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Rh(I)-CATALYZED FORMATION OF TWO CONFORMERS DUE TO CIS-1,2-CYCLOHEXANEDIOL

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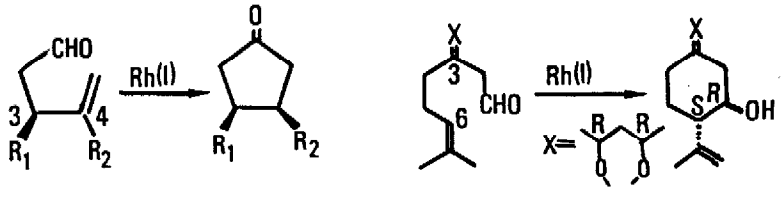
Summary: Two 6-octen-1-als (I and II) with cis-1,2-cyclohexanedioxy function at the C_3-position are cyclized by Rh(I)-complex(Wilkinson-complex) to afford two conformers due to cis-cyclohexanediol, respectively.

It is well known that cis-1,2-cyclohexanediol and its mirror image are not superimposable, but these isomers are rapidly interconvertible by flipping one chair conformation into the other. That is to say, they exist as a pair of unseparable conformer. Now, we describe the isolation of two conformers due to cis-1,2-cyclohexanedioxy function.

Rh(I)(Wilkinson)-catalyzed cyclization of 3,4-disubstituted 4-penten-1-als to cis-3,4-disubstituted cyclopentanones[1] or 3-substituted 6-octen-1-als to cyclohexanol[2] was developed by our laboratory, and it was found that 6-octen-1-als with chiral cyclic acetal at the C_3-position were diastereoselectively cyclized to the trans-alcohol, in contrast to the case of methyl substituent at the C_3-position to afford a mixture of cis- and trans-alcohols.[3]



When two aldehydes I (polar fraction) or II (less polar fraction)[4] with cis-1,2-cyclohexanedioxy function at the C_3-position were heated at reflux in $CHCl_3$ for 7 h in the presence of equimolar Rh(I)(Wilkinson-complex), each aldehyde afforded two cyclized products, IIIA (polar fraction (24%))[5] and IIIB (less polar fraction (26%)), or IVA (polar fraction (19%)) and IVB (less polar fraction (50%)), respectively.[6] In the ^{1}H-NMR spectra of each cyclized product, two olefinic protons appeared as a broad singlet at δ about 4.90. On the basis of our previous finding[3] that two olefinic protons in the trans-alcohol appear as a broad singlet, while one proton of two olefinic protons in the cis-alcohol shifts remarkably upfield, IIIA and IIIB as well as IVA and IVB were assigned to be 3,4-trans

configuration. More definitive evidence for trans-configuration was obtained by deprotecting each cyclized product with 5% aqueous AcOH/THF to afford trans-3,4-disubstituted cyclohexanone, in addition to cis-1,2-cyclohexanediol.[7] Thus, the formation of isomers may be rationalized by taking the conformers into consideration. Similarity of spectral data (Fig. 1)(see References and Notes 5) of IIIA and IIIB as well as those of IVA and IVB also indicate that IIIA and IIIB (or IVA and IVB) are conformational isomers due to cis-1,2-cyclohexanedioxy function.

The most polar IIIA and the least polar IVB (or IIIB and IVA having closed Rf value) in thin layer chromatography showed remarkable similarity in ^{1}H-NMR spectra. That is to say, two HC-O protons (br s) (IIIA; δ 4.096, IVB; δ 4.073) of 1,2-cyclohexandioxy function in IIIA and IVB appear at more upfield than those of the corresponding conformers (IIIB; δ 4.125, IVA; δ 4.133), and HC-O proton (br t)(IIIA; δ 3.729, IVB; δ 3.732) of the alcohol function was observed at lower field than those of IIIB (δ 3.659) and IVA (δ 3.661).

