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FUNCTIONALIZED VINYLIC ORGANOLITHIUM COMPOUNDS, SYNTHETIC EQUIVALENT OF ω-LITHIO SORBALDEHYDE.

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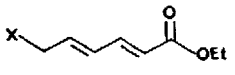
Abstract: Functional vinylic anions 2 and 3 react with aldehydes and ketones leading after hydrolysis to polyenic aldehydes 7. They have been used for the synthesis of navenone B 8.

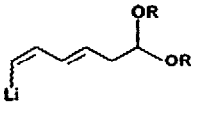
The structure of many natural compounds exhibits a long polyethylenic chain, such as, for instance, fecapentaene (1) and macrolides with antibiotic properties (amphotericine B (2), aureofacine (3)) or mycoticines A and B (4). Considerable interest has also been devoted to studies of the remarkable photophysical properties of several conjugated polyenes (5). In most cases, synthesis of such compounds is performed through a Wittig-like reaction involving for example, the condensation of an aldehyde with the polyenic ester of 1, followed by a two-step conversion of the ester to an aldehyde (reduction then partial reoxidation) on which the next condensation is then carried out (2c, 2d, 7).

Our interest in vinylic carbanions with a masked carbonyle function (8) led us to prepare compounds 2 and 3. Both allow a rapid and convenient conversion of aldehydes and ketones into polyenic aldehydes 7 .



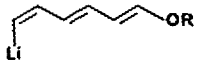
1

X = Ph_3P^+ (7)
$(EtO_2)PO$ (2c)
$(MeO)_2PO$ (2d)



2

a R = Et
b R = Me

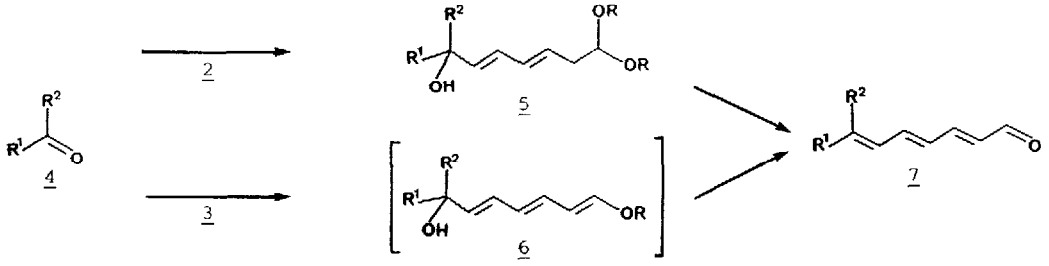


3

a R = Et

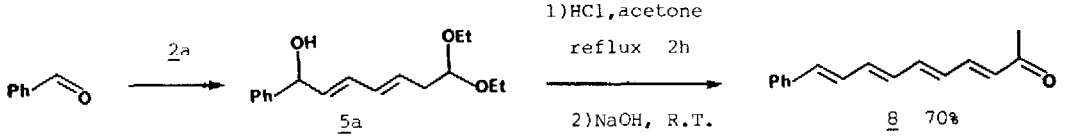
All condensations described hereafter are performed in ether at -20°C or 0°C. Reagent 2 leads to hydroxyacetal 5, which may be purified by silica gel chromatography and then hydrolysed to the aldehyde 7 in refluxing acetone containing a catalytic amount of bromhydric acid. When 3 is used, intermediate 6 is not isolated but directly hydrolysed to

aldehyde 7, using aqueous hydrochloric acid (1N) at room temperature (table 1).

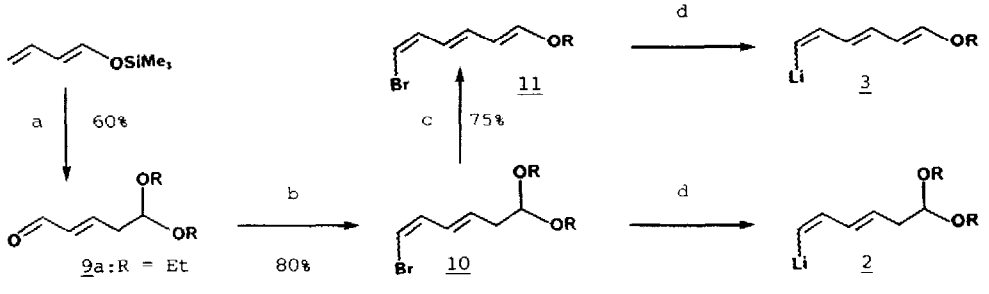


After purification by silicagel chromatography, aldehydes 7 exhibit the whole (7a,b,c,d,g) or major (7c,f) trans configuration. The standard hydrolysis of hydroxyacetal 5b does not give access to aldehyde 7b, which may however be obtained through the condensation of pyridyl-4 carboxaldehyde 4b with lithio enol ether 3a. Aldehydes 7a (9), 7c (10), 7f (11) have been prepared previously using longer methods, some of them leading to stereoisomer mixtures.

