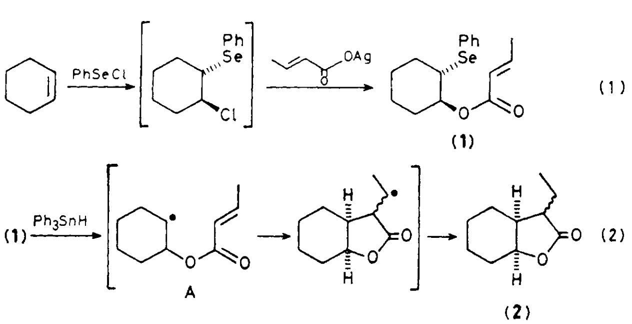
Formation of Carbon–Carbon Bonds by Ring Closure of β-Phenylselenocrotonates

Derrick L. J. Clive* and Pierre L. Beaulieu
Chemistry Department, University of Alberta, Edmonton, Alberta, Canada, T6G 2G2

Successive treatment of olefins with PhSeCl and silver crotonate affords β-phenylselenocrotonates which, on reaction with triphenyltin hydride in the presence of azobisisobutyronitrile, are converted into γ-lactones by a process that introduces a new carbon–carbon bond.

We report a new method, summarized in equations (1) and (2), for making γ-lactones. The first step [*e.g.*, cyclohexene → (**1**)] is an ionic addition of the structural elements of $PhSe^+$ and $MeCH{=}CHCO_2^-$ while the second stage (**1**)→(**2**) involves the generation of a radical. The procedure was suggested by the facts that carbon–selenium bonds undergo homolytic fission [*e.g.*, (**1**) → A] on treatment with Ph_3SnH[1] and that ionic addition of PhSe–OCOR (R = Me,[2] CF_3[3]) to double bonds is a well-established process.[4] Furthermore, as required by equation (1), the double bond in an α,β-unsaturated carboxylic acid is rendered inert, by conjugation, to electrophilic selenium species. For the process summarized in equation (2) to take place, the nucleophile attached to one of the sp^2 carbons in the first stage (here OCOCH=CHMe) should be so constituted



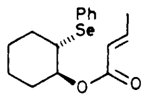
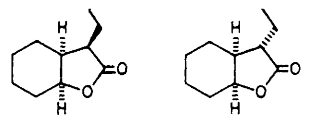
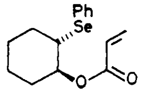
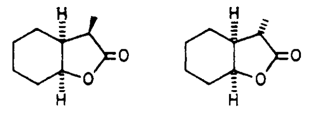
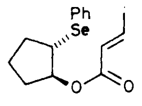
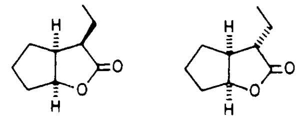
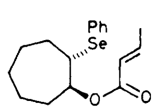
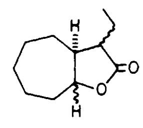
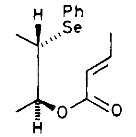
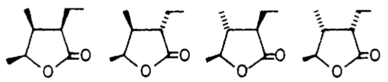
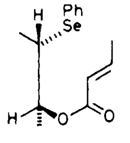
that it is not expelled from the intermediate radical A—at least at a rate competitive with ring closure. The indicated choice of reagents satisfies these requirements.†

In a typical experiment, cyclohexene in dry acetonitrile (0.2 M) was treated with PhSeCl and silver crotonate[6] (1.1 equiv.) was added to the resulting solution. Mechanical or ultrasonic agitation for an arbitrary period of 20 h at room temperature and in the dark then proceeded as shown in equation (1). Several other olefins were converted by this method into the corresponding phenylseleno-esters (see Table 1).

For the ring closure [*e.g.*, equation (2)], individual benzene solutions of Ph_3SnH (1.7—2.2 mmol, 0.17—0.22 M) and azobisisobutyronitrile (AIBN)‡ (0.03—0.06 mmol, 0.003—0.006 M) were injected over 10 h into a refluxing solution of the phenylselenocrotonate (or acrylate) (1.5—2.0 mmol, 0.015—0.020 M) in the same solvent. At the end of the addition, refluxing was arbitrarily continued for 2 h. Evaporation of the solvent, flash chromatography over silica gel with hexane–ethyl acetate mixtures, and Kugelrohr distillation gave the product lactones in the yields shown in Table 1.