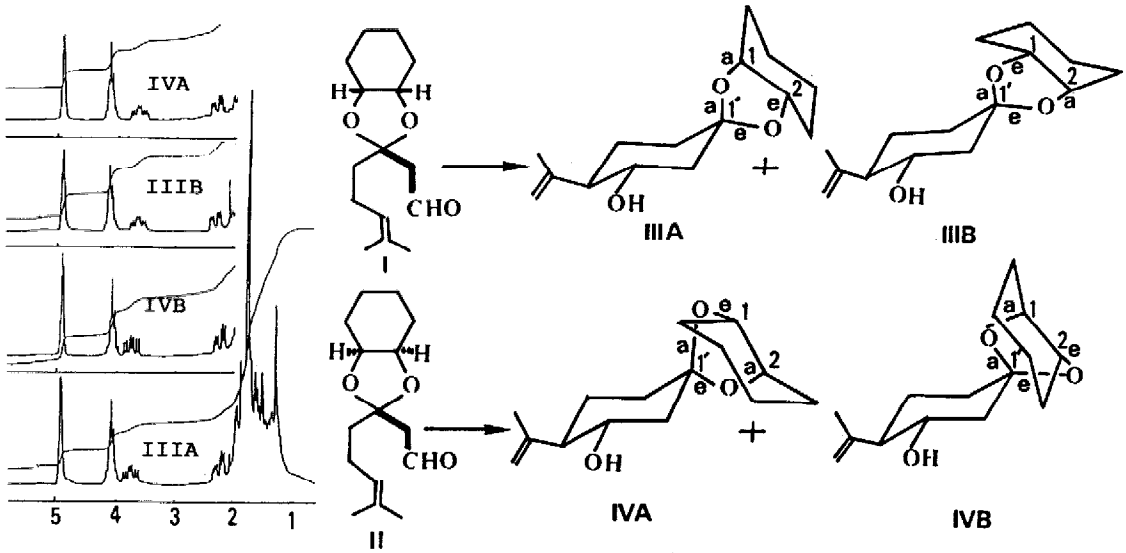


Fig. 1, ^{1}H-NMR spectra of IIIA, IIIB, IVA, and IVB.

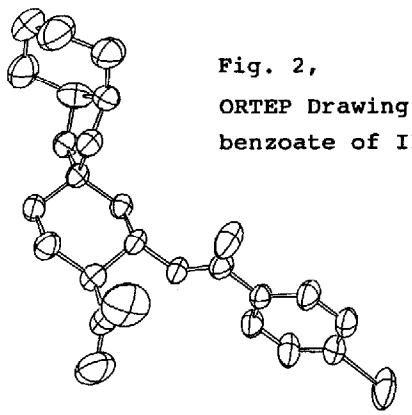


Fig. 2, ORTEP Drawing of p-bromobenzoate of IIIA.

p-Bromobenzoate of IIIA (mp 144°C) was submitted to X-ray analysis,[8] and the structure could be definitively determined to be as shown in Fig. 2. In the dioxolane ring including C_1 and C_2 of cis-1,2-cyclohexanedioxy and C_1, of trans-3,4-disubstituted cyclohexane, two cyclohexane rings are linked by two bonds of the C_1,-axial-O-axial-C_1 and C_1,-equatorial-O-equatorial-C_2. Remarkable similarity of IIIA to IVB in the ^{1}H-NMR spectra indicates strongly that the dioxolane structure in IVB is the same as that of IIIA. Therefore, the structure of IIIB and IVA should be the C_1,-axial-O-equatorial-C_1 and C_1,-equatorial-O-axial-C_2.

$ZnBr_2$-catalyzed cyclization of the aldehyde I afforded only IIIA, and the conformer IIIB was not detected. This interesting finding suggests that Rh(I)-catalyzed cyclization proceed clearly in the different mechanism from the case of Lewis acid.[9]

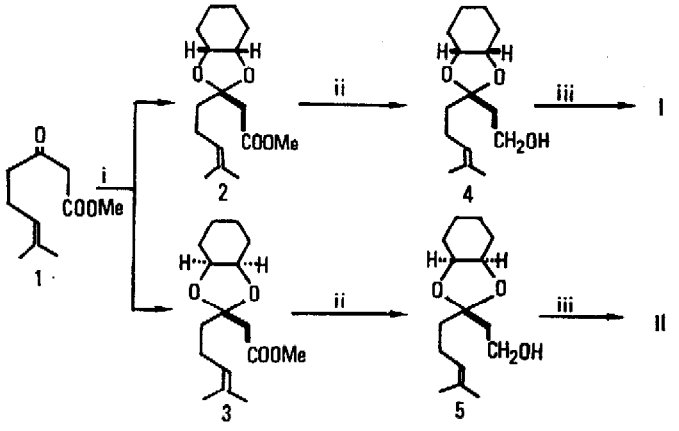
References and Notes

1) K.Sakai, J.Ide, O.Oda, and N.Nakamura, Tetrahedron Lett., 1972, 1287; K.Sakai, Y.Ishiguro, K.Funakoshi, K.Ueno, and H.Suemune, ibid., 25, 961 (1984); R.C.Larock, K.Oertle, and G.F.Potter, J. Am. Chem. Soc., 102, 190 (1980); C.F.Lochow, and R.G.Miller, ibid., 98, 1281 (1976); H.Suemune, K.Oda, S.Saeki, and K.Sakai, Chem. Pharm. Bull., 36, 172 (1988); H.Suemune, H.Maruoka, S.Saeki, and K.Sakai, ibid., 34, 4629 (1986); X.-F.Xie, Y.Ichikawa, H.Suemune, and K.Sakai, ibid., 35, 1816 (1987); K.Ueno, H.Suemune, S.Saeki, K.Sakai, ibid., 33, 4021 (1985); H.Suemune, T.Kawahara, and K.Sakai, ibid., 34, 550 (1986).

2) K.Sakai, and O.Oda, Tetrahedron Lett., 1972, 4375.

3) K.Funakoshi, N.Togo, and K.Sakai, Tetrahedron Lett., 30, 1095 (1989); K.Funakoshi, N.Togo, Y.Taura, and K.Sakai, Chem. Pharm. Bull., in press; K.Funakoshi, N.Togo, I.Koga, K.Sakai, ibid., in press.

