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THE REACTION OF 2,2-DIMETHYL-4-LITHIO-1,3-OXATHIANE 3,3-DIOXIDE. GENERAL SYNTHESIS OF γ-HYDROXYKETONES

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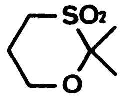
Reactions of 2,2-dimethyl-4-lithio-1,3-oxathiane 3,3-dioxide (2) with alkyl halides and carbonyl compounds proceed smoothly to give 4-substituted heterocycles. A general synthesis of γ-hydroxyketones from aldehydes utilizing 2 is described.

Synthetic potentials of sulfonyl carbanions have been well recognized and reviewed extensively.1,2) As a part of our program for developing the synthetic utility of 1,3-oxathianes,3-7) the reactivity of 4-lithio-derivative 2 derived from 2,2-dimethyl-1,3-oxathiane 3,3-dioxide (1)8) toward electrophiles was examined. Here we describe the reaction of a sulfonyl anion 2 with halides or carbonyl compounds giving substitution products or addition products, respectively, and the application to the synthesis of γ-hydroxy ketones.



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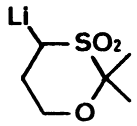
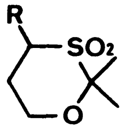


$\equiv$ $\bar{C}H_2CH_2CH_2OH$

2



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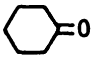
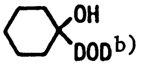
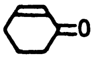
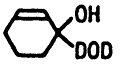
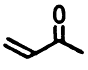
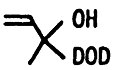
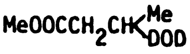
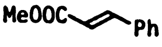
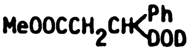
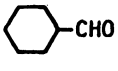
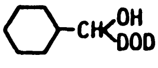
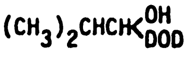
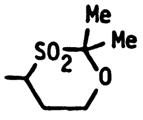
2,2-Dimethyl-1,3-oxathiane9) was easily oxidized with m-chloroperbenzoic acid to afford the corresponding dioxide 1 in 82% yield. The sulfonyl anion 2 generated at -78 °C with n-butyl lithium provides high yields of 4-substituted sulfones on treatment with electrophiles. The results are compiled in Table 1. Not surprisingly, 1,2-addition products were obtained exclusively, when α,β-unsaturated ketones were employed10) (runs 7,8 in Table 1). On the other hand, α,β-unsaturated esters gave 1,4- adducts mainly (runs 9, 10 in Table 1). Methyl cinnamate afforded the 1,4-adduct 8 and an α,β-unsaturated ketone 9, which was obviously derived from in situ desulfonylation of 14 formed by the 1,2-addition.

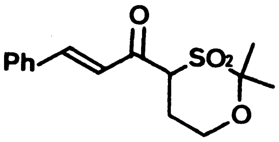
Addition of 2 to aldehydes yielded secondary alcohols 10 - 13. The crude ketones obtained by the Jones oxidation of alchols 10 - 13 were immediately treated with silica gel in hexane-ethyl acetate to afford γ-hydroxy ketones 15 - 18, respectively. Although γ-hydroxypropyl ketones are versatile building blocks not only for the synthesis of 1,4-dicarbonyl compounds but also for the synthesis of α-alkylated prolines,11) few general methods for the syntheses of this class of compounds in the literature.12,13) This process provides a new method for the preparation of γ-hydroxy ketones from the corresponding aldehydes with three carbon unit elongation, and also reveals that 2,2-dimethy-1,4-lithio-1,3-oxathiane 3,3-dioxide (2) can be used as a γ-hydroxypropyl anion equivalent.

Table 1. The Reaction of 2 with electrophiles

Run	Electrophile	Product	Yield/%
1	CD_3COOD	3(R=D)	79
2	CH_3I	3(R=CH_3)	83
3	C_2H_5I	3(R=C_2H_5)	80
4	TMSCl	3(R=TMS)	81
5	$PhCH_2Cl$	3(R=$PhCH_2$)	68
6		4 	87
7		5 	93a)
8		6 	88a)
9		7  $\mathrm{MeOOCCH_2CH}{<}^{\mathrm{Me}}_{\mathrm{DOD}}$	62a)
10		8  $\mathrm{MeOOCCH_2CH}{<}^{\mathrm{Ph}}_{\mathrm{DOD}}$	60a)
		9  $\mathrm{PhCH{=}CH}\overset{\mathrm{O}}{\mathrm{C}}\mathrm{(CH_2)_3OH}$	16
11		10 	80a)
12	$C_5H_{11}CHO$	11  $\mathrm{C_5H_{11}CH}{<}^{\mathrm{OH}}_{\mathrm{DOD}}$	86a)
13	$(CH_3)_2CHCHO$	12  $\mathrm{(CH_3)_2CHCH}{<}^{\mathrm{OH}}_{\mathrm{DOD}}$	74a)
14	PhCHO	13  $\mathrm{PhCH}{<}^{\mathrm{OH}}_{\mathrm{DOD}}$	68a)

a) A mixture of diastereomers.

b) DOD = 



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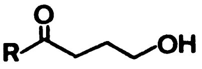

15, R = cyclohexyl 91%
16, R = C_5H_{11} 87%
17, R = $(CH_3)_2CH$ 51%
18, R = Ph 69%

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