The lactones from experiments with (**1**), (**3**), and (**5**) were *cis*-fused (^1H n.m.r., 400 MHz)§ and were composed of *exo* and *endo* isomers. The ratios (**2a**):(**2b**) and (**4a**):(**4b**) were established by spectral comparison with the published[9c] ^1H n.m.r. data for (**4a**) and (**4b**). Differentiation between the *exo* and *endo* isomers (**6a**) and (**6b**) was made on the basis of ^{13}C n.m.r. measurements and equilibration experiments (K_2CO_3 in refluxing tetralin) on samples (preparative g.l.c.) of the individual components. The stereochemistry of (**6b**) is assigned to the more stable isomer and, as expected, the sum of the $\delta(^{13}C)$ values for the methylene carbons is higher (116.0 p.p.m.) for (**6b**) than for (**6a**) (102.5 p.p.m.).¶ The adducts (**7**) and (**9**) from *Z*- and *E*-but-2-ene, respectively, afforded almost identical product mixtures (**8a**—**d**). For these compounds, the stereochemistries shown could be assigned tentatively by comparison with published[12] detailed ^1H n.m.r. data for the four isomeric 2,3,4-trimethylbutyrolactones.**

Table 1[a]

Phenylseleno - adduct (yield %)		Cyclised product (yield %)	
 (1)	(77)[b]	 (**2a**) 80 : 20 (**2b**)	(63)
 (3)	(67)[c]	 (**4a**) 75 : 25 (**4b**)	(24)
 (5)	(74)	 (**6a**) 70 : 30 (**6b**)	(61)
	(76)		(65)
 (7)	(75)	 (**8a**) 34 : (**8b**) 5 : (**8c**) 39 : (**8d**) 22	(66)
 (9)	(88)	(**8a**) 31 : (**8b**) 5.5 : (**8c**) 41 : (**8d**) 22	(65)

[a] Yields refer to isolated products of analytical purity. [b] Sonication. [c] Silver acrylate[7] used.

Some comment is required about several theoretical aspects of the synthetic method reported here.[13] These are (a) the regiochemical outcome (*exo vs. endo* closure—both allowed[14]) of the reaction, (b) the relative stereochemistry of the peripheral substituents in the products, and (c) the ring fusion geometry for the different ring sizes. Free radical addition to crotonates occurs mainly (*e.g.*, 92%) at the β-position.[15] However, in the ring closure of hexen-5-yl radicals there is a kinetic preference, due to stereoelectronic factors, for the 5-*exo* mode of cyclization[16] and the present reactions also show a reversal of the regiochemistry associated with corresponding intermolecular processes.

In the case of (**2a**, **b**), (**4a**, **b**), and (**6a**, **b**) the relative stereochemistry at the three asymmetric centres of the major isomer

---

† The requirements can be met by other systems: *e.g.*, using the iodo-crotonate analogue of (**1**), yields for the two stages were *ca.* 93% and 56%, respectively. The iodo-crotonate was made by the general method of ref. 5.

‡ Ph_3SnH reacts with selenides in the absence of an initiator (ref. 1a). However, the present reaction requires an initiator. For the β-effect on radical stability, see ref. 8.

§ For *cis*-fusion in 2-oxabicyclo[5.3.0]nonan-3-ones the ^1H n.m.r. signal of $HC(R^1)(R^2)O$ occurs at δ 4.3—4.65 (see ref. 9); for *trans*-fusion the signal is at δ 3.60—3.78 (see refs. 9a—d; 10). For *cis*-fusion in 2-oxabicyclo[3.3.0]octan-3-one the corresponding signal is at δ 5.0 (the compound is reported, without spectroscopic data in ref. 1a); the parent hydroxy-acid for the *trans*-fused system is of a type that does not appear to form lactones easily (ref. 11).

¶ ^1H N.m.r. ($CDCl_3$, 400 MHz): (**4a**): =CHO (δ 4.42); Me– (δ 1.14). (**4b**): =CHO (δ 4.52); Me– (δ 1.23). The corresponding methine signals for (**2a**), (**2b**), (**6a**), and (**6b**) are δ 4.37, 4.49, 4.84, and 4.92, respectively.

** Diagnostically significant ^1H n.m.r. signals ($CDCl_3$; 400 MHz) corresponding to MeCH(R)O are: (methine proton, methyl) (**8a**) δ 4.49 (octet), 1.34(d); (**8b**) 4.63(quintet), 1.24(d); (**8c**) 3.99(octet), 1.40 (d); (**8d**) 4.20 (sextet), 1.38 (d).

corresponds to that observed with carbocyclic systems[17] but the proportions tentatively assigned to (**8a**—**d**) are different from those expected[16a] on the basis of analogy with simpler examples. Finally, the *exo*-ring closures reported here that generate [3.3.0], [4.3.0], and [5.3.0] bicyclic systems by formation of a bond to a potential ring junction atom give the same stereochemical result as observed in the formation of halolactones, *i.e.*, *cis*-ring fusion for [3.3.0] and [4.3.0] systems and both *cis*- and *trans*-fusion for [5.3.0].[9d]

All new compounds (as isomer mixtures) were characterized spectroscopically (including mass measurement) and satisfactory combustion analytical data (C and H) were obtained.

