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THE HIGHLY STEREOSELECTIVE SYNTHESIS OF CIS-VINYLOXIRANES

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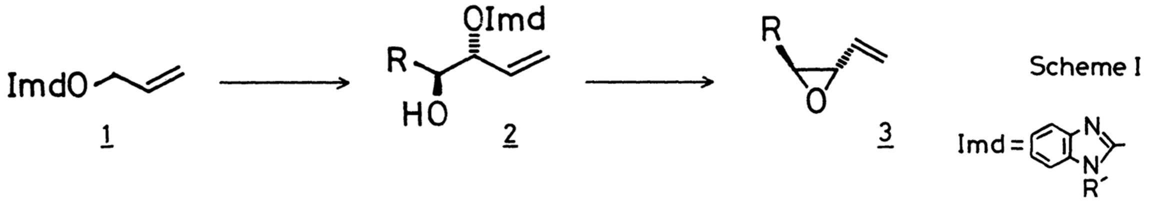
In the presence of triethylaluminum, oxyallyl anions derived from 2-allyloxybenzimidazoles react with aldehydes in highly regio- and stereoselective manner to afford α-adducts in good yields. The adducts are stereospecifically converted to cis-vinyloxiranes in good yields.

Previously, we have shown a useful synthetic method[1] for the stereoselective preparation of trans-vinyloxiranes (3) from allylcadmium compounds (9) and successfully employed it to the stereoselective synthesis[2] of D- and L-ribose (Scheme I).



Scheme I

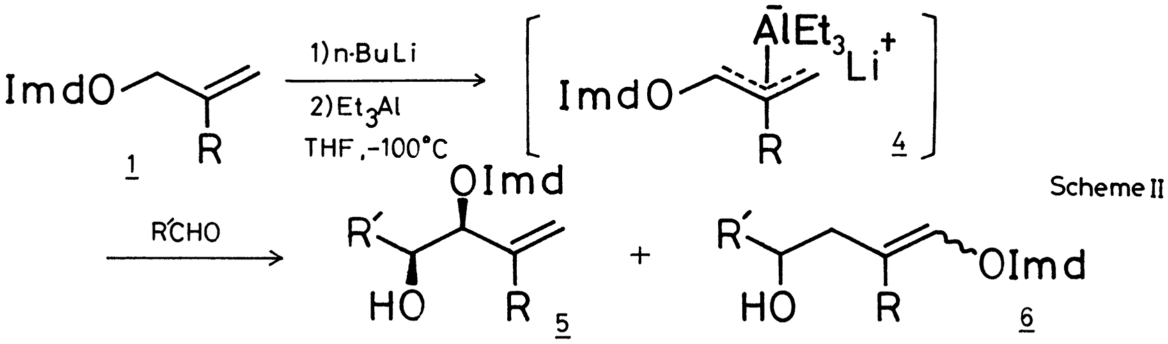
The usefulness of the vinyloxiranes, as a synthetic intermediate, urged us to develop a method for the synthesis of the other isomer —— cis-vinyloxiranes (7), which enables us to prepare various sugar derivatives.

From the screening of various additives in the addition reaction of the oxyallyl anions prepared from 1 and an aldehyde, it was found that the presence of triethylaluminum[3] resulted in high regio- and stereoselectivity to afford the α-adduct (5). Further, it was observed that a higher stereoselectivity was achieved by employing 1 with 3,6,9-trioxadecyl group at 1-position of benzimidazole ring rather than methyl group (Table II).

Thus, a variety of aldehydes are allowed to react with the aluminum ate complex (4) and the adducts (5) are obtained regio- and stereoselectively as shown in Scheme II and Table I. Then, 5 is transformed to cis-vinyloxiranes[4] (7) in good yields according to the procedure described previously[1] (Scheme III, Table II).

As the result of the previous[1] and the present investigation, vinyloxiranes, useful synthetic intermediates, with either trans- or cis-configuration can be selectively obtained starting from the same materials and simply varying the additives.

