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STEREOSELECTIVE ZIRCONOCENE-MEDIATED RING TRANSFORMATION OF 2-VINYLHETEROCYCLES TO VINYLCARBOCYCLES[1,*]

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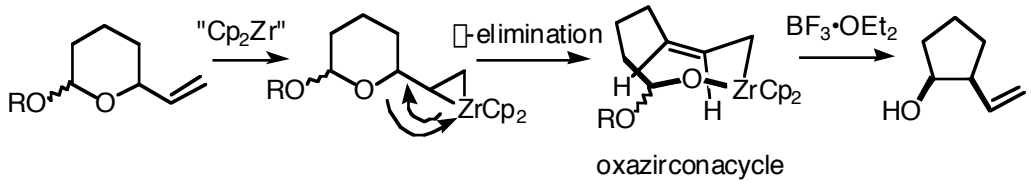
Abstract – Stereoselective ring transformation of 2-vinylheterocycles to vinylcarbocycles was efficiently carried out by the use of a zirconocene equivalent ("Cp_2Zr"). The transformation proceeded through an intramolecular allylation of *Z*-allylic zirconocene species to the epoxide or aziridine ring.

INTRODUCTION

Highly diastereoselective ring contraction reactions of vinyl cyclic acetals to *cis*-2-vinylcycloalkanols through the use of zirconocene-(1-butene) complex (zirconocene equivalent, "Cp_2Zr") have exemplified the usefulness of "Cp_2Zr" as a synthetic reagent (Scheme 1).[2,3] The reaction proceeds *via* a series of reactions, 1) the formation of a zirconacyclopropane by ligand exchange, 2) the formation of an oxazirconacycle containing a *Z*-allylzirconocene portion by β-elimination of *O*-functional group, and 3) the intramolecular allylation to the oxocarbenium ion generated by Lewis acid. The geometry of the allylzirconocene portion in the oxazirconacycle has been proven to be *Z*-stereochemistry,[2] and the diastereoselectivity of the intramolecular allylation reaction was rationalized through a chair-form

* This paper is dedicated to Professor Leo A. Paquette of The Ohio State University on the occasion of his 70th birthday.

transition state between the *Z*-allylzirconocene and the oxocarbenium ion. The methodology has been applied to the preparations of the pyrrolizidine alkaloid[4] from a vinylmorpholine derivative, and the cyclobutane portion of the carbocyclic oxetanocin analogue[5] from a vinylfuranose in an optically pure form, respectively.



Scheme 1. Stereoselective "Cp_2Zr"-mediated ring-contraction of vinyl cyclic acetal

The "Cp_2Zr"-mediated ring-contraction reactions led us to further examine the reaction of 2-vinylheterocycles (**1**, **2**) which possess a leaving group (Y) at a distinct carbon from the ring-carbon bound to heteroatom (X) (Figure 1). In this report, we describe the results of the "Cp_2Zr"-mediated new ring transformation of 2-vinylheterocycles (**1**, **2**, X = O or *N*-Boc, Y = halogen or OTs) to vinylcarbocycles.

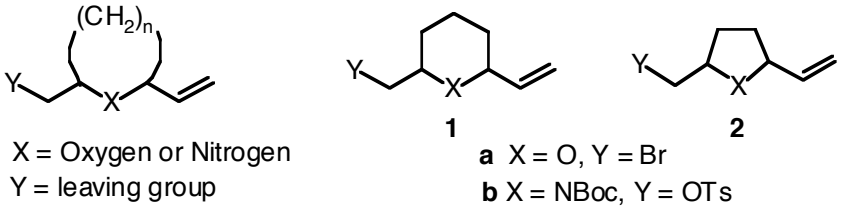
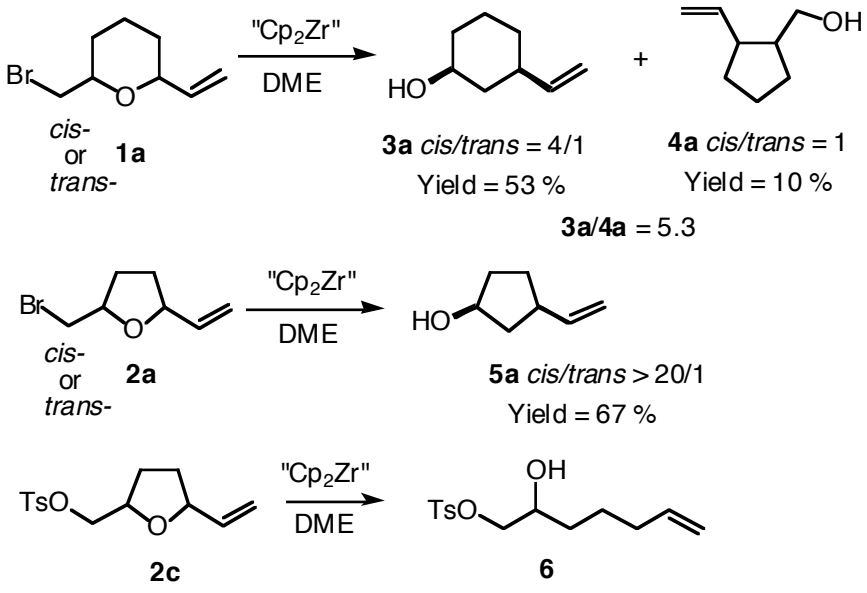


