Tetrahedron Letters, Vol.32, No.34, pp 4353-4354, 1991 Printed in Great Britain

A NOVEL ONE-POT SYNTHESIS OF β -hydroxy 1,3-dienes via allylic ylide-anion

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Summary: A novel one-pot synthesis of β -hydroxy 1,3-dienes via allylic ylideanion with high stereoselectivity is described.

A lot of natural products with biological activity, such as leukotrienes and insect pheromones, bearing the β -hydroxy 1,3-dienes moiety has attracted much attention,¹ and new mothods leading to the formation of the title compounds may be desirable. Ylide-anion with higher reactivity could be generated by deprotonation of the corresponding ylide using sec-butyl- or tert-butyllithium as a base and was applicable with unreactive substrates such as epoxides or hindered ketones.² However, its use as synthetic reagents seems to remain limited.³ and allylic ylide-anion and its synthetic utility have not been reported previously. We now wish to report a novel one-pot synthesis of β -hydroxy 1,3-dienes via allylic ylide-anion affording E,E-isomer exclusively on the basis of NMR spectra.

The reaction sequence is shown as follows:



Allylidenetriphenylphosphorane (2), generated from the corresponding phosphonium salt (1) and n-butyllithium, could be deprotonated by n-butyllithium-TMEDA to give allylic ylide-anion 3, which reacted with the first molecule of carbonyl compounds regiospecifically at 3-position and the second one at 1position stereoselectively, after hydrolysis, affording the title compounds (4). The net result is the formation of one carbon-carbon single bond and one carbon-carbon double bond in this one-pot reaction.

Table l.	\mathbf{The}	preparation	of	β-hydroxy	1,3-dienes
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4	R ¹	R ²	Time(h) ^{a)}	Yield(%) ^{b)}	m.p.(^o C)
a	4-C1C6 ^H 4	Н	2	58	48-50
b	4-BrC ₆ H ₄	н	2	55	65-67
с	C ₆ H ₅	Н	2	53	132/0.5 ^{c)}
d	2-C1C6H4	н	2	46	36-37
е	2.4-Cl ₂ C ₆ H ₃	н	2	48	28-30
f	n-C6 ^H 13	н	8	52	112/0.5 ^{c)}
g	-(CH ₂) ₅ -		14	39	110/2 ^{c)}

a) Reaction time of 3 with R^1R^2CO ; b) Isolated vields;

c) B.p.(^OC/mm).

In a general procedure n-butyllithium (2 mmol) was added dropwise to a stirred suspension of allyltriphenylphosphonium bromide (2 mmol) and absolute THF (10 ml) at 0 $^{
m O}$ C under nitrogen. The reaction mixture was stirred for 1 h at 0 $^{\circ}$ C to give allylic ylide 2, cooled to -78 $^{\circ}$ C, TMEDA (1 ml) and n-butyllithium (2 mmol) was added dropwise. After stirring for 2 h at -78 to -40 $^{\rm O}$ C, the carbonyl compound (4 mmol) was added. The mixture was allowed to warm to 20 ^OC, stirred for several hours (see Table 1), hydrolyzed with 2N HCl (2 drops), diluted with diethyl ether (20 ml), washed with water to neutral and dried with Na₂SO₄. Evaporation of the solvent gave a residue which was purified by column chromatography on silica gel eluting with petroleum ether (bp 60-90 ^OC)/ethyl acetate (9:1) to afford product 4.

The results are shown in Table 1. All products were characterized by IR, NMR, MS and HRMS spectroscopy.

This one-pot synthesis of β -hydroxy 1,3-dienes starting from commercially available substances is quite convenient and should be useful in the synthesis of biologically active compounds.

Acknowledgement The authors thank the National Natural Science Foundation of China and Academia Sinica for financial support.

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(Received in Japan 12 February 1991)