DESILYLATION OF α-TRIMETHYLSILYLMETHYLENE-γ-LACTONES.

A NEW ROUTE TO α-METHYLENE-γ-LACTONES

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Summary: Addition of phenylthiol to α-trimethylsilylmethylene-γ-lactones affords
α-phenylthio(trimethylsilyl)methyl-γ-lactones which, on treatment with tetrabutyl-
ammonium fluoride and methyl acrylate give the corresponding α-methylene-γ-lactones
through a one-pot double deblocking process.

The α-methylene-γ-butyrolactone ring system constitutes a structural feature common to many
natural products which exhibit interesting biological activities.[1] We recently described a new
method for the preparation of α-alkylidene-γ-lactones, which is based on the intramolecular
addition of alkoxycarbonyl free-radicals to acetylenes as displayed in Scheme 1.[2] A variety of
α-alkylidene-γ-lactones 1 in which R^3 represents a phenyl, alkyl or trimethylsilyl group were
obtained in very high yields.[3] However, the extension of this method to the preparation of
α-methylene-γ-lactones 1 (R^3=H) resulted in low to moderate yields.

Scheme I
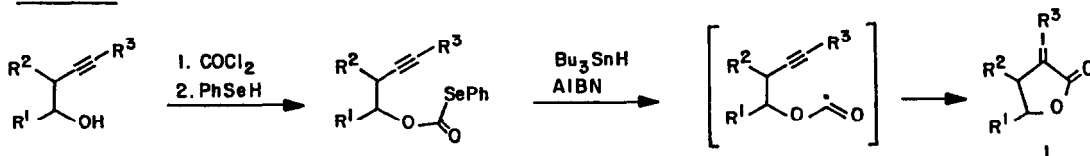

For example, treatment of the selenocarbonate 2[4] in toluene (0.02 M solution) with tri-n-
butylstannane (1.1 equiv) and azobis(isobutyronitrile) (0.1 equiv) at 110°C for 8 h afforded the
α-methylene-γ-butyrolactone 3[5] in 55% yield. In contrast, the trimethylsilyl derivative 4
was obtained, by a similar procedure, in over 92% yield.[2] The ready access to trimethylsilyl-
methylenelactones,[2] represented here by compounds 4 and 5, prompted us to investigate their
potential as intermediates for the preparation of α-methylene-γ-lactones.
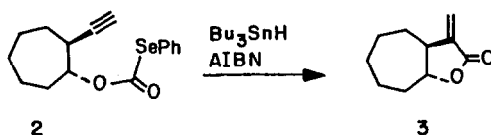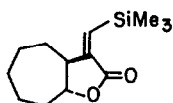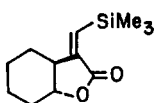
4   5

Whilst the cleavage of the Si-Csp bond in silyl acetylenes by fluoride ions is a common procedure in organic synthesis, the analogous cleavage of the Si-Csp^2 bond in vinyl silanes is rather rare.[6] In fact, the cleavage of this bond in trimethylsilyl-vinyl silanes generally requires an additional driving force which may, for example, be provided by a vicinal hydroxyl group[7] or by a geminal anion-stabilizing group.[8-11] The trimethylsilylmethylenelactones 4 and 5 lack any potential supporting element and indeed, we found that they were not affected by tetrabutylammonium fluoride in either tetrahydrofuran or dimethylsulfoxide.

The trimethylsilylmethylenelactones 4 and 5 were also inert to protodesilylation with trifluoroacetic acid or hydroiodic acid. Vinyl silanes usually undergo protodesilylation on treatment with acids. This reaction is considered to involve protonation of the double bond with the formation of a carbocation of type 6 where the positive charge is centered at a position β to the silicon atom.[6,12] In the case of the lactones 4 and 5, in which the trimethylsilyl group is located at the β-position of an α,β-unsaturated carbonyl system, protonation of the double bond would, by this mechanism, require the formation of an intermediate of type 6 in which R represents a carbonyl group, namely the location of a positive charge in the highly disfavored position α to a carbonyl group.
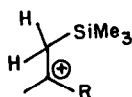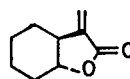

6   13

To circumvent the stability of the α-trimethylsilylmethylenelactones to the conventional deblocking procedures, we conceived the reversible conversion of the exocyclic sp^2 carbon atom into an sp^3 carbon. For this purpose (Scheme 2) the lactone 4 was treated with phenylthiol and triethylamine to give the corresponding adduct 7[5] in practically quantitative yield. Our original plan envisaged fluoride ion desilylation of the adduct 7 to the α-phenylthiomethyl-lactone 8, followed by regeneration of the α-methylene unit by Grieco's method[13] through the sulphoxide 9. Indeed, the now sp^3 trimethylsilyl group in 7 was deblocked by treatment with tetrabutylammonium fluoride (2 equiv

of 1 M solution in moist tetrahydrofuran)[14] and acetic acid (2 equiv) for 1 h to give the α-phenylthiomethyl-lactone 8 (95%)[5]. However, we discovered that when the desilylation was performed as described above, but excluding the acetic acid, the reaction products consisted of a mixture of the phenylthiomethyl-lactone 8 (74%) and the α-methylenelactone 3 (26%). We reasoned that in the double deblocking process, the carbanion 11, formed by fluoride desilylation, underwent proton transfer[15] to give the carbanion 12, which yielded the lactone 3 through β-elimination of phenylthiolate. In the presence of acetic acid, this process was totally blocked by protonation of carbanion 11. We, therefore, postulated that the process leading directly to the methylenelactone 3 would be favored by further decreasing the proton concentration and by the addition of a Michael acceptor that would effectively compete for the phenylthiolate and thus prevent its reverse addition to 3.

