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CARBONYL ADDITION REACTION BY MEANS OF β-SILYLPHOSPHOROUS YLIDE. ANTI-DIASTEREOSELECTIVE VINYLATION OF α-ALKOXY ALDEHYDES.

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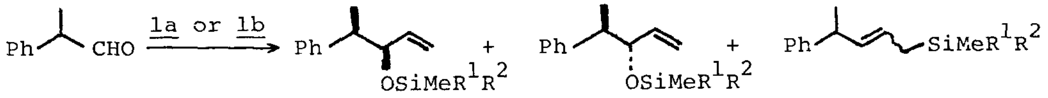
Abstract: β-Silylphosphorous ylide 1c reacts with α-alkoxy aldehydes 2 to give exclusively vinylation product 3, with high anti-diastereoselectivity.

In carbonyl addition reaction of α-alkoxy aldehydes,[1] syn-diol derivatives are usually obtained by the reagent capable of chelating to the substrate,[2] whereas the methods which give anti-diol compound selectively are limited.[3] In this paper we report a new method for anti-diastereoselective vinylation of α-alkoxy aldehydes by means of β-silylphosphorous ylide.

We have recently described that the reaction of β-silylphosphorous ylide 1a with 2-phenypropanal gave a Cram-diastereoselective vinylation product via silyl group migration and concomitant elimination of tris(4-methoxyphenyl)-phosphine, accompanied by a minor amount of allylsilane derivative, the Wittig olefination product.[4] The formation of the allylsilane was throughly supressed by the use of 1b, in which a methyl group on silicon atom was substituted by an electron negative isopropoxy group (Scheme 1).[5] Now the feasibility of this method for the diastereoselective vinylation of α-hydroxy aldehyde derivatives 2 is investigated (Scheme 2). We first checked the

Scheme 1

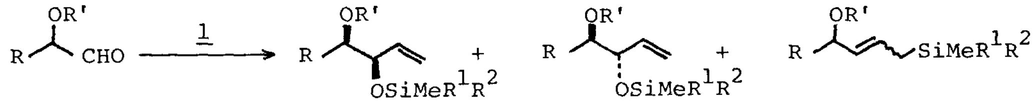


1a;	15	:	1.0	:	1.6
1b;	15	:	1.0	:	0

$(4\text{-MeOPh})_3P{=}CHCH_2SiMeR^1R^2$

1a : $R^1 = R^2 = Me$
1b : $R^1 = Me,\ R^2 = OPr^i$
1c : $R^1 = R^2 = Ph$

Scheme 2

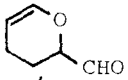
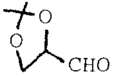


2 syn-3 anti-3 4

reaction selectivity (vinylation product 3 versus allylsilane 4) in the reaction of β-silylphosphorous ylides 1 with 2-benzyloxypropanal (2f) in tetrahydrofuran (THF) at -78°, and found that 1b and 1c gave exclusively vinylation product 3f, whereas 1a gave a 10 : 1 mixture of 3f and 4f. The substitution of electron negative group(s) on silicon atom is essential for the exclusive formation of the vinylation product 3.

Then diastereoselectivities of the vinylation reactions were examined using the β-silylphosphorous ylide 1c and the results are summarized in Table 1. The reaction was carried out by the addition of aldehydes to 1.2 eq of

Table 1. anti-Diastereoselective vinylation of α-alkoxy aldehydes 2 with (4-MeOPh)$_3$P=CHCH$_2$SiPh$_2$Me (1c).[a]

entry	aldehyde 2			ratio of 3[b]			yield[c] of 3 (%)	δ(CD$_3$Cl)[d]	
		R	R'		syn : anti			syn	anti
1	2a	PhCH$_2$CH$_2$	CH$_2$Ph	3a[e]	1 : 15	(2 : 1)	82	4.18	4.35
2	2b	PhCH$_2$CH$_2$	CH$_3$	3b	1 : 15[f]		82	4.10	4.32
3	2c	PhCH$_2$CH$_2$	COCH$_3$	3c[g]	1 : 5.6		64	3.97	4.11
4	2d	PhCH$_2$CH$_2$	SiPh$_2$Bu^t	3d[g]	1 : 1.1		84		
5	2e	PhCH$_2$CH$_2$	SiMe$_2$Bu^t	3e[g]	1.6 : 1	(1 : 4)	84		
6	2f	CH$_3$	CH$_2$Ph	3f	1 : 20	(2.9 : 1)	80	3.96	4.25
7	2g	cyclohexyl	CH$_2$Ph	3g	1 : 31[f]	(3.4 : 1)[f]	70	4.20	4.29
8	2h	Ph	CH$_3$	3h	1 : 8.3	(11 : 1)	74	4.19	4.25
9	2i			3i	1 : 39	(1.9 : 1)	90	4.10	4.27
10	2j			3j	1 : 23	(1 : 1.3)	70	4.05	4.31

