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A NOVEL ROUTE TO SUBSTITUTED PHOSPHONATES VIA CONJUGATE ADDITION OF ORGANOMETALLICS TO 1-(FUNCTIONALLY)SUBSTITUTED ALKENE PHOSPHONATES

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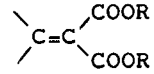
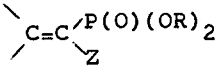
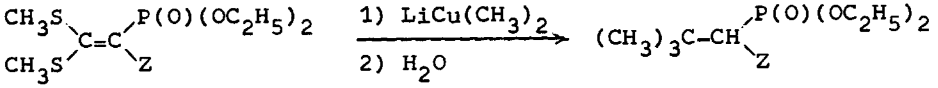
Summary : Organometallics readily add to the double bond of 1-(functionally) substituted alkene phosphonates to give highly substituted phosphonates.

Whereas the conjugate addition of organometallics to alkylidene malonic esters 1 is a well known reaction (1-3), it appears from the literature that such a conjugate addition has not been described with 1-(functionally) substituted alkene phosphonates 2 (Z= CN, COOR', CO-CH_3).

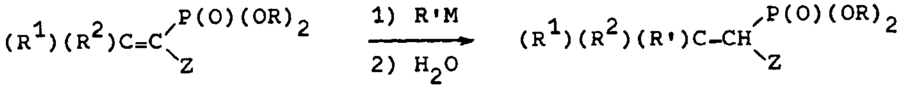
1

$>C=C(COOR)_2$


$>C=C(P(O)(OR)_2)(Z)$
2

During the course of a study on the reactivity of activated double bonds towards organometallics, we therefore decided to consider the case of type 2 ethylenic compounds. A recent publication (4) dealing with the formation of 4 from 3 and lithium dimethylcuprate, prompts us to report the first results we have obtained so far.

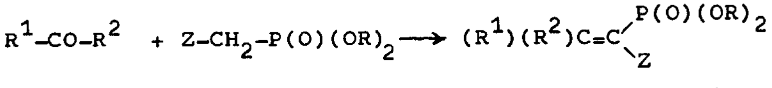
3

$$(CH_3S)_2C=C(P(O)(OC_2H_5)_2)(Z) \xrightarrow[2)\ H_2O]{1)\ LiCu(CH_3)_2} (CH_3)_3C-CH(P(O)(OC_2H_5)_2)(Z)$$
4

The reaction of saturated and allylic lithium organocuprates, methylmagnesium iodide and allylzinc bromide with the 1-(functionally) substituted alkene phosphonates 5 gives with a good yield the phosphonates 6 arising from a conjugate addition (Table)(5).

5

$$(R^1)(R^2)C=C(P(O)(OR)_2)(Z) \xrightarrow[2)\ H_2O]{1)\ R'M} (R^1)(R^2)(R')C-CH(P(O)(OR)_2)(Z)$$
6

This reaction is an easy way to substituted phosphonates which cannot be prepared easily by using the Michaelis-Arbuzov rearrangement (6).

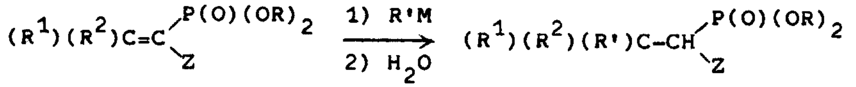
The starting alkene phosphonates were prepared by using the following reaction (7-10) :


$$R^1-CO-R^2 + Z-CH_2-P(O)(OR)_2 \longrightarrow (R^1)(R^2)C=C(P(O)(OR)_2)(Z)$$

Two of the phosphonates 6 we have obtained have been used in a Wittig-Horner reaction. Thus, the phosphonate 6b, reacted with sodium hydride in tetrahydrofuran and then with benzaldehyde, gave the 2-substituted cinnamonitrile 7 (Yield : 50%).

$$C_6H_5-CH=C\left[C(CH_3)_2-nC_4H_9\right]-CN \qquad \underline{7}$$

Table

5  6

$$(R^1)(R^2)C{=}C\begin{smallmatrix}\diagup P(O)(OR)_2\\ \diagdown Z\end{smallmatrix} \xrightarrow[2)\ H_2O]{1)\ R'M} (R^1)(R^2)(R')C{-}CH\begin{smallmatrix}\diagup P(O)(OR)_2\\ \diagdown Z\end{smallmatrix}$$

