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O-SILYLATED ENOLATES IN ORGANIC SYNTHESIS: α-ALKYLATION OF CARBONYL COMPOUNDS BY 1,3-DITHIENIUM FLUOROBORATE.

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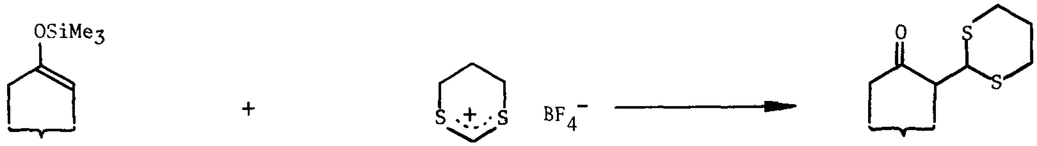
Summary: The *O*-silylated enolates of ketones, aldehydes, esters, and lactones can be regiospecifically alkylated by 1,3-dithienium fluoroborate to give the selectivity protected β-dicarbonyl compounds.

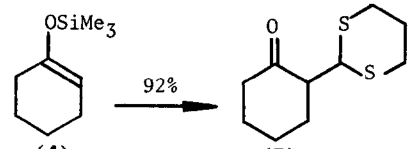
We have found that the reaction of *O*-silylated enolates with α-chloroalkyl phenyl sulphides (PhSCHClR) is a useful method for the regiospecific α-alkylation and alkylidenation of carbonyl compounds.[1,2] This phenylthioalkylation reaction usually requires the presence of a suitable Lewis acid (e.g. $\mathrm{ZnBr_2}$, $\mathrm{TiCl_4}$, or $(\mathrm{Pr^iO})_2\mathrm{TiCl_2}$), and presumably involves the generation of an intermediate thiocarbocation, or an undissociated complex between the reagent and the Lewis acid, as the reacting electrophile. As an extension of this work, we were interested in examining the direct reaction of *O*-silylated enolates[3] with some stable thiocarbocations.[4]



(1) **(2)** **(3)**

We now report that *O*-silylated enolates (**1**) are readily alkylated by the thiocarbocation salt, 1,3-dithienium fluoroborate (**2**),[5] leading to the regiocontrolled introduction of the 1,3-dithiane unit at the α-position of carbonyl compounds. The alkylation products, selectively protected β-dicarbonyl compounds (**3**),[6] are potentially useful synthetic intermediates.[7] For example, the 1,3-dithiane substituent may, if desired, be hydrolysed to a formyl group, or converted into a methyl group by reductive desulphurisation.

The electrophile (**2**)[5] is readily prepared by hydride abstraction from 1,3-dithiane by trityl fluoroborate[8] ($\mathrm{CH_2Cl_2}$, reflux 2h, 81%). Its reaction with *O*-silylated enolates (**1**) was found to



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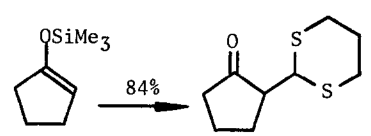

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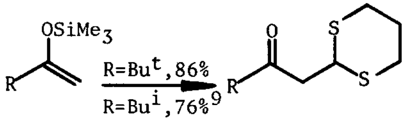

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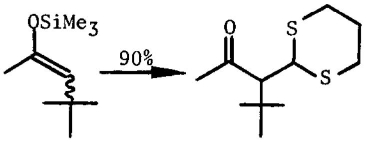

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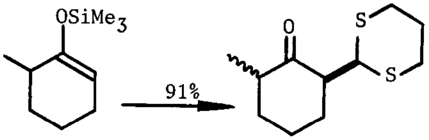

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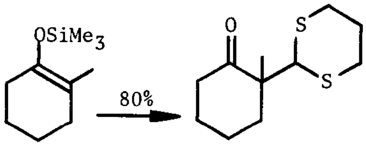

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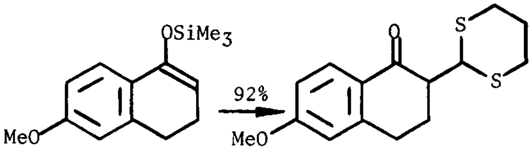

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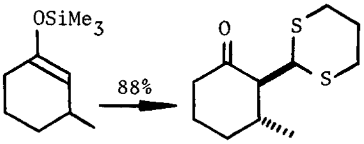

