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A 1,3-DIENE-2-CARBOXYLIC ESTER SYNTHESIS;
REACTION OF ALKYLIDENE-γ-LACTONES WITH POTASSIUM AND SODIUM PHENYL SELENOATE

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Recent reports by Liotta[1a] and Smith[1b] have described the S_N2-type opening of lactones with various forms of the sodium salt of the anion derived from phenyl selenol. In connection with other work, we were interested in converting the lactone **1a** to diene **2a** and decided to investigate the use of this methodology.

(*E*)-Ethylidene-γ-lactone (**1b**)[2] (13.5 mmol) was reacted with 1.1 equivalents of potassium phenyl selenoate (PhSeK) in 10% HMPA/THF at 80°C for 6 hours. The selenoate was prepared by heating a dry THF solution (15 ml) of diphenyldiselenide (7.7 mmol) in the presence of potassium metal (14.9 mg atom) at 80°C for 3 hours in a resealable sealed tube.[3] Progress of the reaction was monitored by observing the disappearance of lactone and appearance of carboxylate stretching frequencies in the ir spectra of crude aliquots. Isolation of the crude acid (see procedure in ref. 1a), esterification (CH_2N_2, Et_2O), and purification by chromatography on silica gel (6:1/hexanes:EtOAc) provided the selenide **3b**[4] in 71% yield. Interestingly, a slight amount (∿5%) of isomerization of **1b** to (*Z*)-ethylidene-γ-lactone (**5**) could be detected by gas chromatographic analysis of the reaction mixture at low conversion. This implies the reversible formation of a lactone enolate ion from Michael attack of PhSeK to the unsaturated lactone However, no products resulting from net Michael addition to **1b** nor from S_N2 opening of the (*Z*)-lactone **5** were ever detected. The only undesirable material isolated from this reaction was the diselenide **6**[4] (*vide infra*).

Nucleophilic opening of the lactone ring in the more complex substrate **1a**[5] provided the phenylselenide **3a**[4] (62%) after esterification and chromatography. Again, no Michael adducts or *E-Z* isomerized products were observed. The presence of the free hydroxyl group in **1a** also did not interfere with the reaction, nor was any diselenide product analogous to **6** observed.

We initially used the potassium rather than sodium salt of phenyl selenol almost exclusive ly because the reduction of PhSeSePh in THF was much more rapid with potassium metal than with sodium (3 hr/K° vs 15 hr/Na°) when solid chunks of metal were used. However, we have since observed that use of sodium sand[6] allows for the generation of PhSeNa in less than one hour (0.5 M, 3 mmol) in refluxing THF. Attempts to accurately compare the relative nucleophilic reactivities of these two reagents in 10% HMPA/THF or THF/18-crown-6 (5 mole %)[1a] with γ-butyrolactone (**7**) were hampered by solubility differences (0.5 M PhSeNa gave a homogeneous solution while 0.5 M PhSeK was only partially soluble in 10% HMPA/THF at 80°C and both mixtures were heterogeneous in the presence of the crown ether). Qualitatively, little difference in the overall rate of lactone openings was observed for any of these systems. A disadvantage to the use of the potassium reagent was the production on two occasions of small amounts (6-15%) of diselenides **6** (from **1b**) and **8**[4] (from **7**). We suspect these arose from overreduction of PhSeSePh by potassium to generate small amounts of reduced selenium metal[7] which then opened lactones **1b** and **7**. No dialkyl diselenides were observed when sodium was used as the reductant.

Completion of the preparations of dienes **2a** and **2b** involved oxidation of the pure selenides **3a** and **3b** (40% peracetic acid, $CHCl_3$, R.T., 5-10 min) to the selenoxides **4a** and **4b** which were isolated by rapid extraction (CH_2Cl_2 or $CHCl_3$) from a bicarbonate quenching medium. Elimination of these selenoxides in refluxing CH_2Cl_2 or $CDCl_3$ (50°C)[8] led to the dienes **2a**[4] and **2b**[4] as the sole products observable by nmr spectroscopy of the reaction mixture and in 73 and 68% yield respectively after chromatography. The ready availability of a variety of(*E*)-γ-butyrolactones[9] coupled with their stereospecific conversion to dienes by the method described herein provides a versatile route to 1,3-diene-2-carboxylic esters of predictable geometry.