Figure 1. 2-Vinyl heterocycles

RESULTS AND DISCUSSION

The reaction of 2-vinyl-tetrahydropyranyl compound (*cis*-**1a**; X = O, Y = Br) with "Cp_2Zr" in DME gave a mixture of 3-vinylcyclohexanol (**3a**, *cis*/*trans* = 4 : 1)[6] and 1-hydroxymethyl-2-vinylcyclopentane (**4a**, *cis*/*trans* = 1)[7] in 5.3 : 1 ratio (63% yield) (Scheme 2). Identical products without significant differences in the yield and selectivity were obtained from *trans*-**1a**. These results suggest that the "Cp_2Zr"-mediated ring transformation of **1a** is not affected by stereochemistry at the allylic carbon of the starting

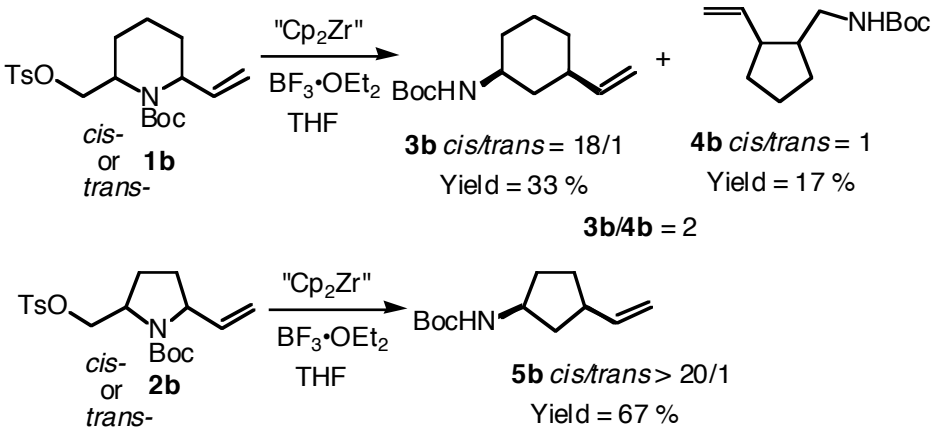
material (**1a**). The major pathway is the transformation to **3a** which has the same ring size with **1a**, and the ring-contraction to **4a** was a minor process in the reaction of **1a**. Unlike the poorly selective reaction of **1a**, the "Cp_2Zr"-mediated reaction of 2-vinyltetrafuranyl compounds (*cis*- and *trans*-**2a**, X = O, Y = Br) proceeded to give **5a** in 67% yield with a high *cis*-selectivity (*cis* : *trans* > 20 : 1),[8] and the supposed ring contraction-product, cyclobutane derivative, was not detected. It is interesting to note that the reaction of **2c** (X = O, Y = OTs) with "Cp_2Zr" gave monotosylate (**6**), and failed to yield the cyclic product (**5a**).



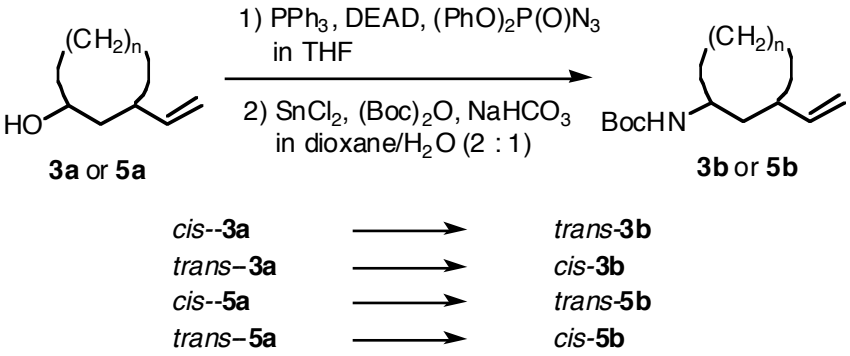
Scheme 2. Ring transformation of oxygen heterocycles

In the reactions of nitrogen vinylheterocycles (**1b** and **2b**)[9,10] with "Cp_2Zr", the addition of a stoichiometric amount of BF_3•OEt_2 and the use of THF as a solvent are necessary for the reaction to yield product in fair amounts. Thus, the "Cp_2Zr"-mediated reaction of *N*-Boc-2-vinylpiperidine derivative (**1b**) (X = *N*-Boc, Y = OTs) gave a mixture of *N*-Boc-3-vinylcyclohexylamine (**3b**) (*cis* : *trans* = 18 : 1) and ring-contraction product (**4b**) (*cis* : *trans* = 1) in a 2 : 1 ratio (50% yield), and *N*-Boc-2-vinylpyrrolidine derivative (**2b**) gave *N*-Boc-3-vinylcyclopentylamine (**5b**, *cis* : *trans* >20 : 1) in 67% yield (Scheme 3). The relative stereochemistry of **3b** was confirmed by the conversion of *cis*-**3a** to *trans*-**3b** or by the conversion of *trans*-**3a** to *cis*-**3b**, respectively, under the S_N2-reaction conditions, and the stereochemistry of *cis*-**5b** was analogously confirmed by the reactions of *cis*- and *trans*-**5a** (Scheme 4). In the reactions of

nitrogen heterocycles (**1b** and/or **2b**) with "Cp_2Zr", the *p*-toluenesulfonate leaving group is employed for the present purpose. It is worth mentioning that fair to high *cis*-stereoselectivity has been obtained in the formation of **3a**,**b** and **5a**,**b** while the formation of **4a**,**b** was non-stereoselective.



