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O-SILYLATED ENOLATE PHENYLTHIOALKYLATION
A SYNTHESIS OF α,β-UNSATURATED 5- AND 6-MEMBERED LACTONES

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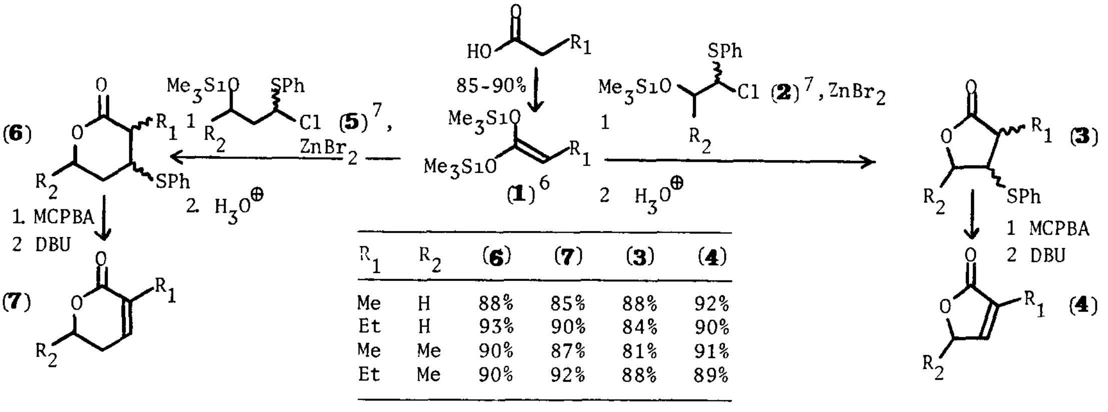
Summary $ZnBr_2$-catalysed phenylthioalkylation of ketene bis(trimethylsilyl)acetals, obtained from carboxylic acids, with appropriate α-chlorosulphides can be used to prepare γ- and δ-lactones

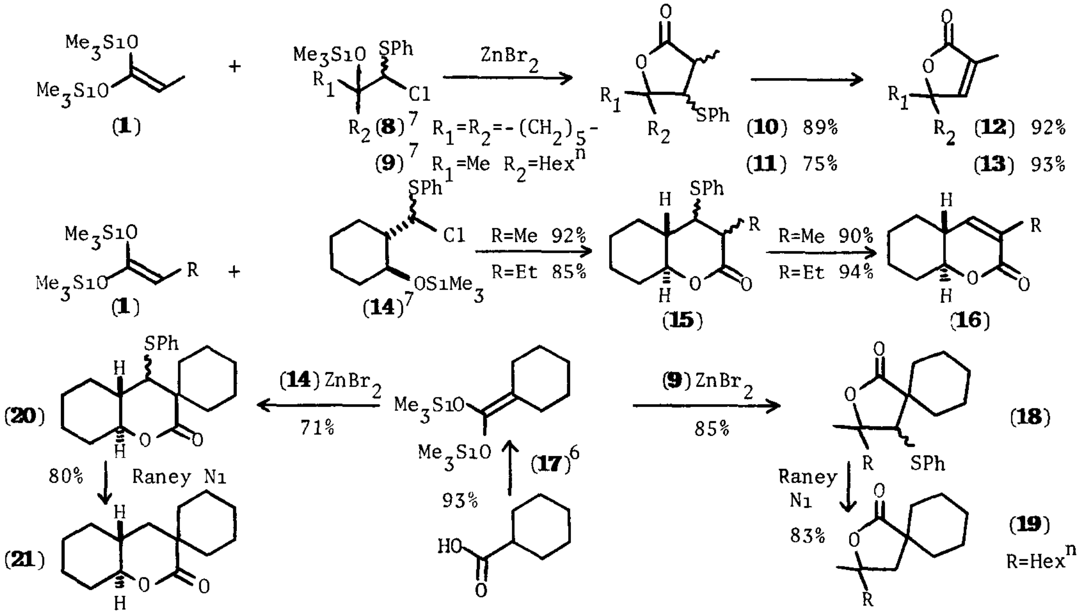
O-Silylated enolate chemistry has recently produced new and improved methods for forming carbon-carbon bonds next to the carbonyl group[1-3] In particular, alkylation of *O*-silylated enolates of ketones and esters by α-chloroalkyl phenyl sulphides (PhSCHClR),[2,3] under Lewis acid-catalysis, leads overall to α-alkylation or α-alkylidenation after a suitable sulphur removal step[3]

