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PREPARATION AND UTILIZATION OF TWO C_5 CONJUGATED KETENE DITHIOACETALS AS ISOPRENE SYNTHONS. SYNTHESIS OF (-)(E)-LANCEOL.

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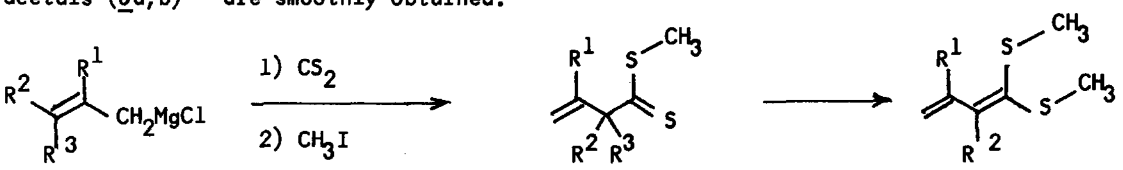
While investigating methods of producing several unsaturated sulfur systems which may be useful for the syntheses of natural products, we have noted that few procedures [1-3] are available for the preparation of conjugated ketene dithioacetals in the 1,3-dithiane series, and fewer still [4,5] for similar compounds bearing various S-alkyl, -alkenyl or -aryl groups. It was therefore desirable to seek a practical and inexpensive synthesis of isoprenic ketene dithioacetals (3a,b).

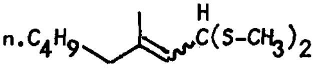
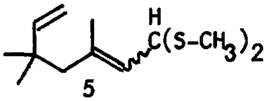
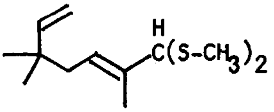
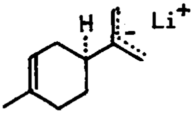
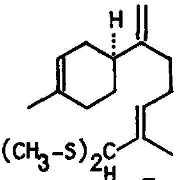
A simple route would be the S-methylation [6] of unsaturated dithioesters, but at the outset of our work, these compounds were scarcely described in the literature [7]. The known reaction of carbon disulfide with Grignard derivatives [6a,8] can be successfully adapted to the more reactive allylic Grignard reagents on condition that the reaction is carried out at -78° (inverse addition) in an ether- tetrahydrofuran mixture. Then methylation affords the dithioesters (2a-c) bearing an inversed allylic chain as expected [7]. After treatment of the dithioesters (2a,b) first with lithium diisopropylamide (1,1 eq) in THF at -78° for 30 min, then with methyl iodide, the two isoprenic ketene dithioacetals (3a,b) [9] are smoothly obtained.



1	R^1	R^2	R^3	Ratio ether:THF	2 (% yield)	3 (% yield)
1a	CH_3	H	H	2 : 1	2a (47)	3a (83)
1b	H	CH_3	H	1 : 1	2b (86)	3b (80)
1c	H	CH_3	CH_3	0 : 1	2c (85)	

It is now possible to utilize the two stable[10] and readily available isoprene synthons (3a,b) for the preparation of terpenoid compounds. Whereas conjugate addition of n.butyl-lithium to 2-(1-methyl-2-propenylidene)-1,3-dithiane is known[11], the ability of S-methyl compounds (3a,b) to undergo such additions with various organo-lithium reagents remained to be examined. Table I summarizes some of the results obtained using n.butyl-lithium and two allylic C_5 or C_{10} lithium reagents. In each case, addition to the isoprenic dithioacetals (3,a,b) is clean and rapid and after protonation affords the compounds 4 and 5, each as a mixture of E and Z isomers while the two adducts 6 and 7 from 3b are homogeneous. The additions of 3-methyl-2-butenyl-lithium with inversion of the allylic chain are noteworthy.

Table I. Conjugate addition of organo-lithium reagents to the isoprenic dithioacetals

Substrate	R-Li[a] (equiv)	Product[9]	% Yield[b] (E/Z)
3a	$n.C_4H_9Li$ (1,2)	 4	56 (6/4)
3a	 (1,3)[12]	 5	61 (6/4)
3b	 (1,3)[12]	 6	75[c]
3b	 (-) (1,4)[13]	 7	53[c]

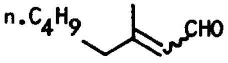
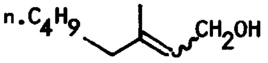
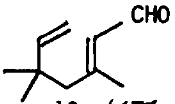
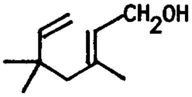
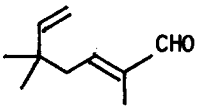
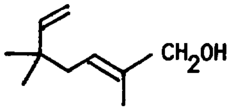
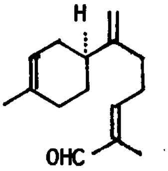
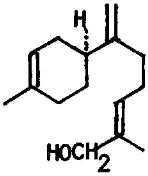
a. THF as solvent; after 60-120 min at -78°, the mixture was allowed to warm to -20° during 30-50 min; then hydrolyzed.

b. Yield of product after isolation and purification by column chromatography (SiO_2).

c. Only one isomer isolated.

The dithioacetals 4-7 are smoothly hydrolyzed using cupric chloride-cupric oxide in aqueous acetone [14] (2 hrs at 20°), and the corresponding aldehydes reduced with $LiAlH_4$. The compounds 8 and 9 have the same ratios of isomers E/Z as the dithioacetal precursor 4. However the mixture of (E+Z)-dithioacetals 5 affords only the (E)-aldehyde 10 and then the (E)-alcohol 11 [15]. The pure dithioacetals 6 and 7 give the (E)-compounds 12 [16], 13, 14 and (-)(E)-lanceol 15 [17].

Table II. Conversion of dithioacetals to aldehydes and alcohols.

Dithioacetal	Aldehyde [9] % yield (E/Z)	Alcohol [9] % yield (E/Z)
4	 8 61% (6/4)	 9 70% (6/4)
5	 10 67%	 11 72%
6	 12 66%	 13 76%
7	 14 73%	 15 78%

We are currently investigating the ability of the isoprene compounds (3a,b) to undergo conjugate additions with other various organometallic reagents.

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