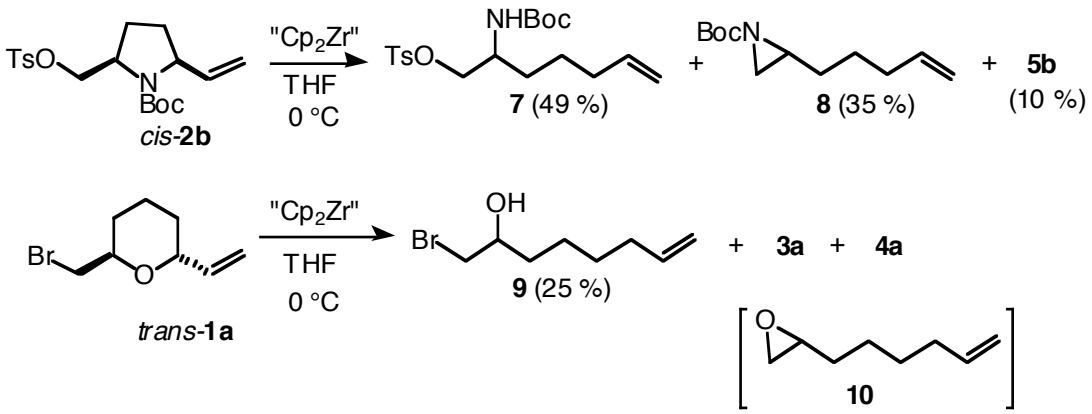
Scheme 3. Ring transformation of nitrogen heterocycles



Scheme 4. The S_N2 conversion of **3** and **5**

In the early stages of the reaction of *cis*- or *trans*-**2b**, the existence of two products was assumed by the analysis of silica gel thin layer chromatography (TLC). Thus, the exisitence of **5b** (10%), *N*-Boc-aminoalcohol tosylate (**7**) (49%) and *N*-Boc-aziridine (**8**) (35%) was confirmed by quenching the reaction mixture with aqueous HCl (1M solution) after the consumption of *cis*-**2b** (Scheme 5). The pursuit of the reaction of *cis*-**2b** by TLC revealed the first appearance of **7** at 0 °C-ambient temperature, and the further stirring at ambient temperature indicated a gradual increase in **5b** and **8**, in a simultaneous decrease in **7**. For the smooth conversion to **5b**, the addition of BF_3•OEt_2 (one equivalent) to the reaction

mixture was required. In an analogous experiment of *trans*-**1a** with "Cp_2Zr", bromohydrine (**9**) (25%) was isolated in addition to **3a** and **4a** by quenching the reaction at the early stage. Oxirane compound (**10**), however, was neither detected nor isolated at the stage of the consumption of *trans*-**1a**.



Scheme 5. Quenching at the early stage of the reaction

Our previous reports about the "Cp_2Zr"-mediated ring-contraction of 2-vinyl cyclic acetals derivatives[2] and the isolation of products (**7**, **8** and **9**) at the early stage of the present reactions suggest that the intervention of zirconacycle intermediate has a *Z*-allylzirconocene portion in the beginning of the reaction, cf. Scheme 1. Since **2c** did not give the ring transformation product (Scheme 2), the compound (**2c**) was used for the NMR spectral study to analyze the initial stage of the reaction. The NMR spectral analysis of the intermediate (**11**) in benzene-d_6, which was generated by the reaction of **2c** with "Cp_2Zr", indicates that the geometry of the allylzirconocene portion ($J_{\text{olefinic-H}}$ = 10.7 Hz, NOE correlation) is *Z*-geometry (Figure 2). The addition of aqueous HCl (1M solution) to **11** indicated a formation of monotosylate (**6**).

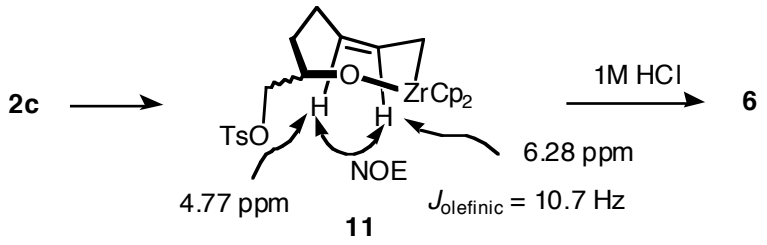
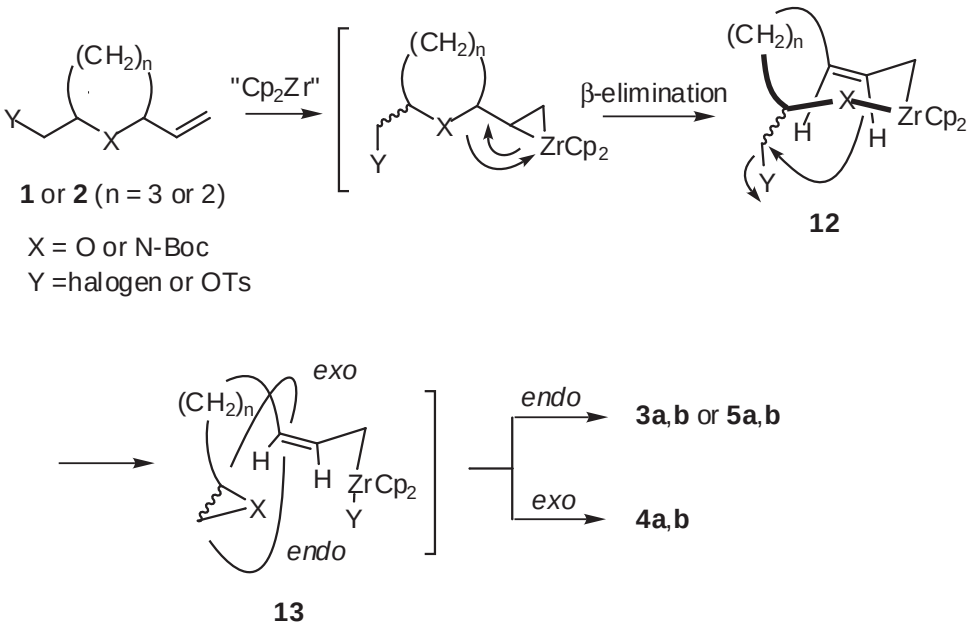


Figure 2. NMR spectra of zirconacycle (**11**) in benzene-d_6

Based on the observed results, we propose the transformation of **1** and **2** to products (**3**, **4**, and **5**) through 1) the formation of a zirconacycle (**12**) containing a *Z*-allylic zirconocene portion, 2) the formation of a

Z-allylic zirconocene oxirane or aziridine intermediate (**13**), and 3) the *endo*- or *exo*-cyclization of the *Z*-allylic zirconocene species to the oxirane or aziridine ring in **13** (Scheme 6).



