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## Metalloporphyrin Cr(TPP)Cl-catalyzed Claisen rearrangement of simple aliphatic allyl vinyl ethers and its unique stereoselectivity

Toshikatsu Takanami, Mikiko Hayashi and Kohji Suda\*

Meiji Pharmaceutical University, 2-522-1 Noshio, Kiyose, Tokyo 204-8588, Japan

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Abstract—The catalytic Z-selective Claisen rearrangement of simple aliphatic allyl vinyl ethers can be achieved using a chromium(III) porphyrin complex, Cr(TPP)Cl, as a catalyst: Cr(TPP)Cl significantly enhances reversal of E-Z selectivity in the thermal Claisen rearrangement of allyl vinyl ethers, especially, 4,5- and 4,6-disubstituted derivatives, at low catalyst loading. © 2005 Elsevier Ltd. All rights reserved.

The Claisen rearrangement of allyl vinyl ethers is among the most powerful synthetic tools for the construction of carbon–carbon bonds.<sup>1,2</sup> The reaction leads to formation of  $\gamma$ , $\delta$ –unsaturated carbonyl compounds, and virtually all cases proceed with high selectivity for the products with *E* configuration.<sup>1a,3,4</sup> However, there is scarcely any precedent for the rearrangement with the opposite *Z*-selectivity.<sup>4–6</sup> The only reported example of a Lewis acid-mediated *Z*-selective rearrangement requires the use of superstoichiometric quantities of a bulky organoaluminum reagent, methylaluminum bis(4-bromo-2,6-di-*tert*-butylphenoxide) (MABR).<sup>4</sup>

Recently, we have demonstrated that high-valent metalloporphyrin complexes work as an efficient and easy-tohandle Lewis acid catalyst for the highly regio- and stereoselective rearrangement of epoxides to carbonyl compounds.<sup>6,7</sup> Reported herein is a chromium(III) tetra-phenylporphyrin chloride Cr(TPP)Cl-catalyzed Claisen rearrangement of simple aliphatic allyl vinyl ethers **1** at low catalyst loading (5 mol %), wherein the *Z*-isomers of  $\gamma$ , $\delta$ -unsaturated aldehyde **2** are predominantly produced from 4,5- and 4,6-disubstituted allyl vinyl ethers. These are, to the best of our knowledge, the first example of *catalytic Z*-selective Claisen rearrangement.

We commenced our studies with the rearrangement of vinyl ether of *trans*-3-octen-2-ol **1a** using different por-

phyrin-based catalysts at 83 °C in dichloroethane.<sup>8</sup> The representative results are summarized in Table 1. Heating **1a** under similar conditions without catalysts for 48 h gave a 97:3 mixture of 3-*n*-butyl-4-heptenal **2a** with

 Table 1. Evaluation of metalloporphyrin catalysts in the rearrangement of vinyl ether of *trans*-3-octen-2-ol 1a



Entry	Catalyst	Time (h)	Yield (%) <sup>a</sup>	Ratio $(E/Z)^{b}$
1	Cr(TPP)OTf	4	37	21:79
2	Cr(TPP)Cl	12	62	28:72
3	MABR <sup>c,d</sup>	0.5	28	27:73
4	None	48	48	97:3
5	Mn(TPP)Cl	30	69	97:3
6	Fe(TPP)Cl	30	64	99:1
7	Cr(salen)Cle	30	36	83:17
8	Mn(salen)Cl <sup>f</sup>	30	57	94:6

<sup>a</sup> Isolated yield.

*Keywords*: Allyl vinyl ether; Chromium(III) porphyrin complex; Claisen rearrangement; Lewis acid catalyst; (Z)- $\gamma$ , $\delta$ -unsaturated aldehyde.

<sup>\*</sup> Corresponding author. Tel./fax: +81 4249 58780; e-mail: suda@ my-pharm.ac.jp

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<sup>&</sup>lt;sup>b</sup> Determined by 300 MHz <sup>1</sup>H NMR.

<sup>&</sup>lt;sup>c</sup> MABR: bis(4-bromo-2,6-di-t-butylphenoxide).

 $<sup>^{\</sup>rm d}$  The reaction was carried out with 200 mol % MABR in CH\_2Cl\_2 at  $-78~^{\rm o}{\rm C}.$ 

<sup>&</sup>lt;sup>e</sup> Cr(salen)Cl: (*S*,*S*)-(+)-*N*,*N*'-bis(3,5-di-*t*-butylsalicylidene)-l,2-cyclohexanediamino chromium(III) chloride.

