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Polyunsaturated aldehydes by direct polyvinylogation of carbonyl compounds using functionalized phosphonates.

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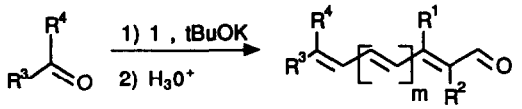
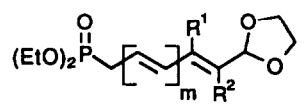
Summary: Carbonyl compounds are converted into polyethylenic aldehydes in a one pot reaction with the anions of phosphonates 1, followed by a mild acidic hydrolysis.

The polyvinylogation of carbonyl compounds is an important synthetic reaction, the newly formed polyethylenic carbonyl compound bearing or not substituents on the double bond. In this note we show that this change can be effected quite simply, using phosphonates 1 bearing a protected aldehyde group.



	1a	1b	1c	1d	1e
m	0	0	0	1	1
R^1	H	CH_3	H	H	CH_3
R^2	H	H	CH_3	H	H

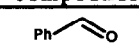
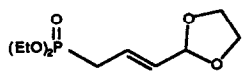
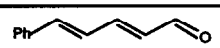
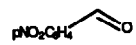
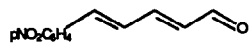
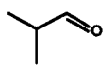
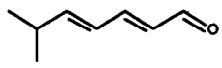
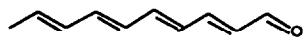
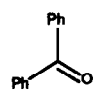
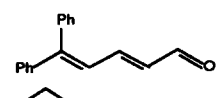
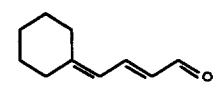
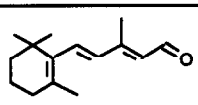
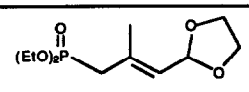
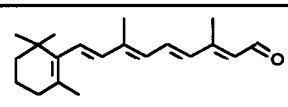
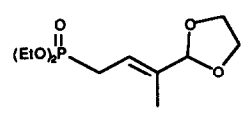
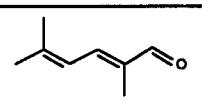
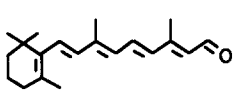
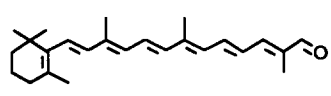
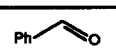
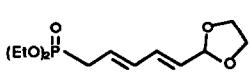
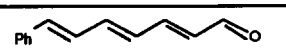
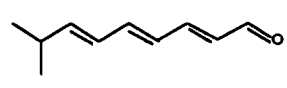
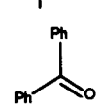
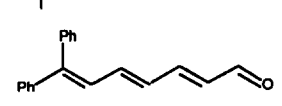
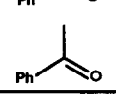
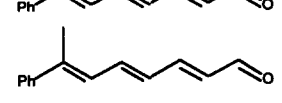
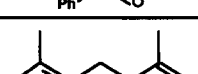
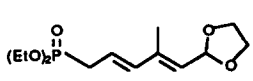
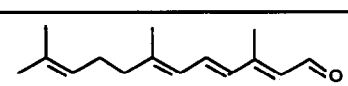
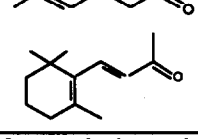
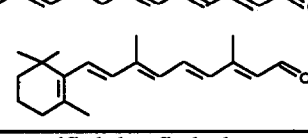


1

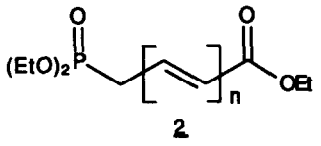
Recent results of the literature show that, to introduce a long polyolefinic chain, multistep processes are used. The most useful reagents are the triethyl phosphonoesters 2 (1-3). The condensation of their anions with a carbonyl compound leads to a conjugated ester with one, two or three supplementary double bonds, which are transformed in two steps into an aldehyde on which the precedent operations are repeated (1c,d; 2c,d; 3a,b).

Our interest in this area led us to study reagents allowing the introduction of several double bonds and leading directly to carbonyl compounds. We have already described organometallic vinylic reagents with a masked carbonyl such as 3 (Y=NR_2, $OSiMe_3$ or their synthetic equivalents) and we propose now for the polyvinylogation the use of anions of 1.