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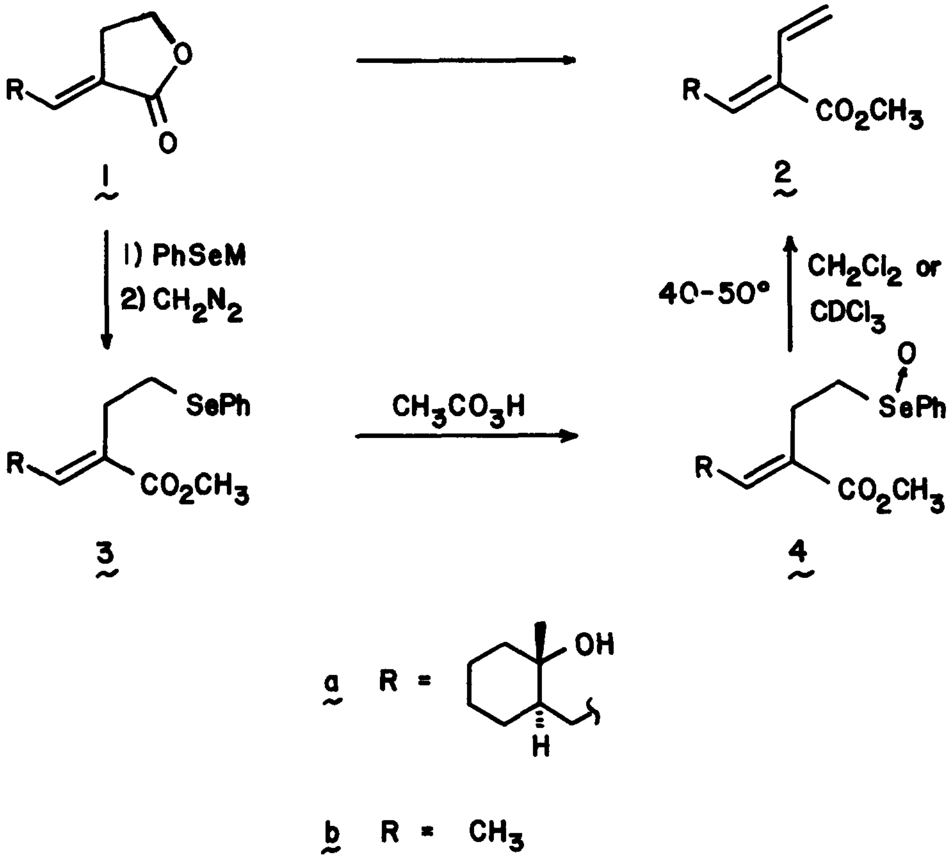
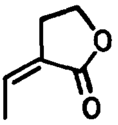
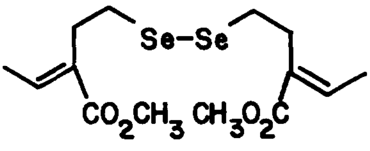
References and Notes:

1. (a) D. Liotta, W. Markiewicz, and H. Santiesteban, *Tetrahedron Letters*, 4365 (1977) and D. Liotta and H. Santiesteban, *Tetrahedron Letters*, 4369 (1977).
   (b) R. M. Scarborough, Jr. and A. B. Smith, III, *Tetrahedron Letters*, 4361 (1977).
2. C. P. Casey and W. R. Brunsvold, *J. Organomet. Chem.*, **102**, 175 (1975) and K. Ohga and T. Matsuo, *Bull. Chem. Soc. Jap.*, **46**, 2181 (1973).
3. Assembled from the following components available from Fischer & Porter Co. (Lab-Crest Scientific Division): flanged glass pipe (1/4", 1/2", 3/4"), aluminum glass coupling, teflon insert, neoprene gasket, aluminum sealing disc, and neoprene-asbestos insert strips.

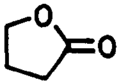

1
2
1) PhSeM
2) CH2N2
40-50°
CH2Cl2 or
CDCl3
CH3CO3H
SePh
CO2CH3
3
4
a R =
OH
H
b R = CH3


O
O

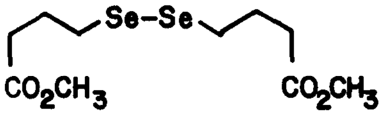
5


Se-Se
CO2CH3 CH3O2C

6


O
O

7


Se-Se
CO2CH3
CO2CH3

8

4. **2a**: NMR ($CDCl_3$) δ 1.15 (s, CH_3), 2.10 (br d,d; J = 15, 7 Hz; C$\underline{H}$HCH=C), 2.68 (d,d,d; J = 15, 7, 3 Hz; CH$\underline{H}$CH=C), 3.74 (s, OCH_3), 5.32 (br d, J = 11 Hz, $H_t\underline{H}_c$C=CHR), 5.55 (br d, J = 18 Hz, $\underline{H}_tH_c$C=CHR), 6.47 (d,d; J = 18, 11 Hz; H_tH_cC=C$\underline{H}$R), 6.74 (br t, J = 7 Hz, CHHC$\underline{H}$=C); IR (CCl_4) 3580, 3070, 3010, 1720, 1670, 1615 cm^{-1}; Calcd. for $C_{14}H_{22}O_3$: 238.1568; Found: 238.1561.