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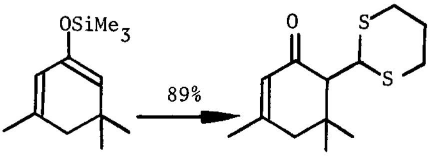

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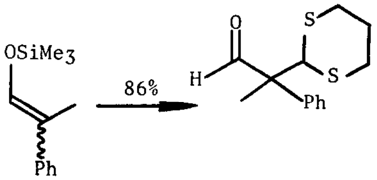

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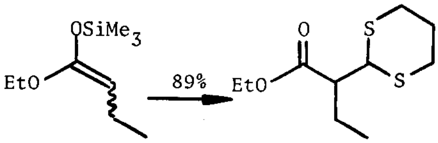

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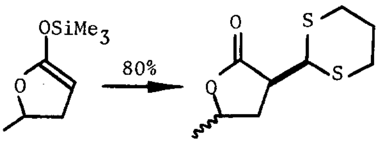


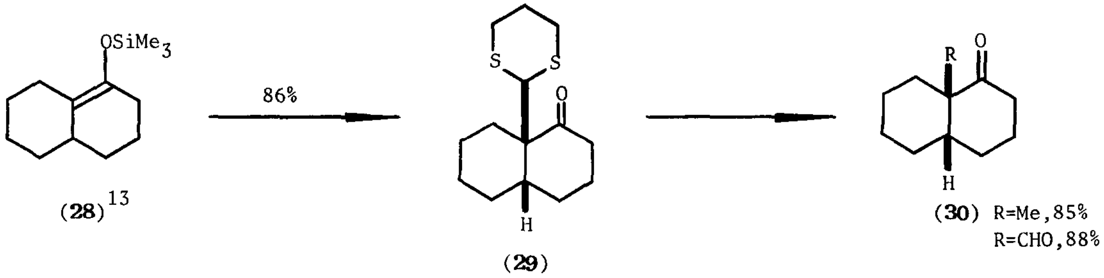
(26) (27)

be remarkably rapid and high yielding: reaction was essentially over directly after the addition of a solution of **2** (CH_3NO_2) to a solution of substrate (CH_2Cl_2) at -78°. Successful reaction was obtained with a range of ketone-derived *O*-silylated enolates, as well as for aldehyde (**22**), ester (**24**), and lactone (**26**)-derived substrates.

Silyl enol ether regiointegrity is usually,[1,2] but not always,[10] retained in Lewis acid-mediated alkylation reactions. With the highly reactive electrophile (**2**), regiospecific introduction[11] of the 1,3-dithiane group into unsymmetrical ketones was found to be straightforward, as in **8** → **9** for R = Bu^i, **10** → **11**, **12** → **13**, **14** → **15**, **18** → **19**, and **28** → **29**. Alkylation of the cross-conjugated *O*-silylated dienolate (**20**) also proceeded smoothly to give the enone derivative (**21**).

In certain cases the reaction with the 1,3-dithiane cation (**2**) also showed useful kinetic stereoselectivity. Alkylation of **18** gave only the *trans*-isomer (**19**), while **12** gave a 6:1 mixture of diastereoisomers (**13**) (presumably *axial*-attack of the electrophile favours the *trans*-isomer[12]). In the case of the *O*-silylated lactone enolate (**26**) ,we obtained the products (**27**) as a 7:1 mixture of diastereomers (stereochemistry undetermined).

We previously examined the regio- and stereo-selectivity of alkylation of the 1-decalone-derived silyl enol ether (**28**) with chloromethyl phenyl sulphide ($PhSCH_2Cl$) in the presence of $TiCl_4$.[1] We obtained the bridgehead-alkylated product as a 4:1 mixture of *cis* and *trans*-isomers.



(**28**)[13]

(**29**)

(**30**) R=Me,85%
R=CHO,88%

For reaction of **28**[13] with 1,3-dithienium fluoroborate (**2**) (-78°, 10 min), the alkylation stereoselectivity was greatly increased and we now isolated a single product (**29**). The stereochemistry was confirmed by hydrogenolysis of **29** with W-2 Raney nickel (Me_2CO, 20°, 4h), which gave cleanly *cis*-9-methyl-1-decalone (**30**, R = Me). Hydrolytic sulphur removal was also possible, treatment of **29** with HgO-BF_3OEt_2 in aqueous THF[14] gave the corresponding aldehyde (**30**, R = CHO).

