Mild and Efficient Preparation of γ-Substituted α,β-Unsaturated γ-Butyrolactones from Epoxides

Stephen Hanessian,* Paul J. Hodges, Peter J. Murray, and Soumya P. Sahoo

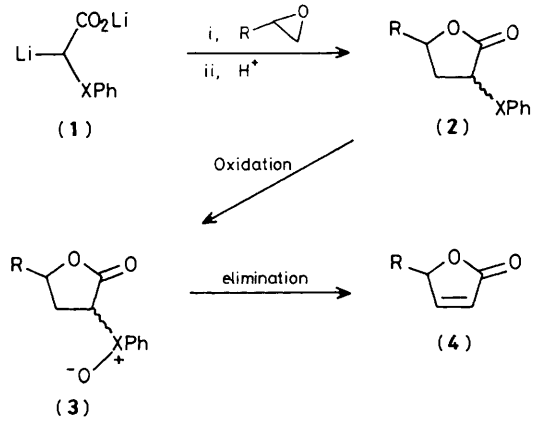
Department of Chemistry, Université de Montréal, Montréal, Québec H3C 3J7, Canada

Reaction of the dilithio derivative of phenylselenoacetic acid with epoxides leads to γ-substituted-α-phenylseleno-γ-butyrolactones, which upon oxidation–elimination, afford γ-substituted α,β-unsaturated γ-butyrolactones in high overall yield.

We have recently shown that γ-substituted α,β-unsaturated γ-butyrolactones can be used as versatile 'chiral templates' for the construction of acyclic units with a 1,3-, 1,4-, or 1,5-substitution pattern.[1] In our continuing effort to synthesize various complex polycyclic natural products utilizing the aforementioned strategy, we required mild methods for the formation of butenolides that would be compatible with other sensitive functional groups present in the substrate. Presently available methodology for the preparation of butenolides from epoxides involves nucleophilic ring opening with the dilithio derivative of phenylthioacetic acid (**1**) (X = S), followed by lactonization, oxidation under carefully controlled conditions, and elimination of the corresponding sulphoxides (**3**) (X = S) at the reflux temperature of toluene.[2]

In an effort to explore alternative conditions for such operations, we turned our attention to the α-phenylseleno derivatives (**2**) (X = Se), which after oxidation should eliminate under very mild conditions.[3] To the best of our knowledge, the dilithio derivative of phenylselenoacetic acid[4] has not been used for the opening of epoxides. Reaction of (**1**) (X = Se) with various epoxides proceeds smoothly as shown by the examples in Table 1.† Lactonization of the intermediate γ-hydroxy-α-phenylselenocarboxylic acids was accomplished with EDAC·HCl–DMAP–CH_2Cl_2.‡ As expected, oxidation–elimination proved to be very rapid with excess of hydrogen peroxide in CH_2Cl_2 at 0 °C.

The following is a representative procedure. To a stirred solution of LDA (7.32 mmol) in THF (13 ml) at 0 °C was added dropwise a solution of phenylselenoacetic acid[4] (3.66 mmol) in THF (3 ml). After stirring for 15 min, the epoxide (**5**) (3.33 mmol) was added as a solution in THF (3 ml). The mixture was stirred at room temperature for 16 h under argon, then it was acidified (1 M HCl) and extracted with ether (3 × 40 ml). The combined organic extracts were washed with water and brine, dried ($MgSO_4$), and evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2 (12 ml) and EDAC·HCl (3.5 mmol) and DMAP (0.333 mmol) were added. The solution was stirred at room temperature for 30 min and then water (20 ml) was added. The mixture was extracted with ether (4 × 30 ml) and the combined organic



Scheme 1. X = S or Se.

† All butenolides illustrated in Table 1 showed satisfactory 400 MHz ^1H n.m.r., high-resolution mass spectral, and i.r. data. Optical rotations were measured in chloroform.

‡ Abbreviations: EDAC = 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide; DMAP = 4-*N*,*N*-dimethylaminopyridine; THF = tetrahydrofuran; LDA = lithium di-isopropylamide.

Table 1.

Epoxide	Butenolide	(% Yield)[a]
Bu^tPh_2SiO (**5**)	Bu^tPh_2SiO (**10**)	(72)
Ph (**6**)	Ph (**11**)	(73)
H, $OSiPh_2Bu^t$ (**7**)[b]	H, Bu^tPh_2SiO (**12**)[e]	(73)
H (**8**)[c]	H, H (**13**)[f]	(71)
OCH_2Ph (**9**)[d]	OCH_2Ph (**14**)[g]	(75)

[a] Overall yields (3 steps) refer to chromatographically isolated product. Compounds (**10**) and (**11**) are recemic. $[\alpha]_D$ values/° (*c*): [b] −1.6 (1.35). [c] −22.4 (0.75). [d] −36.6 (1.24). [e] +31.5 (2.00). [f] +89.3 (1.25). [g] 0 (2.68).

extracts were processed as described above. Flash column chromatography (elution with ethyl acetate–hexanes, 1:9) gave a 1:1 mixture of 2-phenylseleno-γ-butyrolactones (**2**; X = Se, R = $Bu^tPh_2SiOCH_2$) as a pale yellow syrup. This compound was dissolved in CH_2Cl_2 (8 ml) and 30% hydrogen peroxide (4 ml) was added at 0 °C. After 10 min, the mixture was diluted with water (20 ml) and extracted with ether (3 × 20 ml). The combined organic extracts were processed as usual and the residue purified by flash column chromatography (elution with ethyl acetate–hexanes, 3:7) to give the butenolide (**10**) (72% overall).

The presently described methodology for the synthesis of functionalized butenolides and butyrolactones[5] further expands the utility of organoselenium reagents in organic synthesis in general, and natural product chemistry in particular.[6]

We thank the Natural Sciences and Engineering Council of Canada and Le Ministère de l'Education du Québec for generous financial support. We also thank Michael Evans for mass spectra.

Received, 3rd February 1986; Com. 156

References

1 S. Hanessian, P. J. Murray, and S. P. Sahoo, *Tetrahedron Lett.*, 1985, **26**, 5623, 5627.
2 K. Iwai, M. Kawai, H. Kosugi, and H. Uda, *Chem. Lett.*, 1974, 385.
3 K. B. Sharpless, R. F. Lauer, and A. Y. Teranishi, *J. Am. Chem. Soc.*, 1973, **95**, 6137.
4 H. J. Reich, F. Chow, and S. K. Shah, *J. Am. Chem. Soc.*, 1979, **101**, 6638.
5 For a review, see S. Kano, S. Shibuya, and T. Ebata, *Heterocycles*, 1980, **14**, 661.
6 For an excellent recent review on the use of organoselenium compounds in natural product synthesis, see K. C. Nicolaou and N. A. Petasis, 'Selenium in Natural Product Synthesis,' CIS, Inc. Philadelphia, 1984, and references cited therein.