitrile (AIBN) [0.2—0.3 mmol per mmol of (**7**); 0.015 M] were added simultaneously over 10 h by syringe pump to a refluxing solution (0.03 M) of (**7**) in the same solvent.[9] After the addition, refluxing was continued for an arbitrary period of 2 h and the products were isolated in the yields shown (see Table 1) by evaporation of the solvent and flash chromatography.

The cyclization proceeds by 5-*exo* closure of an intermediate radical (see Scheme 1) to give products that are isomer mixtures (^{1}H n.m.r., 400 MHz). Formulation of the products as benzylidenecyclopentanes was made on the basis of the known preference for analogous δ-acetylenic radicals to undergo 5-*exo*, rather than 6-*endo*, closure.[10] In addition, (**8b**) was degraded [O_3, MeOH, −78 °C; then $(MeO)_3P$, −78 to 25 °C] to the expected cyclopentanone system [79%; Fourier-transform i.r. 1760 cm^{-1} (solid cast from CH_2Cl_2)], thereby establishing the regiochemistry of cyclization. The total ozonolysis product was examined by ^{1}H n.m.r. spectroscopy (400 MHz) and, as expected, only one aldehyde signal (due to benzaldehyde) was observed.

In summary, our results show that the present method is a general and efficient route to synthetically useful five-membered carbocycles that are at an oxidation level suitable for further manipulation.

Acknowledgement of financial support is made to the Natural Sciences and Engineering Research Council of Canada.

Received, 8th March 1985; Com. 312

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