Scheme 6. Ring-transformation of **1** and **2**

The formation of the intermediate products (**7**, **8**, and **9**) at the early stage of the reaction, thus, could be explained by the hydrolysis of **12** or **13**. The intramolecular allylation to the oxirane or aziridine carbon in **13** would be considered to occur with the inversion of the configuration,[11] and the added BF_3•OEt_2 in the reaction of **1b** and **2b** could participate in the activation of the less reactive aziridine ring compared to the oxirane ring. Therefore, the 1,3-*cis* selectivity in the formation of **3** or **5** could be explained by the comparison of the two possible transition states (**A** and **B**) for the 5-*endo* and 6-*endo* cyclization modes (Figure 3).

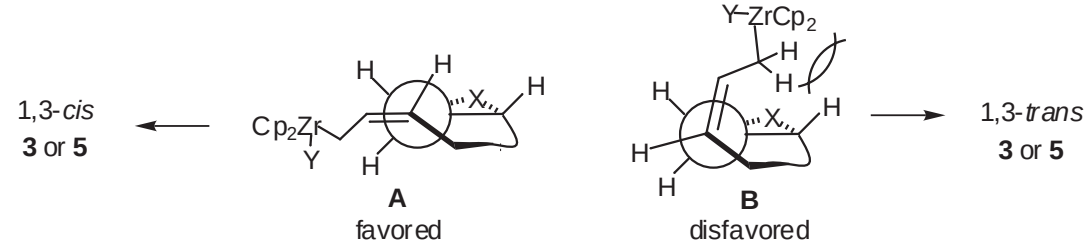
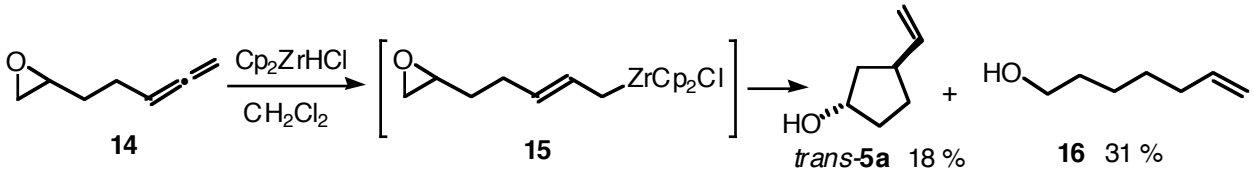


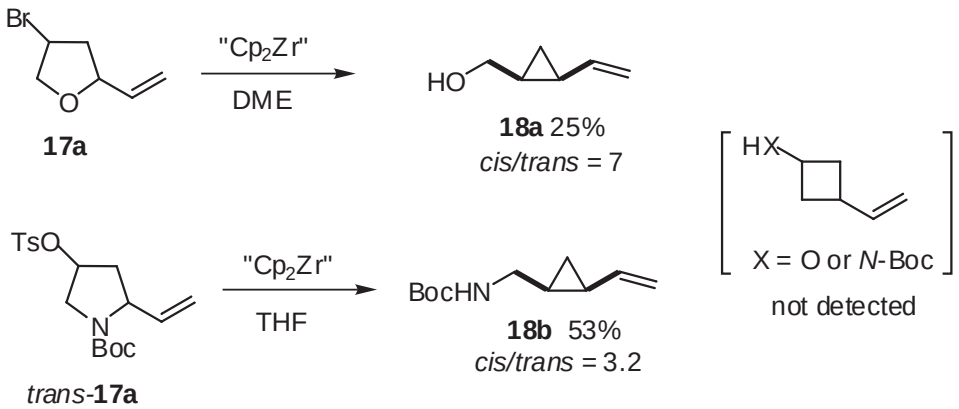
Figure 3. Transition state for 5-*endo* and 6-*endo* cyclization of **13**

In the transition state (**B**), the unfavorable steric interaction between the *Z*-allylic zirconocene portion and the oxirane or aziridine ring hydrogen is present while there is no such steric interaction in the

transition state (**A**). It is worth noting that the hydrozirconation[12] of □-allenenyloxirane (**14**) with an equivalent amount of Schwartz reagent (Cp_2ZrHCl)[13] in CH_2Cl_2 gave a *trans*-isomer of **5a** in 25% yield as a solely cyclized product together with the recovered **14** (43%) and hept-6-en-1-ol (**16**) (31%) (Scheme 7). In this reaction, the addition of BF_3•OEt_2 is necessary for the formation of the *trans*-**5a**. Recently, the formations of *E*-allylzirconocene species by the hydrozirconation of allene derivatives[14] and the chemoselective hydrozirconation to the alkenyl portion of alkenyl oxirane compound[15] have been reported. Thus, oxirane compound (**15)** containing an *E*-allylzirconocene portion would be generated by the hydrozirconation of **14** (Scheme 6). The formation of *trans*-**5a** as a solely cyclized product in the reaction of **14** with Cp_2ZrHCl and a nearly exclusive formation of *cis*-**5a** in the reaction of **2a** with "Cp_2Zr" would indicate that the cyclization of the allylic zirconocene species to oxirane ring would be a stereospecific reaction.[16] These observations provide an indirect evidence for the stereochemistry of zirconacycle intermediate (**12**) in the present reaction.



