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STEREOSPECIFIC SYNTHESIS OF (*E*)-ALKENYLPYRIDINES *VIA* α-SILYL CARBANION[1]

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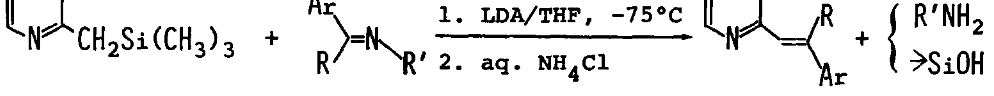
Summary: (E)-2-Alkenylpyridines were stereospecifically prepared from 2-(trimethylsilylmethyl)pyridine and the corresponding (E)-aldimines of anilines by an analogous reaction to the Peterson reaction.

In the previous paper, we prepared 2-alkenylpyridines from 2-(trimethylsilylmethyl)pyridine and carbonyl compounds.[2] By the method, a mixture of (*E*)- and (*Z*)-isomers was obtained, and similar observations have been reported by many workers.[3] Generally, there is no stereoselectivity in the direct Peterson reaction,[4∿6] because of the formation of mixed diastereomers, and it has not been controlled so effectively as the Wittig reaction.[5a] Aldimine reacts with alkyl α-haloacetates in the presence of zinc to form amines and/or β-lactams,[5b,7] and with 2-lithiomethylpyridine to give the corresponding 2-(2-pyridyl)ethylamine derivatives.[8] In the presence of potassium *t*-butoxide, 2-picoline and *N*-(2-pyridylmethylene)aniline gave (*E*)-bis(2-pyridyl)ethene in low yield (20 ∿ 30%).[9]

We now wish to report a stereospecific synthesis of (*E*)-alkenylpyridines (3) ∿ (6) from 2-(trimethylsilylmethyl)pyridine (1) and (*E*)-imines (2) in good yields (Eq. 1). In a typical run, twenty mmol of (1) was lithiated with LDA in THF at -75 °C, and the resultant solution was treated with a THF solution of imines (2a



(1) (2a ∿ 2g) (3) ∿ (6) (Eq. 1)

∿ 2g) at -75 °C to afford (*E*)-2-alkenylpyridines (3) ∿ (6). The result obtained is shown in Table. *N*-Benzylideneaniline (2a) gave (*E*)-2-styrylpyridine (3) in high yield (84% isolated), and the (*Z*)-isomer was not found. The product (3) was also obtained in high yield (84% HLC) in the reaction with *N*-benzylidene-*p*-chloroaniline (2b), but (3) was difficult to be isolated from the liberated *p*-chloroaniline by a recrystallization from ethanol. *N*-(2-Pyridylmethylene)aniline (2c) and *N*-cinnamylideneaniline (2d) gave (*E*)-bis(2-pyridyl)ethene (4) and 1-phenyl-4-(2-pyridyl)-1,3-butadiene (5) in moderate yields (54, 68% isolated), respectively. On the other hand, a ketimine (2e) was not so reactive as the aldimines. When (1) was treated with (2e) under the same condition, (*E*)-2-phenyl-1-(2-pyridyl)propene (6) was obtained in low yield (10.5% GC) together with the (*Z*)-isomer (1.5% GC yield), and the unreacted starting materials were recovered. This lower reactivity of (2e) may be due to a steric hindrance. The reaction with *N*-benzylidenealkylamines (2f,g) also gave unsatisfactory results (see Table).[10] This shows that the aldimines of anilines are more suitable for

Table Yields and Physical Properties of the Products (3) ∿ (6)

2	Ar	R	R'	Product	(*E*)-isomer^{a}		*E*/*Z* ratio	
					Yield (%)	Mp (°C)	This work (by GC)	Previous work^{b}
a	C_6H_5	H	C_6H_5	3	84 (86)	87 ∿ 89^{c}	100 : 0	25 : 75
b	C_6H_5	H	p-ClC_6H_4	3	32 (84)^{d}	88.3^{c}	100 : 0	25 : 75
c	2-Py^{e}	H	C_6H_5	4	54 (67)	118 ∿ 120^{f}	100 : 0	——
d	$C_6H_5CH{=}CH$	H	C_6H_5	5	68	120.7 ∿ 121^{g}		
e	C_6H_5	CH_3	C_6H_5	6	(10.5)^{h}	——	87.5 : 12.5	40 : 60
f	C_6H_5	H	CH_3	3	(10.2)^{i}	——	99.6 : 0.4	25 : 75
g	C_6H_5	H	t-C_4H_9	3	(0.5)	——		