(a) All the reaction were carried out on 1 mmol scale. Unless otherwise specified, syn/anti ratio was determined on the desilylated alcohol by capillary GC (CBP20, 25 M), and the assignment of the diastereomers was based on the empirical rule with the chemical shift of allylic proton δ(syn)<δ(anti), and/or of the coupling constant of vicinal glycol protons J(syn)>J(anti).

(b) The ratios in parentheses denote the selectivity observed in the reactions with vinylmagnesium bromide in THF at 0°.

(c) All the yields correspond to chromatographically purified products.

(d) Chemical shift of allylic proton of the desilylated alcohol.

(e) The assignment was established by conversion of the major isomer to the dioxane derivative 5. (See ref. 17)

(f) This ratio was determined on the corresponding desilylated alcohol by 400 MHz ^{1}H-NMR.

(g) The assignment was based on the chemical correlation with the corresponding diol derived from 3a.

light orange THF solution of silyl ylide 1c, which had been prepared from 2-methyldiphenylsilylethyltris(4-methoxyphenyl)phosphonium iodide[6] and n-butyllithium at 0°, 30 min, and then room temperature, 30 min. The yields of vinylation products 3 are usually over 70 %, and the formation of allylsilanes 4 was not detected. The products 3 were purified by silica gel column chromatography and the syn/anti ratios were determined by 400 MHz ^{1}H-NMR and/or capillary GC. The effect of the nature of the hydroxyl substituents in 2 on the diastereomeric selectivity is exemplified in the case of 2-hydroxy-4-phenylbutanal. In the reaction of benzyloxy aldehyde 2a and methoxy aldehyde 2b with 1c,[7] good anti-diastereoselectivities are observed (entries 1 and 2). In contrast corresponding acetoxy aldehyde 2c, and silyloxy aldehydes 2d and 2e showed poor or none of the selectivity (entries 3-5). For comparison vinylation reactions by means of vinylmagnesium bromide in THF were also performed with 2a and 2e , and the selectivity of syn to anti in these reactions was 2 : 1 and 1 : 4 respectively, which is explained by the chelation transition state model in the former,[8] and the non-chelation transition state model in the latter, since the basicity of the hydroxyl oxygen is lowered in the silyl ether 2e.[9] The anti-diastereoselectivity observed in the reaction of β-silyl ylide 1c with α-alkoxy aldehydes should be ascribed to non-chelation transition state, Felkin-Anh model,[10] or more likely dipole model.[11] The reversed diastereoselectivity in the reaction of silyloxy aldehyde 2e might be rationalized by the intramolecular chelation of silicon atom to carbonyl oxygen.[12] The reactions of β-silyl ylide 1c with the other α-alkoxy aldehydes 2f-2i (entries 6-9) and 2,3-O-isopropylideneglyceraldehyde (2j)[13] were found to show good to excellent anti-diastereoselectivity. The products in these reactions could be important intermediates for the syntheses of natural products. For instance 3j and the dihydro derivative of anti-3i are known to be key intermediates for the synthesis of pentoses[14] and endo-brevicomin,[15] respectively.

The vicinal diol derivatives obtainable in the reaction described above are differently protected, and their vinyl group could be used for further functionalization[16] and carbon chain extension. These advantages would be valuable for the synthesis of natural products under acyclic control. Application of our method in this line is now in progress.

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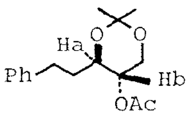
17. The conversion of *3a* to dioxane *5* in 6 steps: (1) 3N HCl, (2) Ac$_2$O/Py, (3) O$_3$, then Et$_3$N, (4) Zn(BH$_4$)$_2$, (5) H$_2$/Pd-C, (6) Me$_2$C(OMe)$_2$/CSA. In the ^{1}H-NMR of *5*, coupling constant J_{ab} is 9.0 Hz indicating H$_a$ and H$_b$ are *trans* diaxial.



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