2b: NMR ($CDCl_3$) δ 1.91 (d, J = 7 Hz, CH_3), 3.73 (s, OCH_3), 5.35 (br d, J = 11 Hz, $\underline{H}_cH_t$C=CHR), 5.53 (br d, J = 17 Hz, $H_c\underline{H}_t$C=CHR), 6.44 (d,d; J = 11, 17 Hz; H_cH_tC=C$\underline{H}$R), 6.80 (br q, J = 7 Hz, C$\underline{H}$$CH_3$); IR (neat) 3100, 3040, 3000, 2960, 2920, 2860, 1725, 1640, 1590 cm^{-1}; Anal. Calcd. for $C_7H_{10}O_2$: C, 66.64; H, 7.99; Found: C, 66.48; H, 7.92.

3a: NMR ($CDCl_3$) δ 1.05 (s, CH_3), 2.82 (m, $C\underline{H}_2C\underline{H}_2Se$), 3.70 (s, OCH_3) 6.80 (br t, J = 7 Hz), 7.2 and 7.5 (m, PhSe); IR (CCl_4) 3620, 3080, 3060, 1720, 1645, 1585, 720, 690 cm^{-1}; Calcd. for $C_{20}H_{28}O_3{}^{80}Se$: 396.1201; Found: 396.1180.

3b: NMR ($CDCl_3$) δ 1.73 (d, J = 7 Hz, CH_3), 2.8 (m, $C\underline{H}_2C\underline{H}_2Se$), 3.69 (s, OCH_3), 6.87 (br q, J = 7 Hz, C$\underline{H}$$CH_3$), 7.2 and 7.45 (m, PhSe); IR (CCl_4) 1720, 1650 cm^{-1}; Anal. Calcd. for $C_{13}H_{16}O_2Se$: C, 55.13; H, 5.69; Found: C, 55.43; H, 5.68.

4a: (diastereomeric mixture with some (∿10%) **2a** already present): NMR ($CDCl_3$) δ 1.03, 1.04 (s, CH_3), 3.61, 3.63 (s, OCH_3), 6.9 (m, $\underline{H}$C=C), 7.5 and 7.6 (m, Ph).

4b: (some (∿30%) **2b** already present): NMR ($CDCl_3$) δ 1.79 (d, J = 7 Hz, CH_3), 3.68 (s, OCH_3), 6.90 (q, J = 7 Hz, HC=C), 7.5 and 7.6 (m, Ph).

6: NMR ($CDCl_3$) δ 1.84 (d, J = 7 Hz, CH_3), 2.84 (m, $C\underline{H}_2C\underline{H}_2Se$), 3.70 (s, OCH_3), 6.89 (br q, J = 7 Hz, C$\underline{H}$$CH_3$); IR ($CCl_4$) 1720, 1650, 760 cm^{-1}; Calcd. for $C_{14}H_{22}O_4{}^{78}Se_2$: 409.9863; Found: 409.9861.

8: NMR ($CDCl_3$) δ 2.1 (m, $CH_2C\underline{H}_2CH_2$), 2.45 (m, $C\underline{H}_2CO$), 2.92 (t, J = 7 Hz, $SeC\underline{H}_2$), 3.66 (s, OCH_3); IR (CCl_4) 1740 cm^{-1}; Calcd. for $C_{10}H_{18}O_4{}^{80}Se_2$: 361.9533; Found: 361.9515.

5. (a) Prepared by Wittig reaction of α-(γ-butyrolactonylidene)-triphenylphosphorane[5b] with the hemiacetal arising from reduction (DIBALH, $PhCH_3$, -70°C) of hexahydro-7a-methyl-2(3H)-benzofuranone.[5c] (b) S. Fliszár, R.F. Hudson and G. Salvadori, *Helv. Chim. Acta*, **46**, 1580 (1963). (c) J. Ficini and A. Maujean, *Bull. Soc. Chim. Fr*, 219 (1971).

6. Sodium from Alfa (40% dispersion in mineral oil) was washed several times with petroleum ether. Each washing was followed by centrifugation and decantation.

7. See J.A. Gladysz, J.L. Hornby, and J.E. Garbe, *J. Org. Chem.*, **43**, 1204 (1978) for examples of and references to selenium metalloid anion reactivity.

8. (a) The presence or absence of pyridine[1b] in the thermal PhSeOH extrusion seemed to have little effect. A useful and detailed study of alkylarylselenoxide elimination which describes solvent and substituent effects and competing side reactions (such as readdition of PhSeOH to the newly generated olefin)[8b,c] has recently been reported.[8c] (b) T. Hori and K.B. Sharpless, *J. Org. Chem.*, **43**, 1689 (1978). (c) H.J. Reich, S. Wollowitz, J.E. Trend, F. Chow, and D.F. Wendelborn, *J. Org. Chem.*, **43**, 1697 (1978).

9. G.A. Howie, P.E. Manni, J.M. Cassady, *J. Med. Chem.*, **17**, 840 (1974) and T. Minami, I. Niki, and T. Agawa, *J. Org. Chem.*, **39**, 3236 (1974).

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