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NEW METHOD FOR THE PREPARATION OF POLYENALS FROM δ-ALKOXY-α,β-UNSATURATED ALDEHYDES

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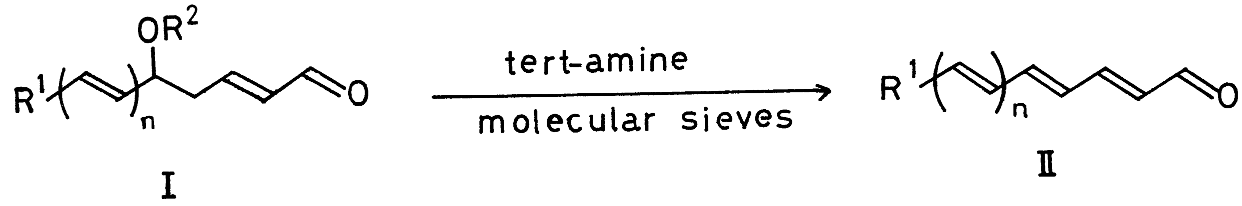
In the presence of tertiary amine and molecular sieves, δ-alkoxy-α,β-unsaturated aldehydes were easily converted into the corresponding polyenals, useful intermediates in carotenoid synthesis, in good yields under mild conditions.

It is generally known that β-alkoxy aldehydes are easily converted to α,β-unsaturated aldehydes through the elimination of the alkoxyl group under acidic conditions by employing acetic acid-sodium acetate,[1] dilute hydrochloric acid,[2] and so on.[3] However, the yields of the desired products are very low[4] when the elimination reaction of δ-alkoxy-α,β-unsaturated aldehydes are carried out according to the above mentioned procedures.

In this communication, we wish to report a new and practically useful method for the preparation of polyenals by the treatment of δ-alkoxy-α,β-unsaturated aldehydes with tertiary amine in the presence of molecular sieves 3A or 4A as shown in the following equation.



5-Methoxy-2,6-decadienal(Ia) was used to determine the optimum experimental condition. The conversion of 5-methoxy-2,6-decadienal(Ia) to 2,4,6-decatrienal (IIa)[5] was examined by using various tertiary amines such as pyridine, triethylamine, 1,8-bis(dimethylamino)naphthalene(Proton Sponge), 1,4-diazabicyclo[2.2.2]-octane (DABCO), 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), and 1,5-diazabicyclo[5.4.0]-undec-5-ene (DBU) in the presence of molecular sieves 3A (see Table I).

As shown in Table I, it is evident that, in the case of the elimination of δ-methoxyl group of Ia, trienal(IIa) was obtained in good yield by employing DBU or DBN as a tertiary amine in CH_2Cl_2 at room temperature.

Table I. The Effect of Amines and Solvents in the Preparation of 2,4,6-Decatrienal(IIa) from 5-Methoxy-2,6-decadienal(Ia)

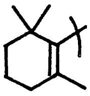
	Base	Ratio of Base/(Ia)	Reaction Conditions			Isolated
			Solvent	Temp.	Time(hr)	Yield(%)
1)	Pyridine	4.0	CH_2Cl_2	refl.	24	5
2)	$(C_2H_5)_3N$	4.0	CH_2Cl_2	refl.	24	5
3)	Proton Sponge	2.0	CH_2Cl_2	refl.	24	17
4)	DABCO	2.0	CH_2Cl_2	r.t.	24	51
5)	DBU	0.5	C_6H_6	refl.	0.8	64
6)	DBU	2.0	C_6H_6	r.t.	4	75
7)	DBU	2.0	THF	r.t.	6	69
8)	DBU	2.0	CH_3CN	r.t.	0.5	72
9)	DBU	2.0	CH_2Cl_2	r.t.	3	81
10)	DBN	2.0	CH_2Cl_2	r.t.	3	82

The following experiment provides a typical procedure for the conversion of δ-alkoxy-α,β-unsaturated aldehyde to dienal, trienal or other polyenal. To a dichloromethane (10 ml) solution of 5-methoxy-2,6-decadienal (364 mg, 2.0 mmol) were added a dichloromethane (5 ml) solution of DBU (608 mg, 4.0 mmol) and molecular sieves 3A (500 mg) at room temperature under an argon atmosphere. The reaction mixture was stirred for 3 hr and poured into a mixture of ice cold brine (10 ml) and acetic acid (180 mg, 4.1 mmol). The organic layer was separated and washed with brine. 2,4,6-Decatrienal(IIa) was obtained in 81% (243 mg) yield after purification by thin layer chromatography on silica gel. Similarly, IIa was obtained in 80% yield when molecular sieves 4A was employed in place of molecular sieves 3A.

In a similar manner, various δ-alkoxy-α,β-unsaturated aldehydes were easily converted to the corresponding dienal or trienal as shown in Table II.