a) Only the (*E*)-isomer was obtained in all cases examined except for (2e,f), and recrystallized from an indicated solvent and identified by a comparison of the spectral data or R_t value of GC with those of an authentic sample;[2] GC yield in parenthesis. *b)* Prepared from the corresponding carbonyl compound and determined by NMR.[2] *c)* From ether or ethanol (lit.[2] 88.5 ∿ 89.0 °C). *d)* HLC yield in parenthesis. *e)* 2-Py: 2-pyridyl. *f)* From ether (lit. 118 °C, E. Bayer and E. -G. Witte, *J. Coord. Chem.*, 7, 13(1977)). *g)* From petroleum ether (lit.[2] 120 ∿ 121.5 °C). *h)* 1.5% of the (*Z*)-isomer was found. *i)* A trace of the (*Z*)-isomer was found.

the preparation of 2-alkenylpyridines than those of aliphatic amines.

Of particular utility is the result that this reaction is highly stereospecific. In all cases of aldimines of anilines examined, more than 99.5% of the product was found to be the (*E*)-isomer by means of GC analysis.[11] The reaction is expected to proceed by a step-wise process like the Peterson reaction. That is, the first step is the formation of an intermediate β-silylamine (7) and the second step is the elimination of *N*-trimethylsilylanilide from (7). In the Table the ratio of the isomers (*E*)/(*Z*) obtained in this work was compared with the values obtained in the previous work,[2] in which the corresponding carbonyl compounds were employed as electrophiles. The high stereospecificity in this work may be caused by the facts that the configuration of the imine (2) is (*E*)-form and that the plane of the *N*-phenyl group is perpendicular to the plane of the carbon-nitrogen double bond. This geometrical structure of (2) makes the occupied *p*-orbitals of the *N*-phenyl group interact with the vacant *d*-orbital of silicon atom in the transition state of the first-step reaction,[12] and the *threo*-β-silylamine may exclusively be formed. This speculation is confirmed by the following facts; (a)an unsatisfactry result was obtained in the reaction with (2f) and (2g), (b)the reaction with (2a) gives exclusively (3) as a product together with the unreacted starting materials and the liberated aniline in the quenching experiment with water at -75 °C after 5 or 60 min reaction period,[11] that is, the intermediate (7) and 2-picoline formed by a destruction of (1) could not be observed, (c)anilines were quantitatively recovered in all cases examined,[13] (d) a reaction of 2-lithiomethylpyridine with (2a) did not give (3),[8] and (e)the trimethylsilyl group is easily transferred from carbon atom to nitrogen atom.[14] The fact (a) suggests the importance of the orbital interaction and the fact (b) suggests that the first-step reaction is slow and the second step is very fast. The second-step reaction may be a *syn*-elimination. If it proceeds by a mechanism analogous to E2, it will never give only the (*E*)-isomer.[15]

In a comparison with the Peterson reaction employing a carbonyl compound,[2,3] the present method has advantages of a higher stereospecificity and a higher yield, while it has regrettably a disadvantage of a lower conversion in the case of ketimines. Further investigation is now in progress.

Experimental procedure has been reported previously.[2] To the reaction mixture was added aq. saturated ammonium chloride instead of water at 0 °C after stirring for 1 h at -75 °C and then for 2 h at room temperature. The result obtained is shown in Table.

References and notes

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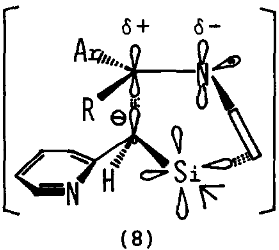
10. Most of the unreacted (2g) was recovered from the reaction mixture, while (2f) was completely destructed to produce a by-product. The structure was not identified.
11. The reaction mixture quenched with water after 5 (or 60) min reaction period gave 43% (or 50%) of (3), 0.2% of the (*z*)-isomer, 26% (or 17%) of the unreacted (2a), the unreacted (1) and the liberated aniline.
12. For example, the following formula (8).



(8)

13. In the reaction with (2b), 84% (by HLC) of *p*-chloroaniline was formed.
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