Although Taylor and LaMattina[6] have described the synthesis of some α-(1,3-dithian-2-yl)-aldehydes and ketones (3) by enamine alkylation with 2-chloro-1,3-dithiane,[15] we feel the reaction of *O*-silylated enolates with 1,3-dithienium fluoroborate has the advantages of greater generality, efficiency, and mildness. Moreover, as a two-step methylation procedure, it also has some advantages over our earlier phenylthiomethylation method:[1] alkylation occurs under milder conditions with higher stereoselectivity, while, more significantly, greater γ-selectivity is obtained in the reaction of *O*-silylated dienolates.[16]

The *O*-silylated enolates used were prepared by standard methods.[1-3] In a typical alkylation reaction, a solution of 1,3-dithienium fluoroborate (**2**)[5] (206 mg, 1 mmol) in dry nitromethane (1 ml) was added dropwise, over 1 min, to a stirred solution of *O*-silylated enolate (1 mmol) in dry dichloromethane (3 ml) at -78° under Ar. After 10 min, the reaction mixture was partitioned between saturated $NaHCO_3$ solution and ether. The organic phase was separated, dried, and evaporated *in vacuo* to give, after flash chromatography on silica gel, the alkylated carbonyl compound.

NOTES and REFERENCES:

[1] I. Paterson and I. Fleming, *Tetrahedron Letters*, 993 and 995 (1979).

[2] I. Paterson and I. Fleming, *ibid.*, 2179 (1979).

[3] J. K. Rasmussen, *Synthesis*, 91 (1977).

[4] For alkylation reactions with some other stable carbocations see: S. Danishefsky, M. Prisbylla, and B. Lipisko, *Tetrahedron Letters*, 850 (1980); L. F. Kelly, A. S. Narula, and A. J. Birch, *ibid.*, 4107 (1979); K. M. Nicholas, M. Mulvaney, and M. Bayer, *J. Amer. Chem. Soc.*, *102*, 2508 (1980).

[5] E. J. Corey and S. W. Walinsky, *ibid.*, *94*, 8932 (1972). We followed a slightly modified procedure of using a longer reaction time (2h), then decanting off the solvent from the precipitated product, and liberally washing with dry cold ether followed by dichloromethane, before drying. The light beige-coloured reagent was then free of any residual trityl-containing contaminants.

[6] E. C. Taylor and J. L. LaMattina, *Tetrahedron Letters*, 2077 (1977), T. Mukaiyama and M. Hayashi, *Chemistry Letters*, 15 (1974); A. Pelter, P. Rupani, and P. Stewart, *J.C.S. Chem. Comm.*, 164 (1981).

[7] In principle, the dithioacetal substituent might first be metallated and alkylated etc., before hydrolysis or hydrogenolyis. B.-T. Gröbel and D Seebach, *Synthesis*, 357 (1977); E. J. Corey and D Seebach, *Angew. Chem., Int. Ed.*, *4*, 1075 (1965).

[8] H. J. Dauben, L. R. Honnen, and K. M. Harmon, *J. Org. Chem.*, *25*, 1442 (1960).

[9] **8**:regioisomer in the proportion 88:12; **12**:**14** in the proportion 99:1, **14**:**12** in the proportion 88:12.

[10] I. Paterson, *Tetrahedron Letters*, 1519 (1979).

[11] In detail, the amount of regioisomer produced was proportional to the amount of the corresponding silyl enol ether in the starting material.[9]

[12] Base equilibration of **13** (K_2CO_3/MeOH, 20°, 3h) gave a 1:3 mixture, where the now minor isomer (*trans*) corresponded to the major component from alkylation. For the stereochemistry of enolate anion alkylations, see: H. O. House, *Modern Synthetic Reactions*, 2nd edn., W. A. Benjamin, Menlo Park, Cal. (1972), chapter 9.

[13] **28** was separated from a small amount of regioisomer by flash chromatography on silica gel.

[14] E. Vedejs and P. L. Fuchs, *J. Org. Chem.*, *36*, 366 (1971).

[15] In a preliminary study, we found this alternative electrophile to be less easily handled than **2**. It gave only low yields of alkylated product in reaction with *O*-silylated enolates.

[16] See the following paper.

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