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1,4-ADDITION OF LITHIATED DERIVATIVES FROM 1,3-DITHIANES TO α-UNSATURATED ALDEHYDES : A WAY TO δ-CARBONYL ALDEHYDES

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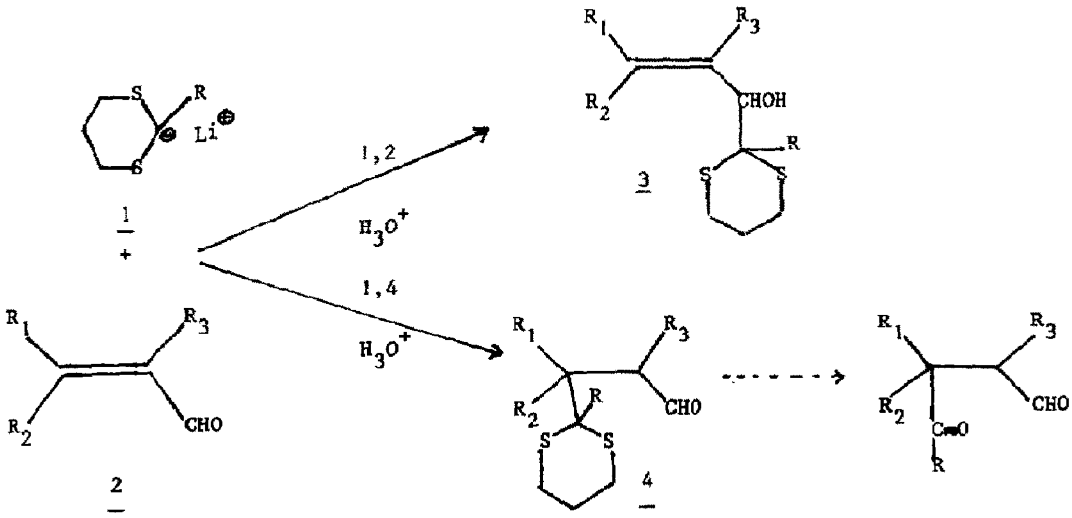
1,4-Addition of the lithiated derivatives of the 1,3-dithiane and 2-phenyl-1,3-dithiane on α-unsaturated aldehydes is performed in THF-HMPA ; this reaction could be an interesting way to δ-carbonyl aldehydes.

1,4-Addition of several types of nucleophilic reagents can be easily achieved on α-enones (1) ; however, with α-unsaturated aldehydes, excepted in a few cases (2), 1,2-addition is generally predominant (3).

Actually, from results obtained in our group (4) and recent reported data (1a,5) it turns out that the use of THF-HMPA as a reaction medium (at -70°C) yields practically the sole 1,4-addition in the case of α-enones. We have also shown that, under the same conditions, 1,4-addition of lithiated anions derivated from arylacetonitriles on α-unsaturated aldehydes can be performed (6). Moreover, 1,4-addition can be realized by using THF alone at higher temperature (4a,7).

In order to synthesize δ-carbonyl aldehydes, which are interesting precursors in organic synthesis, we examine in this paper the action of masked acyl anions the lithiated derivatives from 1,3-dithiane 1a and from 2-phenyl-1,3-dithiane 1b on selected unsaturated aldehydes 2a-d, in THF as well as in THF-HMPA (scheme).



Experimental results

1) In THF

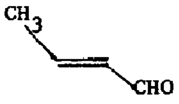
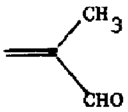
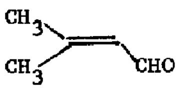
a) At -70°C, 1a prepared according to Seebach (8) reacts with the four aldehydes 2a-d leading to the allylic alcohols 3a-d (ex 1, 6, 10, 15). However 1b (8) gives with 2a-c the products 3 and 4 resulting both from 1,2 and 1,4-addition, (exp. 3, 8, 12) the 1,2-addition being only observed with 2d (exp. 17).

b) Reactions carried out at higher temperature (30 mn at -70°C then 2 h at 20°C) both with 1a and 1b (exp. 4, 13) do not show any change of the 1,2/1,4 ratio. It should be pointed out that these results are different from our previous observations concerning the reaction of arylacetonitriles and unsaturated aldehydes (6b) as well as those of Ostrowski and Kane with 1b and cyclohexenone (7b). The latter case can be explained by the higher stability of secondary alcoholates versus tertiary ones (9).

2) Using THF-HMPA (80-20), which is a medium strongly solvating lithium, at -70°C, we have shown that 1,4-addition is enhanced, particulary in the case of 1b (exp. 2, 5, 7, 9, 11, 14, 18). Furthermore 1,4-addition is kinetically controlled, the lithiated alcoholates being stable in this medium.

Reaction of 1 on unsaturated aldehydes 2

THF 30 mn at -70°C

aldehyde	Reagent	N° ex.	Ad.	1,4/1,2	yield % (1,2 + 1,4)
 2a	1a	1	------	0/100	70
	1a	2	HMPA	45/55	70
	1b	3	------	35/65	75
	1b	4 *	------	35/65	70
	1b	5	HMPA	95/5	80
 2b	1a	6	------	0/100	70
	1a	7	HMPA	25/75	75
	1b	8	------	15/85	75
	1b	9	HMPA	65/35	75
 2c	1a	10	------	0/100	70
	1a	11	HMPA	55/45	70
	1b	12	------	35/65	80
	1b	13 *	------	35/65	70
	1b	14	HMPA	95/5	80
 2d	1a	15	-----	0/100	80
	1a	16	HMPA	0/100	55
	1b	17	-----	0/100	75
	1b	18	HMPA	35/65	50

* The experiments 4 and 13 are then allowed to stand 2 h at 20°C. All the products are identified by I.R., N.M.R. and mass spectroscopy. Yields were calculated by ^{1}H NMR using internal standard p-CN-C_6H_4-CHO.

Discussion

1) In THF-HMPA, both substrate and reagent substitution effects can be interpretated by repulsive interactions between occupied orbitals of the nucleophile and electrophile ; these interactions, more important on C-2 than on C-4 of the substrate, disfavour 1,2 more than 1,4-addition (10). On the other hand, repulsive interactions on C-2 should be weaker for unsaturated aldehydes than for α-enones. Hence, the 1,2-addition should be favoured in the former case. This is what we actually observe with 1a. We have also shown with 1a that : 1,2- and 1,4-additions are practically of the same importance by introducing one methyl group on C-4 (exp. 2) whereas only 1,2-addition results from the introduction of two methyl groups on C-4 (exp. 16). In the first case the repulsive interactions are likely to be of the same order of magnitude on C-2 and C-4, whereas they are very important on C-4 in the second case.

The fact that 1,4-addition is always more important with 1b than with 1a can be interpreted by the structure of the reagent, the number of occupied molecular orbitals (10) and the type of hybridization of the carbon reactive site (10, 11).

2) In THF, we have noticed that 1,2-addition is favoured, due to a carbonyl-lithium interaction (12). However, 1,4-addition is again more important with 1b than with 1a, due to the reagent structure. It has recently been pointed out that steric hindrance either of the reagent or of the substrate favours 1,4-addition in THF (13).

In conclusion, since it is difficult in THF to carry out the 1,2 rather than 1,4-addition of lithio derivatives on unsaturated aldehydes, the addition of HMPA is necessary to obtain a synthetically useful 1,4-addition.

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