

ORGANOSELENIUM CHEMISTRY II. A METHOD FOR THE PROTECTION OF  
 $\alpha$ -METHYLENE LACTONES<sup>1</sup>

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The use of protecting groups which prevent Michael-type additions of nucleophilic reagents to the reactive sites of  $\alpha$ -methylene lactones has received little attention. The need to effect protection of an  $\alpha$ -methylene lactone function as a result of work in our laboratories involving the synthesis of complex molecules possessing  $\alpha$ -methylene lactone moieties, has led to a search for a mild and potentially useful new blocking sequence. It has been reported that dimethylamine<sup>2</sup> and thiols<sup>3</sup> undergo a reversible addition to conjugated  $\alpha$ -methylene lactones. The removal of these protecting groups involves conversion to their corresponding methiodides and subsequent treatment with saturated aqueous sodium bicarbonate solution.<sup>3,4</sup> We wish to report a new blocking sequence for the protection of highly reactive conjugated  $\alpha$ -methylene lactones.

Our approach employs a) a Michael-type addition of phenyl selenium anion to the  $\alpha$ -methylene lactone and b) a "retro-Michael" reaction via the corresponding selenoxide which reestablishes the  $\alpha$ -methylene unit. The method is based on the observations by Sharpless<sup>5</sup> and Jones<sup>6</sup> that alkyl phenyl selenoxides readily undergo elimination to form olefins.

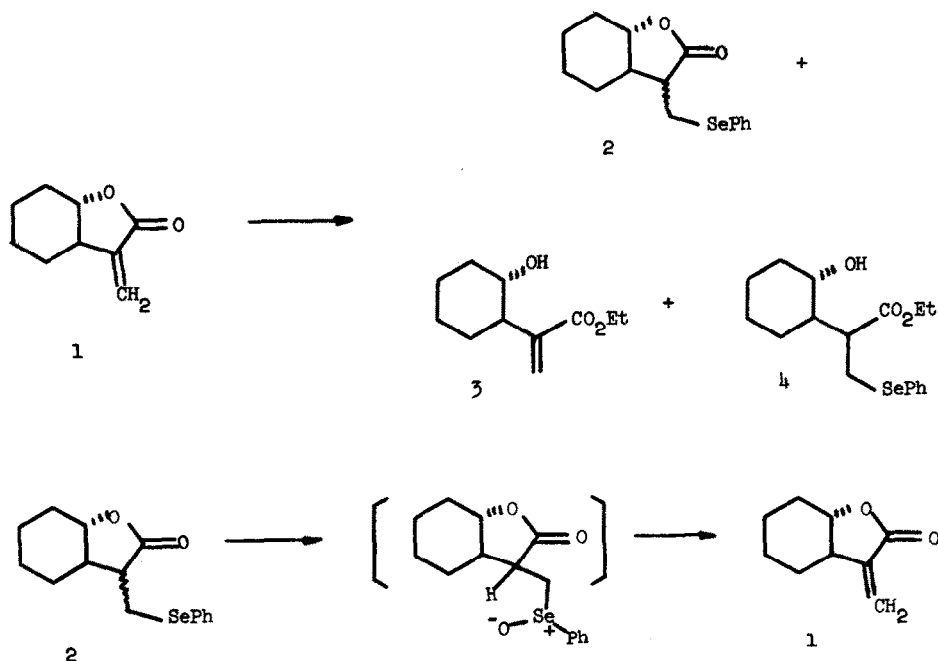
To an ethanolic solution of phenyl selenium anion [prepared by addition of 29 mg (0.77 mmol) of sodium borohydride to 126 mg (0.04 mmol) of diphenyldiselenide in 3.5 ml of absolute ethanol] at room temperature was added rapidly dropwise 97 mg (0.65 mmol) of lactone (1)<sup>7</sup> in 1.5 ml of absolute ethanol. The resultant mixture was stirred for 1.3 hr. The reaction was quenched by the addition of 0.1 N hydrochloric acid. Work-up afforded a crude yellow oil which after chromatography on silica gel gave 118 mg (60%) of pure crystalline lactone 2, mp 75-76°. Anal. Calcd. for C<sub>15</sub>H<sub>18</sub>O<sub>2</sub>Se: C, 58.25; H, 5.86. Found: C, 58.42; H, 5.95. In addition, chromatography afforded a 6% yield of the substituted ethyl acrylate 3 and a 6% yield of the protected ethyl

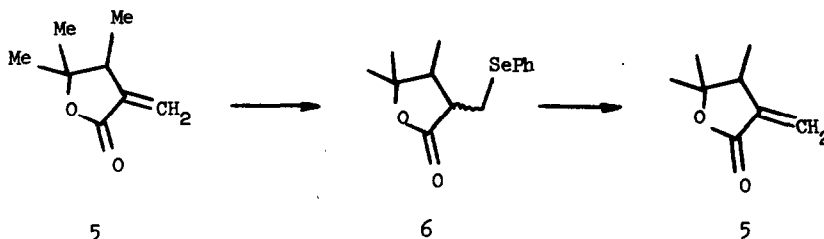
acrylate 4. Regeneration of the  $\alpha$ -methylene unit was achieved in 97% yield by treatment of phenylselenenyl lactone 2 with 30% hydrogen peroxide in tetrahydrofuran containing a trace of acetic acid at 0° for 30 minutes. The product 1 was identical in all respects (ir, nmr, tlc, glc) with a sample of 1 prepared by an alternative procedure.<sup>7</sup>

Similarly when the Michael-type addition of phenyl selenium anion was applied to  $\alpha$ -methylene lactone (5)<sup>8</sup>, there was obtained a 54% isolated yield of pure adduct (6)<sup>9</sup>. Employing the usual oxidation procedure resulted in exclusive formation of 5 in 99% isolated yield. Ir and nmr spectra of 5 were identical with those of a sample prepared previously in our laboratory.<sup>8</sup>

This new blocking sequence for the protection of  $\alpha$ -methylene lactones should prove useful in view of the observed ease of the "retro-Michael" reaction of selenoxides. Attempts are currently underway to improve the yield of the initial Michael adducts. Studies on the application of this blocking sequence to synthesis are continuing.

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## References

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5. Sharpless has also made the observation that phenyl selenium anion undergoes a Michael addition to cyclohexenone affording  $\beta$ -phenylseleno cyclohexanone which upon oxidation readily regenerates cyclohexenone [K. B. Sharpless, M. W. Young, and R. F. Lauer, Tetrahedron Letters, 1979 (1973)].
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9. Yields have not been optimized for the Michael adducts  $\tilde{2}$  and  $\tilde{6}$ .