Though the reaction mechanism is not fully clear, these differences in the

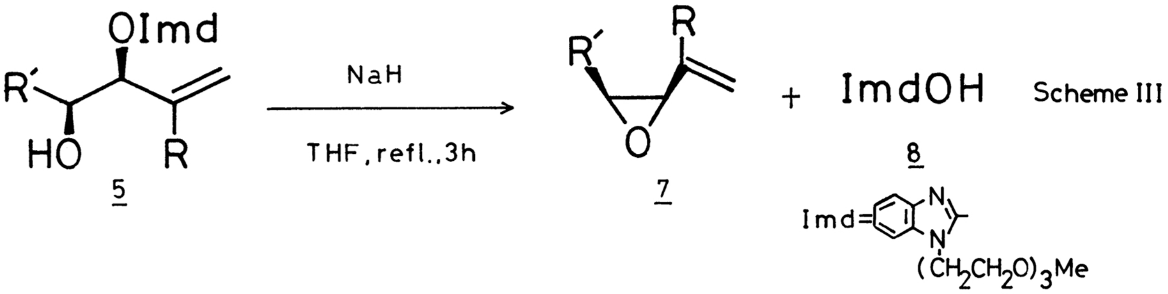


Scheme II

Table I. The Addition Reaction of Oxyallylanions.

R	R'CHO	Yield (5+6, %)a)	5 : 6
H	PhCHO	91	82 : 18
		91	88 : 12b)
	$PhCH_2CH_2CHO$	78	91 : 9
	n-$C_{11}H_{23}CHO$	64	70 : 30
	 CHO	77	> 90 : 10
Me	PhCHO	87	> 90 : 10
	$PhCH_2CH_2CHO$	87	> 90 : 10

a) All the products gave satisfactory NMR and IR spectra.
b) 1-Methyl-2-(2-propenyloxy)benzimidazole was employed.



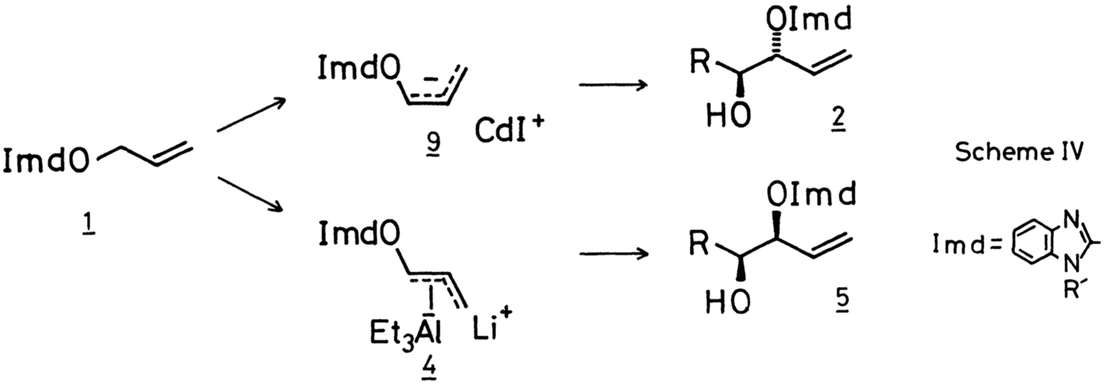
Scheme III

Table II. The Synthesis of Cis-Vinyloxiranes.

R	R'	Yield (7, %)a)	cis : trans
H	Ph	86	90 : 10 7)
		86 d)	82 : 18
	$PhCH_2CH_2$	78b)	> 95 : 5
	n-$C_{11}H_{23}$	75b)	> 95 : 5
		71c)	> 95 : 5
Me	Ph	quant.	90 : 10
	$PhCH_2CH_2$	96	> 95 : 5

a) All the products gave satisfactory NMR and IR spectra.
b) Satisfactory elemental analyses were obtained.
c) A mixture of C-6 epimers in 1 : 1 ratio.
d) 1-Methyl-2-(2-propenyloxy)benzimidazole was emploxyed.

stereoselectivity caused by the additives may be explained as follows: Concerning the configuration of the oxyallyl anions, it is presumed that the previous allyl cadmium compounds (9) exist exclusively as (Z)-form and the present ate complexes (4) prefer (E)-form. These presumptions are supported by the results that the γ-adduct (6), a by-product of the addition reaction, are exclusively (Z)-form5) in the trans-vinyloxirane synthesis and predominantly (E)-form5) in the present reaction. We consider that these differences in the configuration of the allyl anions consequently influence the stereochemistry of the α-adducts, for example, via a boat-like transition state (Scheme IV).6)



Scheme IV

It should be noted that cis-vinyloxiranes (7) are synthesized stereoselectively starting from 2-allyloxybenzimidazoles (1) and aldehydes in the presence of triethylaluminum.