Acknowledgement of financial support is made to the Natural Sciences and Engineering Research Council of Canada and to the Alberta Heritage Foundation for Medical Research. P. L. B. holds an N.S.E.R.C. Postgraduate Scholarship.

Received, 9th November 1982; Com. 1281

References

1 (a) D. L. J. Clive, G. J. Chittattu, V. Farina, W. A. Kiel, S. M. Menchen, C. G. Russell, A. Singh, C. K. Wong, and N. J. Curtis, *J. Am. Chem. Soc.*, 1980, **102**, 4438; (b) for a recent application see S. D. Burke, W. F. Fobare, and D. M. Armistead, *J. Org. Chem.*, 1982, **47**, 3348.

2 PhSe–OCOMe represents the formal structure of the reagent: K. B. Sharpless and R. F. Lauer, *J. Org. Chem.*, 1974, **39**, 429.

3 D. L. J. Clive, *J. Chem. Soc., Chem. Commun.*, 1974, 100; PhSe–OCOCF$_3$ is the actual structure of the reagent: H. J. Reich, *J. Org. Chem.*, 1974, **39**, 428.

4 D. L. J. Clive, *Tetrahedron*, 1978, **34**, 1049.

5 R. C. Cambie, R. C. Hayward, J. L. Roberts, and P. S. Rutledge, *J. Chem. Soc., Perkin Trans.* 1, 1974, 1858.

6 *Beilstein Hauptwerk*, **2**, 410.

7 *Beilstein Hauptwerk*, **2**, 399.

8 D. H. R. Barton, W. Hartwig, and W. B. Motherwell, *J. Chem. Soc., Chem. Commun.*, 1982, 447.

9 (a) A. Itoh, K. Oshima, and H. Nozaki, *Tetrahedron Lett.*, 1979, 1783; (b) W. Herz and L. A. Glick, *J. Org. Chem.*, 1964, **29**, 613; (c) T. K. Das Gupta, D. Felix, U. M. Kempe, and A. Eschenmoser, *Helv. Chim. Acta*, 1972, **55**, 2198; (d) W. Herz and L. A. Glick, *J. Org. Chem.*, 1963, **28**, 2970; (e) M. Bertrand, J. P. Dulcere, G. Gil, J. Grimaldi, and P. Sylvestre-Panthet, *Tetrahedron Lett.*, 1976, 3305.

10 P. L. Creger, *J. Org. Chem.*, 1972, **37**, 1907.

11 A. I. Meyers, E. D. Mihelich, and R. L. Nolen, *J. Org. Chem.*, 1974, **39**, 2783.

12 M. Petrzilka, D. Felix, and A. Eschenmoser, *Helv. Chim. Acta*, 1973, **56**, 2950.

13 For radical cyclizations onto a carbon–carbon double bond, in which the starting material is prepared in several steps, see ref. 1(a); M. D. Bachi and C. Hoornaert, *Tetrahedron Lett.*, 1981, 2689, 2693; *cf.* Y. Ueno, K. Chino, and M. Okawara, *ibid.*, 1982, 2575; S. Danishefsky, S. Chackalamannil, and B.-J. Uang, *J. Org. Chem.*, 1982, **47**, 2231; G. Stork and N. H. Baine, *J. Am. Chem. Soc.*, 1982, **104**, 2321; D. J. Hart and Y.-M. Tsai, *ibid.*, p. 1430; J.-K. Choi, D. J. Hart, and Y.-M. Tsai, *Tetrahedron Lett.*, 1982, 4765.

14 J. E. Baldwin, *J. Chem. Soc., Chem. Commun.*, 1976, 734.

15 B. Giese and S. Lachhein, *Angew. Chem., Int. Ed. Engl.*, 1981, **20**, 967.

16 (a) A. L. J. Beckwith, *Tetrahedron*, 1981, **37**, 3073; (b) T. W. Smith and C. B. Butter, *J. Org. Chem.*, 1978, **43**, 6; (c) C. Walling and A. Cioffari, *J. Am. Chem. Soc.*, 1972, **94**, 6059; (d) S. Wolff and W. C. Agosta, *J. Chem. Res. (S)*, 1981, 78.

17 A. L. J. Beckwith, G. Phillipou, and A. K. Serelis, *Tetrahedron Lett.*, 1981, 2811, and references therein.