We now report that α,β-unsaturated 5- and 6-membered lactones, versatile synthetic intermediates[4] as well as a structural feature of many natural products,[5] are easily prepared by this phenylthioalkylation method by using the *O*-silylated enolate derivatives of carboxylic acids[6] Zinc bromide-catalysed alkylation of these ketene bis(trimethylsilyl)acetals (**1**) with suitable α-chlorosulphides (e g **2**) gives, after acidic workup, the phenylthiolactones (**3**) Sulphur oxidation and β-elimination then gives the corresponding $\Delta^{\alpha,\beta}$-butenolides (**3** → **4**) Similarly, unsaturated 6-membered lactones can be successfully prepared (**1** → **6** → **7**) using γ-silyloxy substituted chlorides (e g **5**)



R_1	R_2	(**6**)	(**7**)	(**3**)	(**4**)
Me	H	88%	85%	88%	92%
Et	H	93%	90%	84%	90%
Me	Me	90%	87%	81%	91%
Et	Me	90%	92%	88%	89%

Further examples of unsaturated lactones, prepared in this way, are **12**, **13**, and **16** (for R = Me, Et) The α-chlorosulphides (**2**, **5**, **8**, **9**, and **14**) used were all made by NCS chlorination of the corresponding phenyl sulphides (CCl_4, 70°, 2-3 h, >95%),[2] which were prepared by various routes[7] The phenylthioalkylation reactions were carried out in the usual way,[2] using a catalytic amount of $ZnBr_2$ in CH_2Cl_2 (20°, 45 min), but were now given an aqueous acidic workup (2*M* HCl) leading to hydrolysis and lactonisation of the intermediate alkylation products[8] The β-phenylthiolactones obtained were generally diastereomeric mixtures at the α- and β-carbons,such that sulphoxide cycloelimination, which we had used previously,[2] was now unsuitable for introducing the unsaturation. Conversion to the desired α,β-unsaturated lactones was best performed, therefore, by first oxidising to the sulphone with MCPBA (CH_2Cl_2, 20°, 3 h), then directly β-eliminating using DBU as the base (CH_2Cl_2 or $CHCl_3$, 20°, 1 h).



Alternatively, reductive sulphur removal by W-2 Raney nickel (Me_2CO, 20°, 2 h)[2] could be used, giving a synthesis of saturated lactones (e.g. **17** → **18** → **19** and **17** → **20** → **21**).

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NOTES[9] AND REFERENCES

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[3] For other applications of phenylthioalkylation, see H. A. Khan and I. Paterson, *ibid.*, 2399 (1982); R. Tanikaga, K. Miyashita, H. Sugihara, and A. Kaji, *J. C. S. Chem. Comm.*, 1106 (1981).

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[7] Precursor phenylsulphides (H for Cl in diagrams) were prepared as follows: for **2** (R_2=H, Me) and **5** (R_2 = H), reaction of NaSPh with the appropriate chloroalcohol (EtOH, 20°, 16 h) was followed by silylation (Me_3SiCl, DMAP-Et_3N, CH_2Cl_2, 20°, 71-80% overall); for **5** (R_2 = Me), addition of PhSH to methyl vinyl ketone (piperidine, CCl_4, 0°, 16 h), reduction ($LiAlH_4$, Et_2O), then silylation (75% overall); for **8**, **9**, and **14**, $PhSCH_2Li$ addition to cyclohexanone, 2-octanone, or cyclohexene oxide (TMEDA-THF, -23°) was followed by *in situ* silylation (Me_3SiCl, -23° → 20°, 70% for **8**, 87% for **9**, 80% for **14**).

[8] On completion of the phenylthioalkylation reaction,[2] the reaction mixture was poured into 2*M* HCl solution and extracted twice with Et_2O. The combined organic fractions were shaken with 2*M* HCl for a few minutes, then dried and evaporated *in vacuo*. Flash chromatography on SiO_2 gave the corresponding lactones.

[9] Yields quoted are for isolated products (characterised by 200 MHz ^{1}H n.m.r., m.s., and i.r.).

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