Scheme 7. Hydrozirconation of allenyl oxirane (**14**)



Scheme 8. Formation of vinylcyclopropane deivatives

The present transformation was applied for the generation of vinyl cyclopropane derivatives (**18**)[17] in moderate yields and stereoselectivity by treating **17a** and **17b** with "Cp_2Zr" (Scheme 8). In these ring transformations, ring size is reduced by a two-carbon unit, and we were unable to detect cyclobutane

derivatives in the reaction mixture. It should be noted that the reaction of **17b** with "Cp_2Zr" did not require BF_3•OEt_2, which is required for the reactions of **1b** and **2b**. These results suggest that the formation of the three-membered ring is kinetically favored in the 3-*exo* vs. 4-*endo* transition state in the cyclization of the Z-allylzirconcocene to oxirane or aziridine ring. The *cis*-stereoselectivity, albeit low, for the formation of **18** in 3-*exo* cyclization could be analogously explained by the transition state model described in Figure 3.

CONCLUSIONS

A novel "Cp_2Zr"-mediated ring transformation of 2-vinyl heterocyclic compounds has been described. Although the present ring transformation is a logical extension of our previously reported "Cp_2Zr"-mediated ring contraction chemistry of 2-vinyl cyclic acetals, the reaction mechanism and the reaction pattern are notable. Thus, the reaction proceeds through the formation of an acyclic oxirane or aziridine having a *Z*-allylzirconocene unit and the subsequent intramolecular nucleophilic attack of the *Z*-allylzirconocene unit to the oxirane or aziridine ring. The reaction described herein indicates the further usefulness of "Cp_2Zr" as a synthetic reagent.

EXPERIMENTAL

All nonaqueous reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions. THF and DME were distilled from benzophenone ketyl. Dichloromethane and benzene-d_6 were distilled from calcium hydride. NMR spectra were measured at 300 or 400 MHz for ^1H, and 75.5 or 100.6 MHz for ^{13}C. Materials purchased from commercial suppliers were used without further purification unless otherwise noted. Purification of the products was carried out by medium pressure silica gel column chromatography (MPLC) using a UV detector at 254 nm.

cis-2-Bromomethyl-6-vinyloxane (*cis*-1a)

To a pretreated solution of CBr_4 (1.75 g, 5.3 mmol) in CH_2Cl_2 (15 mL) with PPh_3 (2.8 g, 10.6 mmol) at 0°C for 5 min was added a solution of *cis*-2-hydroxymethyl-6-vinyloxane[18] (500 mg, 3.5 mmol) in CH_2Cl_2 (5 mL), and the mixture was stirred at ambient temperature overnight. After addition of H_2O, the mixture was extracted with ether. The combined ether layer was washed with brine and dried over

$MgSO_4$. Concentration of the filtrate *in vacuo* gave crude oil, which was purified by silica gel column chromatography (pentane/ether = 10 : 1) gave *cis*-**1a** (pale yellow oil, 663 mg, 92%). ^{1}H-NMR (300 MHz, $CDCl_3$) □ 1.19-1.38 (m, 2H), 1.54-1.68 (m, 2H), 1.77-1.85 (m, 1 H), 1.87-1.96 (m, 1H), 3.33 (dd, *J* = 5.6, 10.3 Hz, 1 H), 3.42 (dd, *J* = 5.6, 10.3 Hz, 1 H), 3.59 (ddt, *J* = 2.1, 5.6, 11.2 Hz, 1 H), 3.84-3.91 (m, 1 H), 5.11 (ddd, *J* = 1.6, 1.6, 10.6 Hz, 1H), 5.26 (ddd, *J* = 1.6, 1.6, 17.3 Hz, 1H), 5.87 (ddd, *J* = 5.4, 10.6, 17.3 Hz, 1 H); ^{13}C-NMR (75.5 MHz, $CDCl_3$) □: 22.9, 29.4, 30.9, 35.5, 76.7, 78.3, 114.6, 138.7; EIMS *m/z*: 204 (M^+) ; HRMS Calcd for $C_8H_{13}OBr$: 204.0150. Found: 204.0135.

***trans*-2-Bromomethyl-6-vinyloxane (*trans*-1a)**

trans-**1a** (pale yellow oil, 175 mg, 77%) was obtained from *trans*-2-hydroxymethyl-6-vinyloxane[18] (157 mg, 1.1 mmol) by the same procedure described for *cis*-**1a**. ^{1}H-NMR (300 MHz, $CDCl_3$) □ 1.43-1.52 (m, 1H), 1.60-1.80 (m, 5H), 3.38 (dd, *J* = 5.7, 10.4 Hz, 1H), 1.87-1.96 (m, 1H), 3.43 (dd, *J* = 6.3, 10.4 Hz, 1H), 3.88-3.96 (m, 1H), 4.41-4.62 (m, 1H), 5.24 (ddd, *J* = 1.8, 1.8, 10.8 Hz, 1H), 5.28 (ddd, *J* = 1.8, 1.8, 17.6 Hz, 1H), 5.90 (ddd, *J* = 4.3, 10.8, 17.6 Hz, 1H); ^{13}C-NMR (75.5 MHz, $CDCl_3$) □ 18.4, 28.4, 29.0, 35.3, 70.5, 72.9, 116.5, 137.9; EIMS *m/z*: 204 (M^+); HRMS Calcd for $C_8H_{13}OBr$: 204.0150. Found: 204.0151.

