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BIS(DIMETHYLALUMINUM) 1,3-PROPANEDITHIOLATE--A USEFUL REAGENT IN THE CONVERSION OF ESTERS TO UNSATURATED ALDEHYDES AND KETONES

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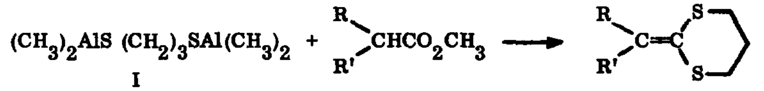
Previously it has been shown that esters and lactones can be protected from nucleophilic attack by conversion to the corresponding dithiolanes or ketene thioacetals. Bis(dimethylaluminum) 1,2-ethanedithiolate was found to be a superior reagent in effecting this transformation (equation 1).[2]

(eq. 1)



$(CH_3)_2AlS\ (CH_2)_3SAl(CH_3)_2$ + $\begin{matrix}R\\R'\end{matrix}\!>CHCO_2CH_3$ ⟶

I

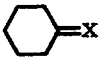
(eq. 2)

We would now like to report further studies of the application of the homologous reagent bis(dimethylaluminum) 1,3-propanedithiolate (I) for synthesis. This reagent, conveniently prepared by dropwise addition of 1,3-propanedithiol to a toluene--methylene chloride solution of trimethylaluminum at ice bath temperature, has been found to react with a variety of methyl esters to produce the corresponding ketene thioacetals in good yield (equation 2). In this way the following products were obtained in the yields indicated:

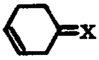
$CH_3CH{=}X$ (50%)

$CH_3(CH_2)_3CH{=}X$ (64%)

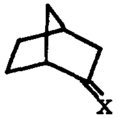
$CH_2{=}CH{-}CH{=}X$ (64%)



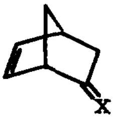
(60%)



(72%)

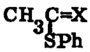


(69%)

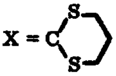


(85%)

$CH_3SCH_2CH{=}X$ (52%)

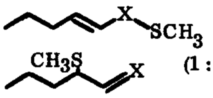
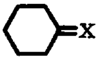
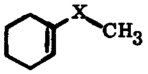
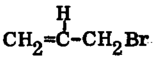
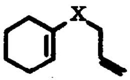
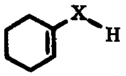
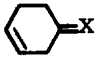
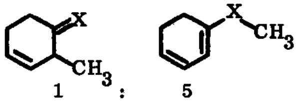
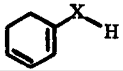
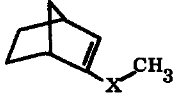
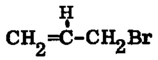
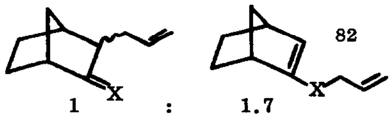
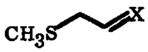
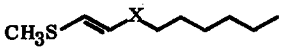


$CH_3\underset{SPh}{C}{=}X$ (65%)

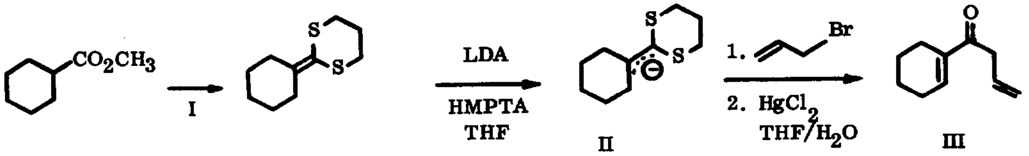


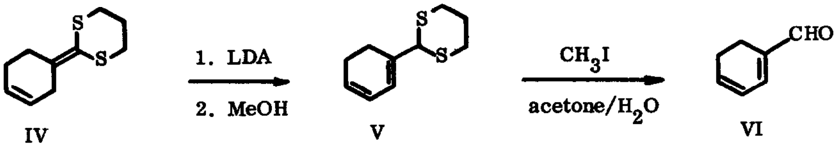
These ketene thioacetals are valuable synthetic intermediates, for they can be metallated in excellent yield with lithium diisopropylamide in the presence of HMPTA to provide the corresponding allyl anions.[4] Reactions of these metallated species with various electrophiles at -78°C were found to occur predominantly at the dithiane 2-position, thus serving as masked α,β-unsaturated acyl anion equivalents (Table 1).