Table 1: Reaction of phosphonates 1 with carbonyl compounds:

Starting carbonyl compounds	Phosphonates 1 (a)	Products	yield % (b)
	 1a		86
			54
			78
			65
			45
			74
	 1b		66
	 1c		65
			51
	 1d		70
			65
			25
			90
	 1e		45(c)
			62

a) for synthetic equivalents see ref. 11. b) products purified by flash-chromatography. NMR and IR spectral data were fully compatible with the structures. c) isolated as dioxolane.



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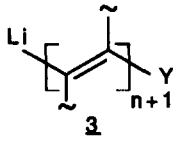
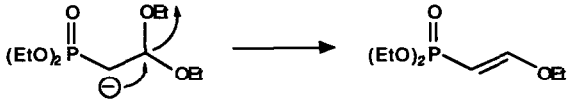


3

2a : n=0 (1) 2b : n=1 (2) 2c : n=2 (3)

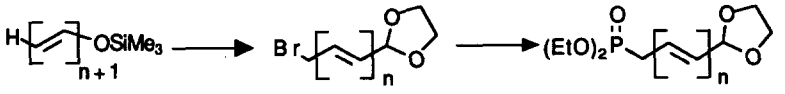
n=0 (4) n=1 (5)
n=2 (5a,6) n=3 (7)

Owing to the observation that an elimination occured when starting from the diethylacetal of diethoxyphosphonoacetaldehyde (8), we used dioxolane as protective group for phosphonate 1.



The anions of 1 were prepared in THF using potassium tert-butoxide as a base. Their condensations with carbonyl compounds led to a conjugated dioxolane which could be deprotected *in situ* in acidic medium. Results are reported in table 1. The all trans configuration was obtained exclusively (starting from 1a, 1b or 1d and aldehydes) or predominantly (in all other cases) (9). In the reaction conditions of 1a with benzaldehyde, the dimethyl acetal analogue of 1a did not lead to the corresponding polyethylenic aldehyde.

Phosphonates 1 are prepared by condensation of the corresponding ω-bromodioxolanes with triethyl phosphite in refluxing toluene. Bromodioxolanes 4a and 4d were obtained in one or two steps by bromination of trimethylsilyl enol ethers of crotonaldehyde or sorbaldehyde with bromine or NBS followed by acetalization.



n=1 4a 54%
n=2 4d 52%

1a 65 %
1d 59%

The preparation of the other phosphonates (9) will be reported elsewhere. We are grateful to Rhône-Poulenc for financial support and scolarship to one of us (J.G.).

References and notes:

1) Synthesis and use of 2a :

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7) L. Duhamel, J. E. Ancel, J. Chem. Research, in press.

8) W. Nagata and Y. Hayase, J. Chem. Soc. (C), 1969, 460.

9) a) J. Guillemont, Ph. D. Thesis Rouen 1989 and patents Rhône Poulenc Santé Patent, SC 89. 15869, (12.01.89); SC 89. 15870, (12.01.89); b) Y. Le Gallic, results to be published

10) tBuOK (0.240 g, 1.05 eq.) is added under argon at -70°C to a solution of 1 (2mmol) in 10 ml of anhydrous THF. After 90 minutes, the carbonyl compound (0.8 eq.) in 1 ml of THF was added to the coulored solution. The mixture is warmed to O°C. After about 2 hours (TLC), HCl 3M (7 ml) was added at -50°C, then the mixture was extracted with ether and chromatographed on silicagel.

11) Synthetic equivalents of 1a :
a) G. Wittig and H. D. Frommeld, Chem. Ber., 1964, 97, 3548; b) E. Vedejs, D. M. Gapinski and S. M. Mc Elvain, Tetrahedron Lett., 1981, 22 , 4913; c) M. J. Berenguer, J. Castells, R. M. Galard and M. Moreno-Manas, Tetrahedron Lett., 1971, 495 ; d) Y. Z. Huang, L. Shi, J. Yang and J. Zhang, Tetrahedron Lett., 1987, 28, 2159; e) T. Rein, B. Akermark and P. Helquist, Acta Chem. Scand., 1988, B 42, 569; f) R. H. Wollenberg, Tetrahedron Lett., 1978, 19, 717; g) (5b).
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Synthetic equivalents of 1d : (6b).
Synthetic equivalents of 1e : (6a), (9a).

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