2-Bromomethyl-5-vinyloxolane (*cis*-2a)

cis-**2a** (pale yellow oil, 308 mg, 94%) was obtained from *cis*-2-hydroxymethyl-5-vinyloxolane[18] (481 mg, 1.7 mmol) by the same procedure described for *cis*-**1a**. ^{1}H-NMR (300 MHz, $CDCl_3$) □ 1.66-1.88 (m, 2H), 2.10-2.23 (m, 2H), 3.37 (dd, *J* = 6.7, 10.1 Hz, 1H), 3.46 (dd, *J* = 4.7, 10.1 Hz, 1H), 4.30 (dddd, *J* = 4.7, 6.7, 6.7, 6.7 Hz, 1H), 4.50 (dtt, *J* = 1.3, 6.1, 6.3 Hz, 1H), 5.11 (ddd, *J* = 1.3, 1.3, 10.3 Hz, 1H), 5.25 (ddd, *J* = 1.3, 1.3, 17.1 Hz, 1H), 5.82 (ddd, *J* = 6.3, 10.3, 17.1 Hz, 1H); ^{13}C-NMR (75.5 MHz, $CDCl_3$) □ 30.6, 32.3, 35.8, 78.1, 80.8, 115.4, 138.4; EIMS *m/z*: 190 (M^+); HRMS Calcd for $C_7H_{11}OBr$: 189.9993. Found: 190.0018.

2-Bromomethyl-5-vinyloxolane （*trans*-2a）

trans-**2a** (pale yellow oil, 179 mg, 77%) was obtained from *trans*-2-(hydroxymethyl)-5-vinyloxolane[18] (346 mg, 1.2 mmol) by the same procedure described for *cis*-**1a**. ^{1}H-NMR (300 MHz, $CDCl_3$) □ 1.67-1.90 (m, 2H), 2.03-2.16 (m, 2H), 3.34 (dd, *J* = 6.8, 10.1 Hz, 1H), 3.46 (dd, *J* = 4.9, 10.1 Hz, 1H), 4.17-4.25 (m, 1H), 4.36-4.43 (m, 1H), 5.11 (ddd, *J* = 1.1, 1.5, 10.4 Hz, 1H), 5.27 (ddd, *J* = 1.1, 1.1, 17.1 Hz,

1H), 5.86 (ddd, *J* = 6.4, 10.4, 17.1 Hz, 1H); ^{13}C-NMR (75.5 MHz, $CDCl_3$) 30.1, 31.6, 35.5, 78.6, 81.2, 115.7, 138.8; EIMS *m/z*: 190 (M^+); HRMS Calcd for $C_7H_{11}OBr$: 189.9993. Found: 189.9994.

4-Bromo-2-vinyloxolane (17a)

To a solution of 5-vinyl-tetrahydrofuran-3-ol[18] (1.26 g, 11.04 mmol) in pyridine (5 mL) was added $MeSO_2Cl$ (1.7 mL, 22 mmol) under ice-cooling and the mixture was stirred at ambient temperature for 2 h. The reaction mixture was poured onto ice-H_2O and extracted with ether. The combined organic layer was washed with saturted aqueous $CuSO_4$ and brine before drying ($MgSO_4$). The filtered solution was concentrated *in vacuo* to give a crude sulfonate, which was directly treated with LiBr (3.8 g, 44.2 mmol) in DMF (10 mL) at 60°C overnight. Upon addition of 1M aqueous solution of HCl to the mixture, the mixture was extracted with ether. The combined ether layer was washed with H_2O, dried over $MgSO_4$, and the filtered solution was concentrated *in vacuo* to dryness to give a crude product. Purification by silica gel column chromatography (pentane/ethyl ether = 10 : 1) gave **17a** (1.1 g, 55%) as a pale yellow oil. ^{1}H-NMR (300 MHz, $CDCl_3$) 2.16 (ddd, *J* = 6.3, 9.0, 13.9 Hz, 1H), 2.43 (ddd, *J* = 2.5, 6.0, 13.9 Hz, 1H), 4.10 (dd, *J* = 3.3, 10.4 Hz, 1H), 4.36 (dd, *J* = 5.1, 10.4 Hz, 1H), 4.48-4.53 (m, 1H), 4.65-4.72 (m, 1H), 5.17 (ddd, *J* = 1.3, 1.3, 10.3 Hz, 1H), 5.33 (ddd, *J* = 1.3, 1.3, 17.1 Hz, 1H); ^{13}C-NMR (75.5 MHz, $CDCl_3$) 43.0, 46.9, 76.2, 78.8, 116.3, 137.0; EIMS *m/z*: 175 (M^+) ; HRMS Calcd for C_6H_9OBr: 175.9837. Found: 175.9846.

***N*-Boc-2-(*p*-toluenesulfonyloxymethyl)-6-vinylpiperidine (*cis*- and *trans*-1b), *N*-Boc-2-(*p*-toluenesulfonyloxymethyl)-5-vinylpyrroridine (*cis*- and *trans*-2b) and *trans*-*N*-Boc-3-(methanesulfonyloxy)-5-vinylpyrroridine (17b)**

Compounds (**1b**, **2b**) were prepared through the reactions of *N*-Boc-2-hydroxymethyl-6-vinylpiperidine (*cis*- or *trans*-)[9] or *N*-Boc-2-hydroxymethyl-5-vinylpyrroridine (*cis*- or *trans*-)[10] with TsCl in pyridine at 0°C, respectively. *trans*-**17b** was similarly prepared by treatment of *trans*-*N*-Boc-3-hydroxy-5-vinylpyrroridine[19] with TsCl in pyridine at 0°C. Compounds (**1b**, **2b**, and **17b**) were directly used without purification for the reaction with "Cp_2Zr".