A typical procedure is described for the synthesis of cis-3,4-epoxy-6-phenyl-1-hexene: To a THF (4 ml) solution of 2-(2-propenyloxy)-1-(3,6,9-trioxadecyl)benzimidazole (160 mg, 0.5 mmol) was added a hexane solution (0.37 ml) of n-butyllithium (0.6 mmol) at -100°C (a methanol-liquid nitrogen bath) under an argon atmosphere, and the mixture was stirred for 30 min to give a pale yellow solution. Then a hexane solution (1 ml) of triethylaluminum (1.4 mmol) was added. After 30 min at -100°C, a THF (2 ml) solution of 3-phenylpropanal (102 mg, 0.75 mmol) was added and the resulted solution was stirred overnight at -78°C. The reaction was quenched with a small amount of ethanol and aqueous ammonium chloride. The organic materials were extracted with ethyl acetate, and the combined extracts were dried over $MgSO_4$. 1-Phenyl-4-[1-(3,6,9-trioxadecyl)benzimidazol-2-yloxy]-5-hexen-3-ol (162 mg, 71%)8) and 1-phenyl-6-[1-(3,6,9-trioxadecyl)benzimidazol-2-yloxy]-5-hexen-3-ol (16 mg, 7%) were isolated by thin layer chromatography (silica gel).

The α-adduct (162 mg, 0.35 mmol) thus obtained was transformed to cis-3,4-epoxy-6-phenyl-1-hexene (48 mg, 78%)9) according to the procedure previously described.1)

References

1) M. Yamaguchi and T. Mukaiyama, Chem. Lett., 1979, 1279.

2) M. Yamaguchi and T. Mukaiyama, ibid., 1981, 1005.

3) Y. Yamamoto, H. Yatagai, and K. Maruyama, J. Org. Chem., 45, 195 (1980).

4) Several recent examples of vinyloxirane synthesis as a mixture of stereoisomers are; M. Ochiai and E. Fujita, Tetrahedron Lett., 1980, 4369; D. Seebach, K.H. Geiss, and M. Pohmakotr, Angew. Chem. Int. Ed. Engl., 15, 437 (1976). P. Van Fnde and A. Kriet, Tetrahedron Lett., 1976, 457.

5) For example, γ-adduct formed by the reaction of the allyl cadmium compound with benzaldehyde as a by-product, was determined to be (Z)-form from the coupling constant of the vicinal vinyl protons in the NMR (δ 4.97 (q, J=6 Hz)). On the other hand, in the case of the reaction of the aluminum ate complex with the aldehyde, a small amount of γ-adduct with (E)-configuration (δ 4.9-5.8 (m)) was given along with α-adduct, a main product.

6) Several examples of the stereoselective addition of thioallyl anions to aldehydes are reported: T. Hayashi, N. Fujitaka, T. Oishi, and T. Takeshima, Tetrahedron Lett., 1980, 303; R. W. Hoffmann and B. Kempfer, ibid, 1980, 4883.

7) J.-C. Paladini and J. Chuche, Bull. Soc. Chem. Fr., 1974, 187.

8) NMR ($CDCl_3$) δ 1.6-2.9 (5H, m), 3.24 (3H, s), 3.43 (3H, s), 3.46 (3H, s), 3.69 (2H, t, J=5Hz), 4.08 (2H, t, J=5Hz), 4.8-5.5 (3H, m), 5.5-6.2 (1H, m), 6.8-7.4 (9H, m). IR (neat) 740, 1620, 3400 cm^{-1}.

9) Bp. 180°C/0.1 mmHg (bath temp.). Found: C, 82.73; H, 8.15%. Calcd. for $C_{12}H_{14}O$: C, 82.72; H, 8.10%. NMR ($CDCl_3$) δ 1.6-2.0 (2H, m), 2.8-3.0 (2H, m) 3.07 (1H, dt, J=4,7 Hz), 3.37 (1H, dd, J=4,6 Hz), 5.2-5.9 (3H, m), 7.21 (5H, s). IR (neat) 925 cm^{-1}.

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