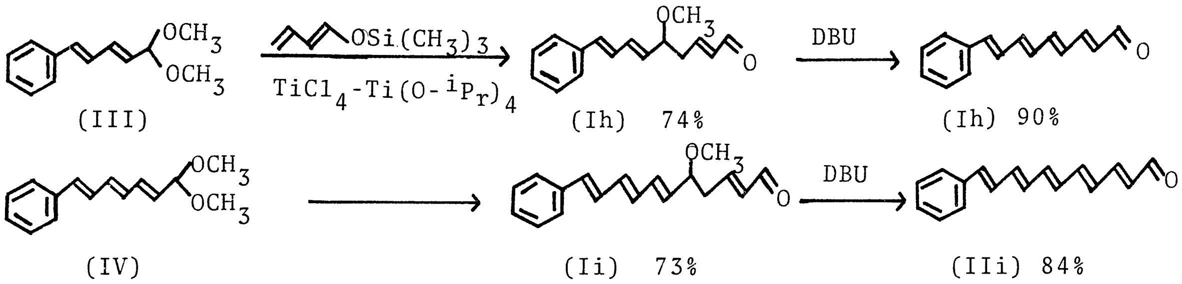
Further, it was found that 5-methoxy-9-phenyl-2,6,8-nonatrienal(Ih) and 5-methoxy-11-phenyl-2,6,9,10-undecatetraenal(Ii) were successfully converted into the polyenals in fairly good yields according to the following procedures. The reaction of 5-phenyl-2,4-pentadienal dimethyl acetal (III) with 1-trimethylsiloxy-1,3-butadiene in the presence of $TiCl_4$ 8) afforded Ih in 74% yield. After treatment of Ih with DBU in the presence of molecular sieves 3A, 9-phenyl-2,4,6,8-nonatetraenal(IIh) was isolated in 90% yield (mp 141-142°C, lit.9) mp 139-141°C). Similarly, 11-phenyl-2,4,6,8,10-undecapentaenal(IIi) was obtained in 84% yield (mp 185-186°C, lit.10) mp 183°C) by treating Ii with DBU.

Table II. The Elimination Reaction of δ-Alkoxyl Group of α,β-Unsaturated Aldehyde with DBU or DBN

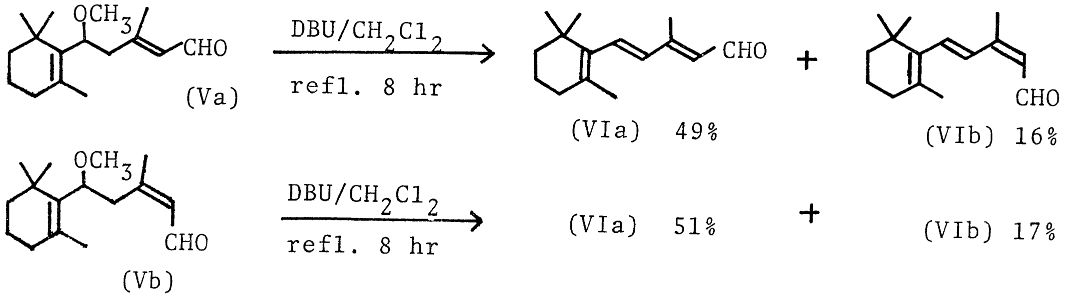
	δ-Alkoxy Aldehyde(I)			Reaction Conditions*1		Yields of II(%)*2	
	R^1	R^2	n	Temp.	Time(hr)	A	B
a)	$CH_3CH_2CH_2$	CH_3	1	r.t.	3.0	81	82
b)	C_6H_5	CH_3	0	r.t.	1.0	82	80[6)]
c)	C_6H_5	C_2H_5	0	r.t.	1.5	79	79
d)	C_6H_5	CH_3	1	r.t.	1.0	92	92[7)]
e)	C_6H_5	C_2H_5	1	r.t.	1.5	92	-
f)	C_6H_5	$CH(CH_3)_2$	1	refl.	2.0	65	-
g)		CH_3	0	r.t.	3.5	72	71

*1 Ratio of tert-amine/δ-alkoxy aldehyde(I) is 2.0. Dichloromethane is used as a solvent.

*2 A) DBU is employed. B) DBN is employed.



3-Methyl-5-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2(E),4(E)-pentadienal(VIa)[11)] and 2(Z),4(E)-isomer(VIb)[11)] were isolated in 49% and 16% yields, respectively, when 5-methoxy-3-methyl-5-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2(E)-pentenal(Va)[13)] was treated with 4 molar amounts of DBU. Further, VIa and VIb were obtained in 51% and 17% yields, respectively, on treating 2-(Z) isomer (Vb)[13)] with DBU under the same condition.



These results indicate that the elimination reactions of the two isomers, Va and Vb, proceed through the same dienolate intermediate to result in the formation of all trans isomer (VIa) as a major product.

Since the δ-alkoxy-α,β-unsaturated aldehydes are easily prepared from the reaction of dienoxysilane with various acetals, this method would provide a simple and practically useful route to polyenals. Further, studies on the synthesis of vitamin A, polyenol skeleton, are now in progress.

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11) The configuration of 3-methyl-α,β-unsaturated aldehyde was determined by the chemical shift of 3-methyl group.[12]
VIa nmr (δ_{TMS} ppm, CCl_4): 2.30 (s, C_3-CH_3), 5.85 (d, J=8Hz, C_2-H), 6.10, 6.65 (2d, J=16Hz, C_4-H, C_5-H), 10.20 (d, J=8Hz, aldehyde-H).
VIb nmr (δ_{TMS} ppm, CCl_4): 2.10 (s, C_3-CH_3), 5.75 (d, J=8Hz, C_2-H), 6.50, 7.10 (2d, J=16Hz, C_4-H, C_5-H), 10.15 (d, J=8Hz, aldehyde-H).

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13) Va nmr (δ_{TMS} ppm, CCl_4): 2.25 (s, C_3-CH_3), 5.80 (d, J=8Hz, C_2-H), 9.95 (d, J=8Hz, aldehyde-H).
Vb nmr (δ_{TMS} ppm, CCl_4); 2.00 (s, C_3-CH_3), 5.80 (d, J=8Hz, C_2-H), 9.85 (d, J=8Hz, aldehyde-H).

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