<sup>&</sup>lt;sup>f</sup> Mn(salen)Cl: (*S*,*S*)-(+)-*N*,*N*'-bis(3,5-di-*t*-butylsalicylidene)-1,2-cyclohexanediamino manganase(III) chloride.

high E selectivity in 48% combined yield (entry 4). On the other hand, the reaction with 5 mol % Cr(TPP)OTf reversed the selectivity and produced a 21:79 ratio of **2a** favoring the Z-isomer (E/Z = 97:3) in 37% combined yield (entry 1). Intriguingly, changing the catalyst to Cr(TPP)Cl, which is a weaker Lewis acid than Cr(TPP)OTf, further improved the reactivity with a minimal loss of the stereoselectivity, the aldehyde 2a being produced in 62% yield with the E/Z ratio of 28:72 (entry 2).9 It is also worth noting that these Zselectivities furnished with these porphyrin catalysts were comparable to that obtained from the corresponding reaction performed with 2 equiv of MABR at -78 °C in dichloromethane (*E*/*Z* = 27:73) (entry 3). Attempts with other catalysts, such as Mn(TPP)Cl, Fe(TPP)Cl, and metallosalen catalysts, Cr(salen)Cl and Mn(salen)Cl,<sup>10</sup> were unsuccessful under the conditions examined, affording the undesired (E)-2a as the major product in modest yields (entries 5-8).

We then examined the scope of the Cr(TPP)Cl catalyst system with several distinct types of allyl vinyl ethers including 4-monosubstituted and 4,5- and 4,6-disubstituted allyl vinyl ethers (Table 2).<sup>8</sup> As a whole, the present catalytic method showed promising functional group compatibility: the substrates bearing phenyl, olefinic, and silvlacetylenic moieties as well as those having simple alkyl chains were tolerated well, the corresponding Claisen products being produced in good to high yields. Several stereochemical features of the catalytic method are as follows: (1) the Cr(TPP)Cl catalyst system provided appreciable Z-selectivities in the rearrangement of 4,6-disubstituted substrates, **1a**-d, which were almost comparable to those obtained from the corresponding stoichiometric reactions with MABR; (2) although Z-

selective rearrangement of 4,5-disubstituted allyl vinyl ethers, 1e-g, was hardly achieved even using the bulky organoaluminum reagent MABR, the use of a  $5 \mod \%$ Cr(TPP)Cl was, to our surprise, quite effective for the Z-selective rearrangement of these substrates;<sup>11</sup> (3) for the rearrangement of 4-mono-substituted substrates, 1i and 1j, the Cr(TPP)Cl catalyst showed only marginal Z-selectivity, whereas MABR could effectively mediate the Z-selective rearrangement of these substrates.

Although details of the present catalytic process are not clear as yet, the preferential formation of the Z-isomers would be interpreted as follows: the Cr(TPP)Cl-catalyzed rearrangement apparently starts with creating coordination of the metal to the oxygen of the substrates, and generates a less likely transition state conformation **B** with the C-4 substituent  $R^1$  axial, which would be favored over a conformation A with the C-4 substituent R<sup>1</sup> equatorial, in view of the 1,2-steric repulsion between the bulky porphyrin macrocycle and the C-4 substituent  $\mathbf{R}^1$  in  $\mathbf{A}$ , furnishing the desired Z-alkenes as major products (Scheme 1). In the case of 4-monosubstituted substrates, however, the conformation **B** initially generated would change to the conformation A due to their relatively long and loose Cr-O coordination, leading to the preferential formation of the undesired E-alkenes. For the rearrangements of 4,5- and 4,6-disubstituted substrates, on the other hand, the substituents at the C-5 and C-6 positions would enhance ring-reversal barriers, preventing the conformational change from **B** to **A**, the desired Z-alkenes thus being obtained successfully.

To elucidate the transition state in the Cr(TPP)Cl catalytic process, we examined the stereo-chemical features

		$ \begin{array}{c c} R^2 & f \\ 5 & f \\ R^1 & 0 & 2 \end{array} $	5 mol % <b>Cr(TPP)Cl</b> CICH <sub>2</sub> CH <sub>2</sub> Cl, 83°C	$\rightarrow \qquad \begin{array}{c} R^2 \\ \downarrow \\ R^1 \\ \end{array}$	õ	
		້1		2		
Substrates	$\mathbf{R}^1$	$R^2$	R <sup>3</sup>	Time (h)	Yield (%) <sup>c</sup>	Ratio $(E/Z)^{d,e}$
1a	Me	Н	"Bu	12 (0.5)	62 (28)	28:72 (27:73)
1b	"Bu	Н	Me	7 (0.25)	59 (72)	30:70 (16:84) <sup>f</sup>
1c	Me	Н	Ph	7 (0.5)	94 (45)	15:85 (15:85)
1d	TMS	Н	Me	0.5 (0.5)	70 (58)	14:86 (6:94)
1e	"Bu	Me	Н	9 (0.25)	64 (58)	25:75 (61:39) <sup>f</sup>
1f	<sup>i</sup> Bu	Me	Н	3 (0.5)	85 (40)	21:79 (64:36)
1g	$H_2C = CH(CH_2)_3$	Me	Н	3 (0.5)	41 (18)	22:78 (69:31)
1h	TMS-	Me	Н	0.5 (0.5)	87 (66)	18:82 (20:80)
1i	"Bu	Н	Н	7 (0.25)	48 (41)	67:33 (9:91) <sup>f</sup>
11	<sup>i</sup> Bu	н	н	6 (0.25)	57 (64)	69.31 (7.93) <sup>f</sup>

**D**2

Table 2. Cr(TPP)Cl-catalyzed Claisen rearrangement of allyl vinyl ethers<sup>a,b</sup>

<sup>a</sup> Conditions: 5 mol % Cr(TPP)Cl, ClCH<sub>2</sub>CH<sub>2</sub>Cl, 83 °C.