General Procedure for the "Cp_2Zr"-mediated ring transformation of 1a, 2a, and 17a

To a solution of Cp_2ZrCl_2 (1.3 equiv.) in DME (5 mL/mmol) was added a solution of n-BuLi in hexane (2.6 equiv.) at -78°C and the mixture was stirred at the same temperature for 1 h. To the reaction mixture

was added a solution of 2-vinyl heterocycle (1 equiv.) in DME (6 mL/mmol) at -78°C and the mixture was stirred at 0°C for 3 h then at ambient temperature for 2 h. After addition of aqueous HCl (1M solution) at 0 °C, the mixture was extracted with ether. The combined ether layer was washed with saturated aqueous $NaHCO_3$, saturated aqueous NaCl and dried over $MgSO_4$. The filtered solution was concentrated *in vacuo* to give a crude product. Purification of the products was carried out by silica gel column chromatography with pentane/ether. Complete separation of the products was carried out by converting the products to corresponding benzoate derivatives (benzoyl chloride/pyridine, 0 °C) and the subsequent separation with MPLC. The relative stereochemistry of the products (**3a,**[6] **4a**,[7] **5a**,[8] and **18a**[17]) was determined by comparison with authentic samples. The products ratio was determined by NMR.

General Procedure for the "Cp_2Zr"-mediated ring transformation of 1b, 2b, and 17b

To a solution of Cp_2ZrCl_2 (1.3 equiv.) in THF (10 mL/mmol) was added a solution of n-BuLi in hexane (2.6 equiv.) at -78°C and stirred at the same temperature for 1 h. To the reaction mixture was added a solution of 2-vinyl heterocycle (1 equiv.) in THF (5 mL/mmol) at -78°C and the mixture was stirred at 0°C for 3 h then at ambient temperature for 1 h. BF_3•OEt_2 (1 equiv.) was added to the mixture and the mixture was stirred for 2 h at ambient temperature. After addition of sat. aqueous $NaHCO_3$, the mixture was extracted with ether. The combined ether layer was washed with sat. aqueous NaCl and dried over $MgSO_4$. The filtered solution was concentrated *in vacuo* to give a crude product which was purified by silica gel column chromatography (hexane/ethyl acetate) and MPLC *t*o give a pure prod*u*ct.

***N*-Boc-3-vinylcyclohexylamine (3b), 1-(*N*-Boc-aminomethyl)-2-vinylcyclopentane (4b)**

cis-**3b**: IR (neat) 3348, 1701 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) 0.91-1.04 (m, 2H), 1.34-1.48 (m, 2H), 1.44 (s, 9H), 1.67-1.84 (m, 2H), 1.93-2.12 (m, 3H), 3.45 (br m, 1H), 4.38 (br m, 1H), 4.90 (ddd, *J* = 1.5, 1.5, 10.4 Hz, 1H), 4.96 (ddd, *J* = 1.5, 1.5, 17.3 Hz, 1H), 5.74 (ddd, *J* = 6.3, 10.4, 17.3 Hz, 1H) ; ^{13}C-NMR (100.6 MHz, $CDCl_3$) 24.6, 28.4, 31.4, 33.2, 39.5, 40.6, 49.6, 79.0, 112.3, 143.2, 155.2; Anal. Calcd for $C_{13}H_{23}NO_2$: C 69.30, H 10.29, N 6.22. Found: C 69.25, H 10.24, N 6.00.

trans-**3b**: IR (neat) 3348 cm^{-1}, 1701; ^{1}H-NMR (400 MHz, $CDCl_3$) 1.24-1.68 (m, 8H), 1.44 (s, 9H), 2.25 (br m, 1H), 3.84 (br m, 1H), 4.60 (br m, 1H), 4.96 (ddd, *J* = 1.5, 1.5, 10.5 Hz, 1H), 5.01 (ddd, *J* = 1.6, 1.6, 17.4 Hz, 1H), 5.78 (ddd, *J* = 6.1, 10.5, 17.4 Hz, 1H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) 24.6, 28.5, 31.5, 33.3, 39.5, 40.6, 49.6, 79.1, 112.3, 143.2, 155.2

A mixture of *cis*- and *trans*-**4b** (1 : 1): IR (neat) ν 3358, 1700 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.22-1.90 (m, 7H), 1.43 (s, 9H), {2.01-2.13 (m), 2.57-2.66 (m), 1H}, {2.98-3.06 (m), 3.16-3.24 (m), 1H}, 4.55 (br m, 1H), 4.92-5.07 (overlap m, 1H), {5.73 (ddd, *J* = 8.3, 10.1, 17.1 Hz), 5.78 (ddd, *J* = 9.0, 10.2, 17.0 Hz), 1H}; ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 23.2, 23.8, 28.4, 28.9, 30.1, 31.2, 33.1, 42.1, 43.9, 44.4, 45.9, 46.0, 49.0, 78.9, 113.9, 114.7, 139.3, 142.4, 156.0; Anal. Calcd for $C_{13}H_{23}NO_2$: C 69.30, H 10.29, N 6.22. Found: C 69.10, H 10.19, N 6.10.

