Tetrahedron Letters No. 1, pp 67 - 70.
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0040-4039/79/0101-0067$02.00/0

GENERATION AND SYNTHETIC USE OF 2-3-DIHYDROPYRANYL-3 LITHIUM

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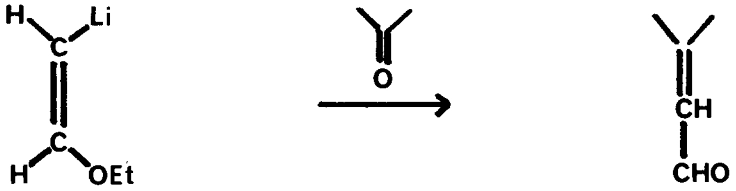
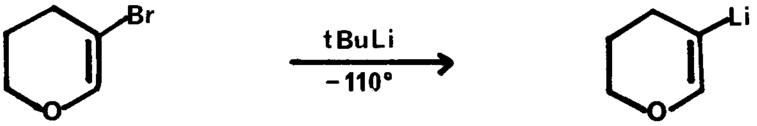
As a part of our investigations on the stability and use of carbanions β to electronegative groups, we have described the formation of vinyllithium 1[1], This useful equivalent of an acetaldehyde enolate converts aldehydes and ketones to α,β unsaturated aldehydes with the addition of two carbon atoms 1 ⟶ 2[1b,2,3] :



1

2

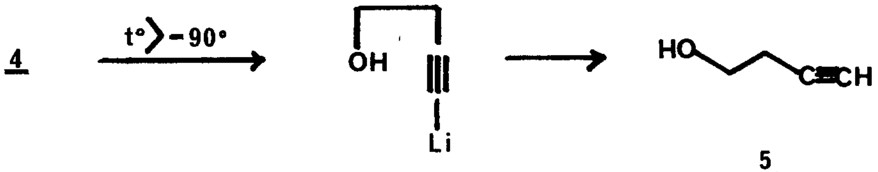
We describe here our first results concerning the generation and synthetic use of the lithium derivative 4 which is the operational equivalent of a functionally substituted aldehyde enolate. The formation of anion 4 from the readily available β-bromodihydropyrane 3 is indeed complete and almost quantitative by halogen-metal exchange with t-butyllithium at very low temperature :



3

4

The new synthon 4, which is the equivalent of a masked δ-hydroxy aldehyde enolate, 5-hydroxy pentanal, in this case, is less stable than 1. It undergoes β elimination more easily than 1 to give the lithium derivative of the acetylenic alcohol 5[4]. As expected[1a,3], the β elimination in 4 is favored by the trans relationship between the oxygen atom and the lithium, which is not present in 1.



4

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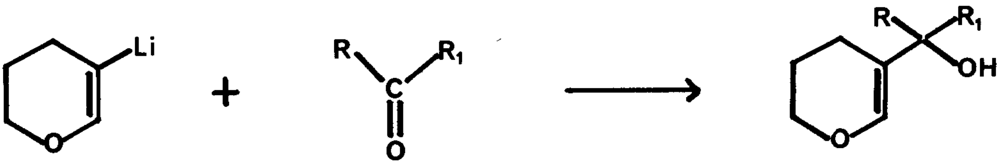
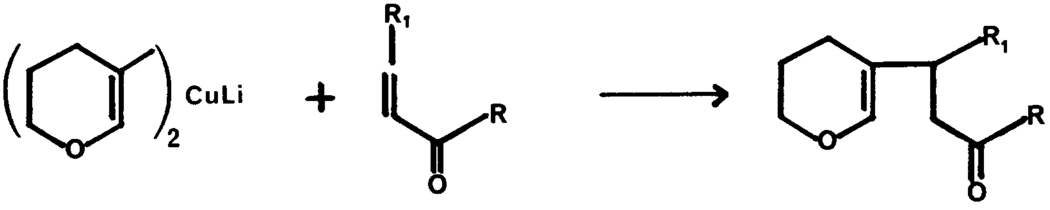
The vinyllithium 4 can nevertheless be used successfully at -110°C, to give good yields (70-85 %) of products, either in hydroxy-alkylation reactions with aldehydes and ketones, 4 ⟶ 6 :



4 5 6

or in conjugate addition with α,β-unsaturated carbonyl compounds in the presence of cuprous ions, 4 ⟶ 7 ⟶ 9 :