Entry	R'M	R^1	R^2	R	Z	temp.°C	Yield %
a	$LiCu(CH_3)_2$*	C_6H_5	H	CH_3	CN	-30 to 20	90
b	$LiCu(nC_4H_9)_2$**	CH_3	CH_3	C_2H_5	CN	-30 to 20	80
c	$LiCu(nC_4H_9)_2$**	C_2H_5	H	C_2H_5	CN	-30 to 20	60
d	$LiCu(CH_3)_2$*	C_6H_5	H	C_2H_5	$COOC_2H_5$	-30 to 20	90
e	CH_3MgI*	C_6H_5	H	C_2H_5	$COOC_2H_5$	20	89
f	$BrZnCH_2{-}CH{=}CH_2$***	C_6H_5	H	C_2H_5	$COOC_2H_5$	20	73
g	$LiCu(CH_3)_2$*	C_6H_5	H	C_2H_5	$CO{-}CH_3$	-30 to 20	82
h	$LiCu(CH_2{-}CH{=}CH_2)_2$****	C_6H_5	H	C_2H_5	$CO{-}CH_3$	-30 to 20	75

Solvent: *ether; **ether/hexane; ***tetrahydrofuran; ****ether/tetrahydrofuran.

The reaction of the phosphonate 6de with an excess of formaldehyde (30 % aqueous solution) in the presence of a saturated solution of potassium carbonate, according to (11) but using more drastic conditions (72h/90°C), gave the 2-substituted acrylic ester 8 (Yield : 45 %).

$$CH_2{=}C\left[CH(CH_3){-}C_6H_5\right]{-}COOC_2H_5 \qquad \underline{8}$$

Generalisation of this work is now under current investigation .

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(5) All compounds obtained in this work showed satisfactory analytical data; yields, based on 5 (0.03 mole) are not optimized and refer to distillated products. 1H NMR(CCl_4): 6a(250MHz):1.5-1.55(2d,3H,CH_3-C,J7Hz);3.35-3.55 (m,1H,C_6H_5-CH);3.6-3.9(2dd,1H,CH-CN,J(H-H)5Hz,J(H-P)22Hz);3.5-3.85(4d,6H, OCH_3,J(H-P)10.7Hz). 6b(60MHz):0.9(t,3H,CH_3-C-C,J6Hz);1.2(s,6H,C(CH_3)$_2$); 1.1-1.7(m,12H,(CH_2)$_3$/O-C-CH_3);2.95(d,1H,CH-CN,J24Hz);3.9-4.5(m,4H,OCH_2). 6c(60MHz):0.8-1.1(m,6H,CH_3-C-C);1.1-1.8(m,15H,CH_2-CH-(CH_2)$_3$/O-C-CH_3);3.05 (dd,1H,CH-CN,J(H-H)4Hz,J(H-P)25Hz);3.9-4.5(m,4H,OCH_2). 6d/e(500MHz):0.9-1.4 (6t,6H,CH_3-CH_2,J7Hz);1.47/1.33(2d,3H,CH_3-CH,J7Hz);3.20-3.26(2dd,1H(CH-P(O), J(H-P)20Hz);3.4-3.5(m,1H,CH-CH_3);3.8-4.3(2m,6H,OCH_2). 6f(250MHz):0.88/1.28 (2t,CO-O-C-CH_3,J6.5Hz);1.02/1.07/1.31/1.32(4dt,P-O-C-CH_3,J(H-H)6.5Hz,J (HC-C-O-P)0.5Hz);4.76-5.7(m,3H,CH=CH_2);7.15-7.40(m,5H,C_6H_5). 6g(60MHz): 0.9-1.6(m,9H,CH_3-CH/CH_3-CH_2);1.85/2.25(2s,3H,CH_3-CO);3.3-4.4(m,6H,OCH_2/CH-CH) ;7-7.4(m,5H,C_6H_5). 6h(60MHz):0.9-1.5(m,6H,O-C-CH_3);1.85/2.30(2s,3H,CH_3-CO); 2.2-2.6(m,2H,CH_2-C=);3.3-4.5(m,6H,OCH_2/CH-CH);4.6-5.8(m,3H,CH=CH_2);7.1-7.5 (m,5H,C_6H_5).

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