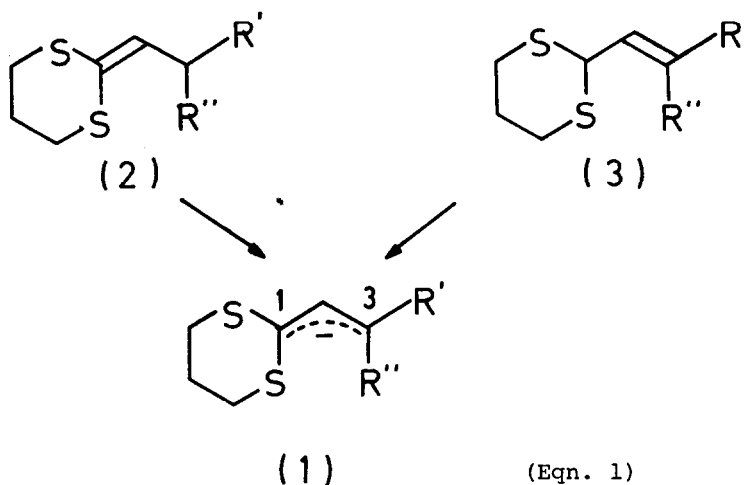


ALKYLATION OF METALLATED KETENE THIOACETALS. EFFECT OF THE HARDNESS OF THE LEAVING GROUP AND ELECTROPHILE

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The harder the leaving group or the Lewis acid end of the alkylating agent, the higher the proportion of C-1 alkylation of lithium ketene thioacetal (6).

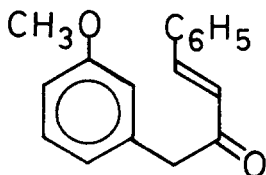
Ketene thioacetals are valuable synthetic intermediates.¹ They serve as masked α , β -unsaturated acyl anion equivalents. The conjugate base (1) can be prepared with *n*-butyl lithium from either the intermediate (2)² or (3)³ (Equation 1). In some instances electrophilic attack on (1) occurs exclusive-



ly at C-1;^{1,2,3,4} in others, simultaneous attack at both C-1 and C-3 has been reported.^{2,4} This latter occurrence has on occasion⁴ seriously limited the synthetic value of the method. An investigation of the factors influencing C-1 vs C-3 alkylation in this type system has not as yet been reported.

We now wish to report the results of our studies on 2-styryl dithiane (5)⁵ which were initiated by the following experiment. We had required the enone (4) for synthetic purposes. We undertook to synthesise it according to

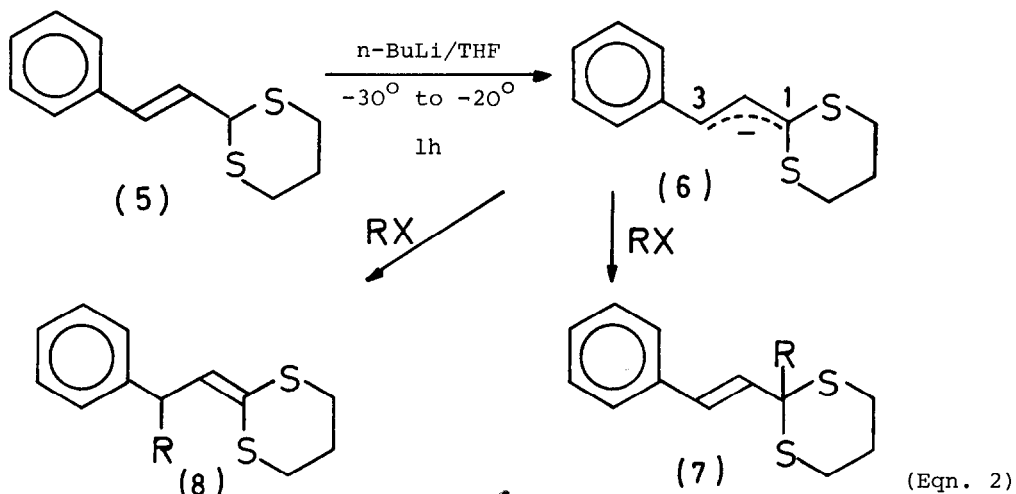
the synthetic scheme (Equation 2), anticipating C-1 alkylation (RX =



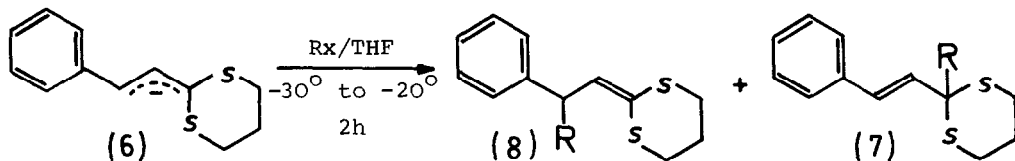
(4)

3-MeOC₆H₄CH₂Br). However the product consisted of a mixture of (7) and (8) in the ratio 10:90. We therefore undertook an investigation of this system.

In the anion (6) C-1 is harder⁶ than C-3. We anticipated, on the



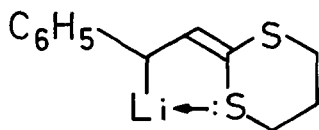
basis of an earlier investigation of allyl anion alkylation⁷, that the hardness of the leaving group would affect the orientation of the alkylation. Our results (Table) dramatically bear out this prediction. The following conclusions can be made: (a) the C-1 to C-3 ratio increases with increasing hardness⁶ of the leaving group I < Br < Cl < OTS < SO₄, (b) in the alkylating agent RX, the influence of X is most dramatic when R = CH₃, (c) very hard acids such as those in Me₃SiCl and D₂O attack the hard C-1 position exclusively, (d) the product of C-1 alkylation is invariably trans. This has been observed by others^{2,4} whichever synthetic method is used (Equation 1). This stereospecificity suggests either the preferential formation of (6) in its W-configuration, or an internally coordinated structure (9)⁸, (e) the site of attack by benzyl halides is due to a combination of the inherent softness of the benzyl group and steric effects. The latter is indicated by a comparison of the results of 3-methoxybenzyl bromide and benzyl bromide (Table).



Rx	R	Yield*, % (7) + (8)	Ratio**	
			(8)	(7)
3-MeO-C ₆ H ₄ -CH ₂ Br	3-MeO-C ₆ H ₄ -CH ₂	69	90	10
phCH ₂ I	phCH ₂	60	90	10
phCH ₂ Br	phCH ₂	75	86	14
phCH ₂ Cl	phCH ₂	66	78	22
phCH ₂ OTS	phCH ₂	74	74	26
n-Propyl-I	n-Propyl	79	37	63
n-Propyl-Br	n-Propyl	57	27	73
CH ₃ I	CH ₃	60	44	56
CH ₃ OTS	CH ₃	80	18	82
(CH ₃) ₂ SO ₄	CH ₃	55	--	100
(CH ₃) ₃ SiCl	Si(CH ₃) ₃	72	--	100
D ₂ O	D	70	--	100

* isolated yield. ** determined by n.m.r.

Specifically, these results increase the synthetic values of ketene thioacetals.^{1,2,4} In general, in the alkylation of allyl anions although the C-1 to C-3 ratio depends on the steric bulk of the substituents on the anion,^{9,10} the nature⁹ and solvation of the counter ion¹¹, and the steric requirements of the alkyl halide¹⁰, still another parameter needs consideration. It is to correlate first the hardness of the ambident anion with the electrophile.¹²



(9)

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