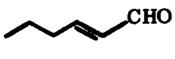
Table 1. Reaction of Metallated Ketene Thioacetals with Various Electrophiles[3] (X = )

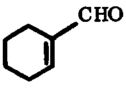
Ketene Thioacetal	Electrophile	Product	Yield (%)
	CH_3I		88
	$CH_3(CH_2)_5I$		81
	CH_3SSCH_3	 (1 : 1)	65
	MeOH		86
	CH_3I		74
	 $CH_2{=}\overset{H}{C}{-}CH_2Br$		86
	MeOH		93
	CH_3I	 1 : 5	78
	MeOH		73
	CH_3I		81
	 $CH_2{=}\overset{H}{C}{-}CH_2Br$	 1 : 1.7	82
	ϕCH_2Br		94
	$CH_3(CH_2)_5I$		93

A simple conversion of methyl ester → α,β-unsaturated ketone is thus at hand. Treatment of the metallated ketene thioacetal with an alkyl halide followed by hydrolysis of the dithiane[5] effects the desired transformation. This is exemplified by the synthesis of the dienone III.






VII


VIII

In addition, treatment of the metallated ketene thioacetal with methanol at -78°C results in protonation predominantly at the dithiane 2-position. Hydrolysis of this newly formed dithiane provides an excellent method for the conversion of an ester to an α,β-unsaturated aldehyde. The generality of this sequence was demonstrated by preparation from saturated esters of the unsaturated aldehydes VI, VII, and VIII. Since such aldehydes are readily oxidized to acids or esters,[6] the methodology described herein allows in a novel way the α,β-dehydrogenation of esters, e.g., $RCH_2CH_2COOCH_3 \rightarrow RCH{=}CHCOOCH_3$.[7]

The following procedures are illustrative:

Bis(dimethylaluminum) 1,3-Propanedithiolate (I). A solution of 61.2 ml of trimethylaluminum (1.63 M in toluene as obtained from Texas Alkyls, Inc.) was diluted with 110 ml of degassed methylene chloride, cooled to 0°C, and treated dropwise with 5.04 ml of dry 1,3-propanedithiol. After addition was completed (ca. 40 min), the cooling bath was removed and the mixture stirred at 25°C for 1 hr to give the reagent.

2-(3-Cyclohexenylidene)-1,3-dithiane (IV). To 88 ml of a toluene--methylene chloride solution of reagent I as prepared above was added a solution of 3.5 g of methyl 3-cyclohexenecarboxylate in 50 ml of methylene chloride in one portion. After two days at room temperature, the reaction mixture was concentrated by rotary evaporation, the residue was diluted with ether, and a few grams of moist sodium sulphate was added. Filtration through dry sodium sulphate and concentration of the ethereal filtrate yielded the partially crystalline ketene thioacetal which was further purified by chromatography on silica gel with 50% benzene--hexane as eluent to provide 3.58 g of pure IV; mp 42-43°.

2-(1, 3-Cyclohexadienyl)-1, 3-dithiane (V). To 1.1 mmol of lithium diisopropylamide in 1 ml of THF cooled to -78°C was added 3 mmol of HMPTA followed by the immediate addition of a solution of 1 mmol of IV in 1 ml of THF.[4] The reaction mixture was allowed to warm to -40°C over 90 min, and then held at -40°C for an additional 30 min. The dark red colored solution was cooled to -78°C and an excess of methanol was added. After several minutes, the now yellow-colored solution was warmed to room temperature, poured into water and extracted with benzene--pentane. The combined organic extracts were washed with water and dried over $MgSO_4$. Concentration by rotary evaporation left a yellow oil which was purified by preparative thick layer chromatography on silica gel with 50% benzene--pentane as eluent to yield 145 mg of V.

References

1. NIH Postdoctoral Fellow, 1974-present.
2. E. J. Corey and D. J. Beames, *J. Amer. Chem. Soc.*, **95**, 5829 (1973).
3. Satisfactory ir, nmr, and mass spectral data were obtained for all new compounds.
4. D. Seebach, *Synthesis*, 17 (1969); D. Seebach, M. Kolb, and B.-Th. Gröbel, *Tetrahedron Lett.*, 3171 (1974). HMPTA = hexamethylphosphoric triamide.
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7. This work was assisted financially by a grant from the National Science Foundation.