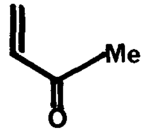
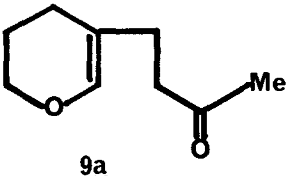
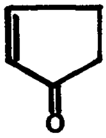
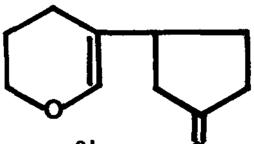
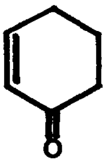
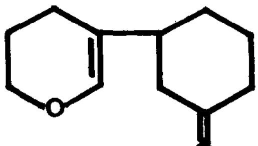


7 8 9

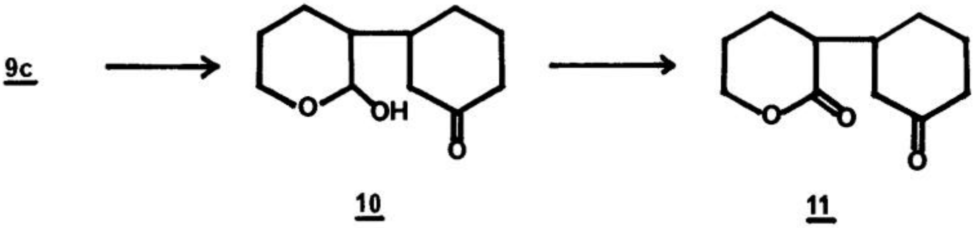
The hydroxyalkylation (4 ⟶ 6) with aldehydes and ketones leading to 6 is illustrated by the reaction with benzaldehyde (5 : R = C_6H_5, R_1 = H ; 75 % yield), heptanal (5 : R = C_6H_{13}, R_1 = H, 72 % yield), cyclohexanone (70 % yield) and cyclohexenone (70 % yield).

The example of cyclohexanone is given here as a typical experiment : to a solution of 1.03 g (6.4 mmol) of bromo-dihydropyran 4 in 20 ml of a mixture ether/THF : 2/1 at -110°C, was added dropwise (0.5 h), 4.2 mL (6.3 mmol) of 1.5 M t butyllithium (pentane). After stirring for 0.5 h at -110°C, 620 mg (6.3 mmol) of cyclohexanone was added over a period of 15 min. The mixture was stirred at -110°C -100°C for 2 h. before an aqueous solution of ammonia saturated with ammonium chloride was added. The mixture was extracted with ether and the isolated crude material was purified by column chromatography on alumina (eluant : ether/pentane : 1/1) to give 795 mg (70 % yield) of the pure adduct 6.

The conjugate addition of cuprate 7 was performed with methylvinyl ketone, cyclohexenone and cyclopentenone under the following conditions : to a solution of 3.6 g (22 mmol) of bromodihydropyran 4 in 50 mL of a mixture ether/dimethoxymethane/THF : 1/2/2, at -110°C was added dropwise (0.5 h), 15 mL (22.5 mmol) of 1.5 Mol. t butyllithium (pentane). A solution of a (11 mmol) of cuprous iodide and 4 mL (60 mmol) of dimethylsulfide in 15 mL of THF was added dropwise over 0.5 h. After stirring for 1 h. at -110°C, 3 mmol of the enone in 15 mL of THF were added over 20 min. The mixture was then warmed to -80°-70°C and stirred at this temperature for 3 h. After addition of an aqueous solution of ammonia saturated with ammonium chloride the mixture was extracted with ether. The crude solution was shaken with ammoniacal silver nitrate (to separate the acetylenic alcohol 5) and purified (after evaporation of the solvent) by column chromatography on alumina (ether/pentane : 1/1). Kugelrohr distillation then gave the desired adducts 9

KETONE 8	ADDUCT 9		
		Yield	bp
	 9a	80 %	bp 65° (0.05 mm)
	 9b	75 %	bp 70° (0.01 mm)
	 9c	90 %	bp 75° (0.01 mm)

We are now exploring the synthetic possibilities of the new vinyllithium derivative 4 not only as a useful equivalent of an δ hydroxy aldehyde enolate but also as an equivalent of a δ lactone enolate. The dihydropyrane moiety of the adducts 9 can be easily transformed indeed into a δ lactone ring *via* the oxidation of an intermediary hemiacetal of type 10 :



As typical experiment, the hemi-acetal 10 prepared with a quantitative yield by hydrolysis of 9c in acidic medium (5 % hydrochloric acid in acetone-water, 0° then,room temperature) leads after oxidation with Collin's reagent[5] to the lactone 11 [bp 140° (0.05 mm)] with a yield of 80 %.

References :

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with bibliography.
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5) The oxidation was performed according to : K. KONDO, E. SAITO, D. TUNEMOTO, Tetrahedron Letters, 2275 (1975).

(Received in UK 20 October 1978)