On the basis of these considerations, phenylthio(trimethylsilyl)methyl-lactone 7 was treated with desicated tetrabutylammonium fluoride[16] (2 equiv) and excess methyl acrylate (10 equiv) in anhydrous tetrahydrofuran at room temperature for 30 min. We were gratified to find that under these conditions the methylenelactone 3 was obtained in 93% yield along with methyl phenylthiopropionate 10 (94%). It is noteworthy that when the phenylthiomethyl-lactone 8 was exposed to the same reaction conditions, the same products were obtained. However, the fact that

Scheme 2
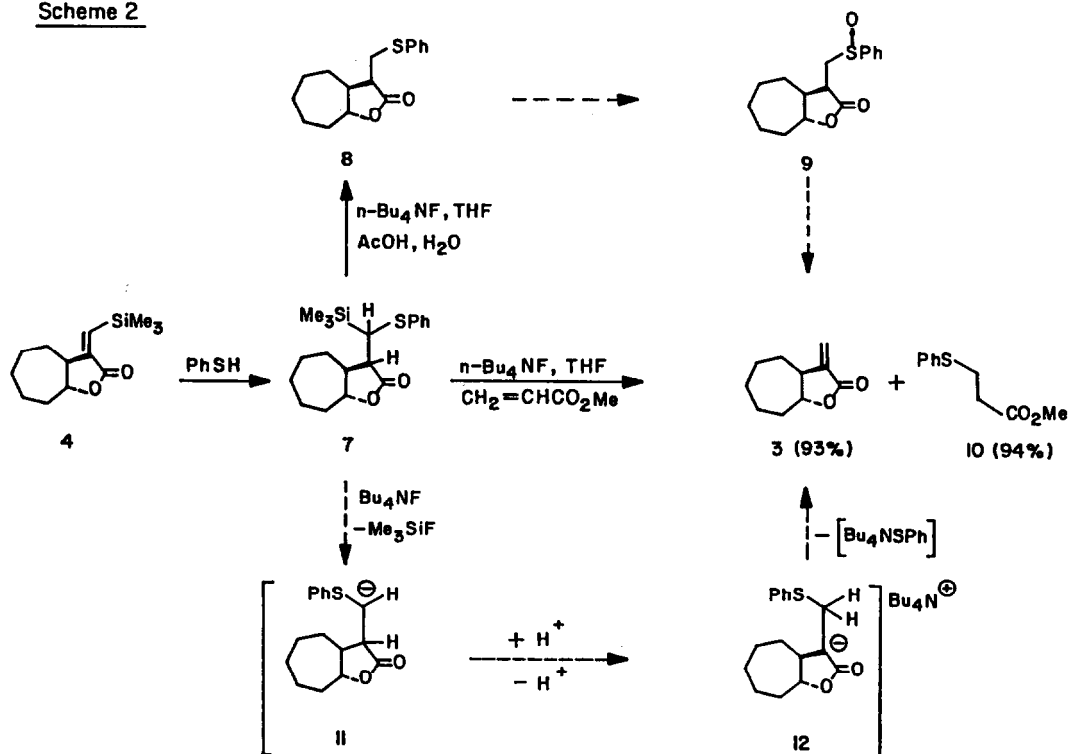
this last reaction required 120 h for completion, in lieu of 30 min, sustains the prevalence of the

proposed mechanism (Scheme 2) rather than a competitive mechanism involving the elimination of

phenylthiolate from 8 by fluoride ion.

Following the same procedure, the trimethylsilylmethylenelactone 5 was desilylated to give, in

excellent yield, the corresponding α-methylene-γ-lactone 13[5].

References

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4. The selenocarbonate 2 was obtained from trans-2-ethynylcycloheptan-1-ol, by the method described in reference 2.

5. All compounds gave analytical data consistent with the assigned structures.

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11. The fluoridolysis of the dimethylphenylsilyl and diphenylmethylsilyl groups was reported (reference 10) to occur also with "simple" vinylsilanes.

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14. A solution supplied by Aldrich, which contains <5 wt. % water was used.

15. The proton transfer leading from 11 to 12 is probably of an intermolecular nature. The alternative concerted [1,2] sigmatropic proton migration is highly unlikely to occur, see: Grovenstein, E. Angew. Chem. Int. Ed. 1978, 17, 313. However, [1,5] proton migration involving the enolic form of 11 cannot be excluded.

16. Tetrabutylammonium fluoride trihydrate, supplied by Fluka, was dried at 40°C/0.05 mmHg for 15 h.[17]

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