We also wish to describe a two-step synthesis, starting from benzaldehyde, of navenone B 8, an alarm pheromone of the mollusc Navanax Inermix (12) found on the Californian coast. Hydrolysis of hydroxyacetaldehyde 5a, was performed using aqueous hydrochloric acid in acetone; soda addition to the medium allows the condensation of acetone enolate on aldehyde 7a formed in situ thus giving the Navenone B 8.



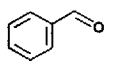
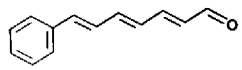
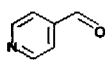
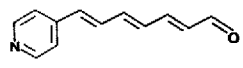
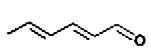
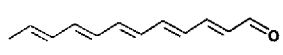
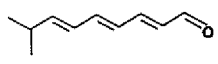
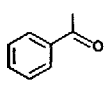
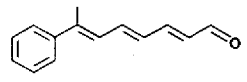
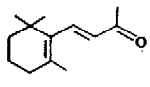
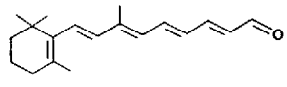
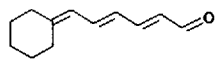
Bromides 10 and 11, precursors of 2 and 3, have been prepared according to the following scheme:



a) $HC(OR)_3$, $ZnCl_2$ - Et_2O, CH_2Cl_2; b) $Ph_3P^+CH_2Br,Br^-$, tBuOK, THF
c)$ISiMe_3$/HMDS, CCl_4, TA 48H; d) tBuLi Et_2O -70°C.

Aldehyde 9 is obtained by condensation of methyl or ethyl orthoformate with trimethylsiloxybutadiene (13) and is then reacted with triphenylbromomethylene phosphorane (14); the bromoacetal 10 (Z/E : 72/28) thus obtained is converted, through the Miller - Mc Kean reaction (15), to the bromo enol ether 11. While bromoacetal 10 may be distilled, the more labile 11 has been used without any further purification.

Table 1: Condensation of carbonyl compounds 4 on 2 or 3 leading to aldehydes 7.

Carbonyle compound 4	Reagent	Conditions[a]	yld % 4→5	yld % 5→7	Aldehyde 7	yld %[b] 4→7
 4a	2a	A	89	85		76[c]
	3a	B				60
 4b	2a	A	68	---		---
	3a	B				42
 4c	2b	A	81	97		79[c]
 4d	2a	A	78	80		62[c]
	3a	B				70
 4e	2a	A	72	94		68[c]
	3a	B				81
 4f	2a	B	43	91		39[c]
 4g	2a	B	70	70		49[c]

a) A:2h,-20°C; B:2h,0°C b) after flash chromatography c) overall yield for two reactions.

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16) Experimental: 1) starting from 2: 3,6 ml tBuLi 1,6M in pentane (1,8 eq) are added under argon and at -70°C to 0.53g (2 mmoles) of bromoacetal 10a in solution in 10 ml anhydrous ether. After 2h at 0°C or -20°C (table 1), 4ml of Na_2CO_3 (5%) is added at 0°C, the hydroxyacetal 5 is extracted with ether and purified by flash chromatography. Hydroxyacetal 5 (1,2 mmoles) is refluxed 5 to 30 mn (TLC monitored) in a solution of 36 ml acetone, 0,2 ml water and 5 µl HBr 47%. The mixture is neutralised (Na_2CO_3), the aldehyde 7 is extracted with ether and flash chromatographed.

2) starting from 3: the halogen-metal exchange and the condensation are carried out as described above. Hydrolysis is performed at -50°C, adding 11 ml of HCl (1N). After two to three hours stirring at room temperature (TLC monitored) the medium is extracted with ether and silica gel chromatographed.

17) Structure and stereochemistry of compounds 5 and 7 have been determined on a 400 MHz Bruker AM NMR spectrometer. The proportion for hydroxyacetals 5 isomers is identical to that measured for bromoacetal 10.

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