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HOMOLOGATIVE TRANSFORMATION OF ALDEHYDES AND KETONES TO α, ß-UNSATURATED KETONES THROUGH METALATED KETENE THIOACETALS

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We report here a simple transformation of saturated carbonyl derivatives 1 to α, ß-unsaturated ketones 2 with the formation of two new C-C-bonds, through the sequence of steps ① through ④ of Scheme I. In a previous paper [1] we presented details of the high yield conversion of carbonyl derivatives 1 to ketene thioacetals 3, step ①, and claimed,[1,2] like other investigators,[3,4] that these compounds are useful synthetic intermediates because they are, among other things,[1-7] precursors to the masked α, ß-unsaturated acylanions 5(= $O=\overset{\ominus}{C}-C=C$, E^1-carbonyl umpolung [7]). However, this has not been

SCHEME I

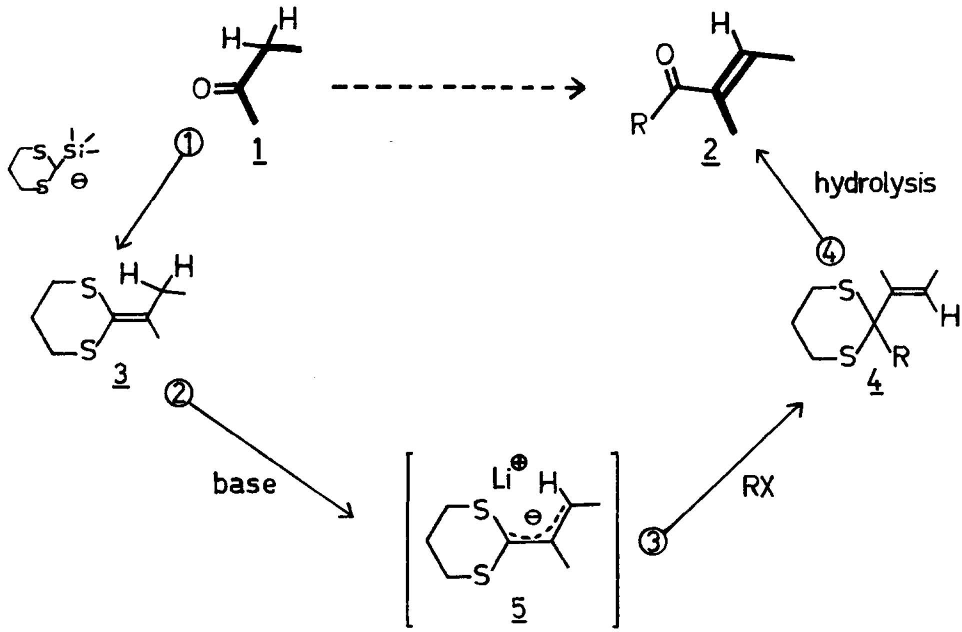
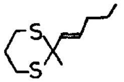
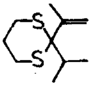
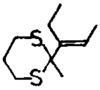
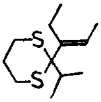
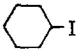
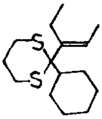
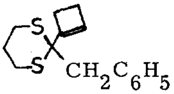
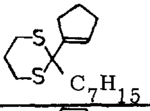
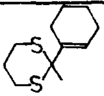
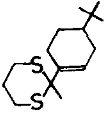
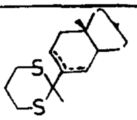


TABLE I: Yields and physical data of the products 4, obtained from metallated ketene thioacetals[10]

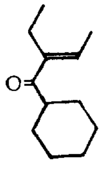
3 from Carbonyl Compound	Alkylating Reagent	Product 4	Yield	B.P.(°C/mm)[a] M.P.(°C)
a: n-pentanal	CH_3I		90	100/1
b: acetone	$(CH_3)_2CHCl$		92	105/0.4
c: diethylketone	CH_3I		87	90/1
	$(CH_3)_2CHCl$		80	120/0.25
			82	130/0.4
d: cyclobutanone	$C_6H_5CH_2Br$		80	82
e: cyclopentanone	n-$C_7H_{15}I$		75	125/0.02
f: cyclohexanone	CH_3I		87	110/1
g: 4-t-butyl-cyclohexanone	CH_3I		77	97
h: cholestanone	CH_3I		75[b]	---[b]

a) Bath temperature in short path distillation.

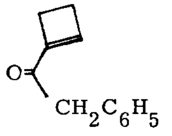
b) The isomeric Δ^2 and Δ^3 olefins are formed in a 3:1 ratio (nmr analysis); m.p. of the mixture broad, > 136°.

demonstrated except for the parent 2-ethylidene-1,3-dithiane,[5] and in fact, a recent paper describes unsuccessful attempts to metalate substituted derivatives 3.[8] In our original investigation of this reaction,[9] we encountered the same problem of sluggish or no allylic proton abstraction at all under ordinary reaction conditions (n-butyllithium in THF, -20°C). However, in the presence of 2-4 moles of HMPTA/mole of ketene thioacetal 3 a smooth conversion to the desired allylic anions 5 occurs[10] in all cases tested. Some examples are shown in Table I. This secures the step ② of the above scheme. As is evident from the table, subsequent alkylation of the anions 5 takes place highly regioselectively (>95%) at the dithiane 2-position, and the derivatives 4 of α, ß-unsaturated ketones are produced in high yields (step ③). One geometrical isomer of 4 is formed from 3a and 3c with greater than 95% preference, as shown by the number of vinylic hydrogens seen in the nmr spectra. In the case of disubstituted double bonds (product from 3a) the E-configuration may be assigned (15 Hz trans-coupling) which is tentatively proposed for the trisubstituted double bonds (products from 3c) as well (see Table I).

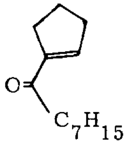
For the final hydrolysis step ④ we found the recently published reagent o-mesitylensulfonylhydroxylamine[11] to be most satisfactory. Other methods have been used successfully for the liberation of α, ß-unsaturated ketones from their thioacetals.[12] The feasibility of this step, and by the same token, the versatility of the overall conversion 1 → 2 is demonstrated by the isolation of the ketones 7 - 10 in the yields shown.



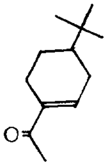
7 (51%)



8 (75%)



9 (60%)



10 (65%)

In favorable cases, transformation 1 → 2 can be achieved with >60% overall yield.

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10. 10 mmoles of 3 in 20 ml THF/4-8 ml.HMPTA are combined at -78°C with 11 mmoles of n-butyllithium or lithium diisopropylamide. After raising the temperature to +20° within 2-3 hours the resulting dark red solution is cooled to -78° and combined with the alkylating reagent.
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