<sup>b</sup> The data in parentheses refer to those in the MABR-mediated rearrangements; conditions: 2 equiv MABR, -78 °C, CH<sub>2</sub>Cl<sub>2</sub>.

<sup>d</sup> Determined by 300 MHz <sup>1</sup>H NMR, except for 2d and 2h E/Z ratios for 2d and 2h were determined by isolation.

<sup>e</sup> The yields and E/Z ratios obtained in the conventional non-catalytic thermal rearrangement (ClCH<sub>2</sub>CH<sub>2</sub>Cl, 83 °C) of 1a-j were as follows: 2a (22%, 97:3); **2b** (44%, 98:2); **2c** (42%, 97:3); **2d** (65%, 48:52); **2e** (40%, 94:6); **2f** (50%, 86:14); **2g** (55%, 84:16); **2h** (82%, 57:43); **2i** (40%, 96:4); **2j** (50%, 93:7). <sup>f</sup> Data quoted from Ref. 4b.

<sup>&</sup>lt;sup>c</sup> Isolated vield.



**Scheme 1.** Plausible reaction pathway for the Cr(TPP)Cl-catalyzed Claisen rearrangement of allyl vinyl ethers: 4-monosubstituted allyl vinyl ether,  $R^2 = R^3 = H$ ; 4,5-disubstituted allyl vinyl ether,  $R^3 = H$ ; 4,6-disubstituted allyl vinyl ether,  $R^2 = H$ .

in the rearrangement of optically active 4,6-disubstituted substrate (*R*)-1k<sup>12</sup> Scheme 2. The rearrangement of (*R*)-1k (91% ee) with Cr(TPP)Cl under the same conditions took place smoothly to provide a mixture of the corresponding aldehydes, (*R*)-(*Z*)-2k, (*S*)-(*Z*)-2k, (*R*)-(*E*)-2k, and (*S*)-(*E*)-2k, in 61% combined yield.<sup>13</sup> The ratio of these isomers was determined to be 4:72:23:1 by capillary GLC analysis after conversion of the aldehydes to the corresponding acetals of (2*R*,4*R*)-2,4-pentandiol. Thus, the chirality of the starting (*R*)-1k was almost perfectly transferred to the major product (*S*)-(*Z*)-2k (90% ee, i.e., 99% chiral transmission),<sup>14</sup> and this result strongly supports the proposed catalytic process via a less likely transition state **B** in Scheme 2.<sup>15</sup>

In summary, a novel and efficient catalyst system utilizing chromium porphyrin, Cr(TPP)Cl, for the Claisen rearrangement of simple aliphatic allyl vinyl ethers has been developed. The most notable advantage of the catalyst system is its unique stereoselectivity: Cr(TPP)Cl significantly enhances reversal of E-Z selectivity in the Claisen rearrangement of allyl vinyl ethers, especially, 4.5- and 4.6-disubstituted derivatives, and dose so in a catalytic fashion (5 mol %). This catalyst system also offers an efficient entry to the highly stereoselective rearrangement of an enantioenriched 4,6-disubstituted allyl vinyl ether to the corresponding optically active Z-olefinic aldehyde: the efficiency of the chiral transfer is almost fully comparable to that obtained from the corresponding stoichiometric reaction with MABR.<sup>3</sup> Ongoing efforts are focused on both improving the stereoselectivity of the present catalysis by tuning the porphyrin peripheral substituents and increasing its scope.

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## Supplementary data

Experimental procedure and characterization data for products 2a-k and Cr(TPP)Cl catalyst are available. Supplementary data associated with this article can be found, in the online version at doi:10.1016/j.tetlet. 2005.02.136.

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Scheme 2. Cr(TPP)Cl-catalyzed Claisen rearrangement of enantioenriched allyl vinyl ether (*R*)-lk. The absolute configurations of the Claisen products were determined according to the literature procedure, see: Ref. 4b.

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- 15. A minimal loss of the optical purity was also obtained in the rearrangement of (R)-1k to (R)-(E)-2k (89% ee, i.e., 98% chiral transmission). Unlike MABR-mediated rearrangement (see Ref. 4), therefore, virtually no ionic mechanism would participate in the present catalytic process.