***N*-Boc-3-vinylcyclopentylamine (5b)**

cis-**5b**: IR (neat) ν 3339, 1701 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.16 (ddd, *J* = 8.5, 9.9, 12.6 Hz, 1H), 1.32-1.53 (m, 1H), 1.44 (s, 9H), 1.76-1.86 (m, 1H), 1.95-2.05 (m. 1H), 2.18-2.27 (m, 1H), 2.43-2.57 (m, 1H), 3.97 (br m, 1H), 4.49 (br m, 1H), 4.90 (ddd, *J* = 1.6, 1.6, 10.2 Hz, 1H), 4.98 (ddd, *J* = 1.6, 1.6, 17.2 Hz, 1H), 5.79 (ddd, *J* = 7.2, 10.2, 17.2 Hz, 1H) ; ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 28.4, 30.3, 32.7, 40.1, 42.2, 51.9, 79.1, 112.8, 142.5, 155.4; Anal. Calcd for $C_{12}H_{21}NO_2$: C 68.21, H 10.02, N 6.63. Found: C 67.85, H 10.00, N 6.49.

1-(*N*-Boc-aminomethyl)-2-vinylcyclopropane (18b)

cis-**18b**: IR (neat) ν 3358, 1715 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.42 (m, 1H), 0.92 (m, 1H), 1.15-1.28 (m, 1H), 1.44 (s, 9H), 1.52-1.65 (m, 1H), 2.87 (ddd, *J* = 4.4, 8.7, 14.0 Hz, 1H), 3.36-3.47 (m, 1H), 4.56 (br m, 1H), 5.02-5.06 (m, 1H), 5.13-5.20 (m, 1H), 5.58 (ddd, *J* = 8.6, 10.2, 17.0 Hz, 1H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 11.1, 18.5, 19.2, 28.4, 40.8, 79.1, 115.5, 136.7, 155.7; CIMS *m/z*: 198 (M+1).

trans-**18b**: IR (neat) ν 3354, 1695 cm-1; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.58-0.67 (m, 2H), 0.96-1.06 (m, 1H), 1.25-1.37 (m, 1H), 1.44 (s, 9H), 3.02-3.07 (m, 2H), 4.61 (br s, 1H), 4.86 (dd, J = 1.5, 10.2 Hz, 1H), 5.05 (dd, J = 1.5, 17.1 Hz, 1H), 5.37 (ddd, J = 8.5, 10.2, 17.1 Hz, 1H); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 12.1, 20.5, 21.0, 28.3, 44.3, 79.1, 112.2, 140.6, 155.8; CIMS *m/z*: 198 (M+1).

Hydrozirconation of 2-penta-3,4-dienyloxirane (14)

To a solution of Cp_2ZrHCl (247 mg, 0.9 mmol) in CH_2Cl_2 (10 mL) was added a solution of **14** (97 mg, 0.8 mmol) in CH_2Cl_2 (3 mL) at -78°C and the mixture was gradually warmed to ambient temperature and stirred for 2 h. To the ice-cooled reaction mixture was added BF_3•OEt_2 (0.09 mL, 0.8 mmol) and the mixture was stirred at ambient temperature overnight. After the addition of saturated aqueous $NaHCO_3$, the mixture was extracted with ether. The combined ether layer was washed with brine and dried over

$MgSO_4$. The filtrate was concentrated in vacuo to give a mixture of products which was separated by silica gel column chromatography (pentane/ether = 3 : 1) to give *trans*-**5a** (32 mg, 25%) and hept-6-en-1-ol **16** (28 mg, 31%). The structure of *trans*-**5a** was confirmed by comparison of the NMR spectra with authentic sample, see ref. 8.

Conversion of *trans*-5a (or *cis*-5a) to *cis*-5b (or *trans*-5b), conversion of *trans*-3a (or *cis*-3a) to *cis*-3b (or *trans*-3b)

To a solution of *trans*-**5a**[8] (110 mg, 0.9 mol) and PPh_3 (353 mg, 1.4 mmol) in THF (10 mL) were added $(PhO)_2P(O)N_3$ (330 mg, 1.2 mol) and DEAD (0.19 mL, 1.2 mmol) at 0°C, and the mixture was stirred at the same temperature for 2 h. After adding saturated aqueous NH_4Cl, the mixture was extracted with ether. The combined organic layer was washed with brine and dried over $MgSO_4$. The solution was filtered and concentrated *in vacuo* to dryness to give the azide product (120 mg), which was used directly in the next reaction. The azide product (120 mg, 0.8 mmol) was stirred with $SnCl_2•2H_2O$ (0.9 g, 4 mmol), $NaHCO_3$ (0.94 g, 11.2 mol) and $(Boc)_2O$ (0.37 mL, 1.6 mmol) in dioxane/H_2O (2 : 1) (5 mL) at ambient temperature for 2 h. After addition of saturated aqueous $NaHCO_3$, the mixture was extracted with ether and dried over $MgSO_4$. Concentration of the filtered solution and the purification of the product by silica gel column chromatography (hexane/ethyl acetate = 5 : 1) gave *cis*-**5b** (95 mg, 50% from *trans*-**5a**), which is identical to the product obtained by the present ring transformation. In the same way, *cis*-**5a** was converted to *trans*-**5b**. *trans*-**5b**: IR (neat) □ 3339, 1701 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) □ 1.16-2.27 (m, 5H), 1.44 (s, 9H), 2.43-2.68 (m, 1H), 4.01 (br m, 1H), 4.49 (br m, 1H), 4.88-4.93 (m, 1H), 4.95-5.02 (m, 1H), 5.76(ddd, *J* = 7.2, 10.1, 17.2 Hz, 1H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) □ 28.4, 31.0, 33.3, 39.7, 41.8, 79.1, 112.8, 142.3, 155.4. Anal. Calcd for $C_{12}H_{21}NO_2$: C 68.21, H 10.02, N 6.63. Found: C 67.96, H 9.98, N 6.55.

The conversion of *trans*-**3a** (or *cis*-**3a**) to *cis*-**3b** (or *trans*-**3b**) was also achieved in the same procedure described.

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