4) The aldehydes I and II were synthesized as follows. Methyl 3-oxo-7-methyl-6-octenoate (1) and cis-1,2-cyclohexanediol in benzene was heated at



Reagents and Reaction Conditios: i; cis-1,2-cyclohexanediol, p-TsOH, reflux in benzene, 2(58%), 3(37%). ii; $LiAlH_4$/ether, 4 (95%), 5(85%). iii; PCC/CH_2Cl_2, I (44%), II(37%).

reflux for 12 h under azeotropic conditions in the presence of p-toluenesulfonic acid. Silica-gel column chromatography of crude product

afforded a polar fraction (2) and a less polar fraction (3) in ratio of 6 to 4 (95% yield). The relative configuration of cyclohexane ring to the methyl ester was determined to be as shown in scheme 1 by analysis (CH_2-COO and HCO-) of the nuclear Overhauser effect difference spectra (NOEDS) of 2 and 3. Reduction of each ester (2 and 3) with $LiAlH_4$ followed by PCC oxidation afforded the aldehydes, I (polar fraction) and II (less polar fraction). **(I)**: IR(neat) ; 1722, 1100, 1040 cm^{-1}. MS m/z; 252(M^+), 234, 210, 169, 140. ^{1}H-NMR($CDCl_3$) δ; 1.688 (3H, s, CH_3), 1.770 (3H, s, CH_3), 2.729 (2H, d, J=3.1 Hz, CH_2CHO), 4.176 (2H, m, HC-O), 5.121 (1H, m, =-H), 9.743 (1H, t, J=3.1 Hz, CHO). **(II)**: IR(neat) ; 1730, 1100, 1040 cm^{-1}. MS m/z; 252 (M^+), 234, 209, 169, 140. ^{1}H-NMR($CDCl_3$) δ; 1.600 (3H, s, CH_3), 1.673 (3H, d, J=1.3 Hz, CH_3), 2.806 (2H, d, J=3.1 Hz, CH_2CHO), 4.184 (2H, t, J=3.8 Hz, HC-O), 5.067 (1H, m, =-H), 9.876 (1H, t, J=3.1 Hz, CHO).

5) **(IIIA)**: colorless oil. IR(neat) ; 3450, 1645, 1445, 1355, 1303, 1240, 1122, 1043, 1035 cm^{-1}. MS m/z; 252 (M^+), 234, 207, 169, 153, 140, 98, 81, 55. ^{1}H-NMR ($CDCl_3$) δ; 1.255-2.301 (14-14.5H, m), 1.732 (3H, s, =C-CH_3), 2.167-2.317 (1.5-2H, br d), 3.729 (1H, br t, HC-OH), 4.096 (2H, br s, HC-O), 4.906 (2H, br s, =CH_2).
(IIIB): colorless oil. IR(neat) ; 3450, 1642, 1445, 1355, 1195, 1135, 1045, 1030 cm^{-1}. MS m/z; 252 (M^+), 234, 207, 169, 140, 99, 81, 43. ^{1}H-NMR ($CDCl_3$) δ; 1.259-2.392 (14-14.5H, m), 1.745 (3H, s, =-CH_3), 2.171-2.392 (1.5-2H, br d), 3.659 (1H, br t, HC-OH), 4.125 (2H, br s, HC-O), 4.909 (2H, br s, =CH_2).
(IVA): colorless oil. IR(neat) ; 3400, 1640, 1440, 1350, 1240, 1120, 1040 cm^{-1}. MS m/z; 252 (M^+), 234, 169, 153, 140, 81, 79, 55. ^{1}H-NMR ($CDCl_3$) δ; 1.257-2.397 (14-14.5H, m), 1.763 (3H, d, J=5.6 Hz, =-CH_3), 2.171-2.397 (1.5-2H, br d), 3.661 (1H, br t, HC-OH), 4.133 (2H, br s, HC-O), 4.922 (2H, br s, =CH_2).
(IVB): colorless oil. IR(neat) ; 3500, 1640, 1442, 1350, 1240, 1120, 1040 cm^{-1}. MS m/z; 252 (M^+), 234, 169, 153, 140, 98, 81, 79, 69, 55. ^{1}H-NMR($CDCl_3$) δ; 1.255-2.326 (14-14.5H, m), 1.741 (3H, d, J=0.8 Hz, =-CH_3), 2.132-2.326 (1.5-2H, br d), 3.732 (1H, br t, HC-OH), 4.073 (2H, br s, HC-O), 4.917 (2H, br s, =CH_2).

6) Even reflux in toluene (8 h) as well as benzene (4 h), interconversion between IIIA and IIIB (or IVA and IVB) was not observed.

7) Each product was confirmed by comparison of spectral data and also the behavior on TLC with those of the standard sample.

8) X-Ray diffractions were measured on a Rigaku AFC-5R apparatus, and R-factor was 6.7%. These data were deposited with the Cambridge Crystallographic Data Center, Univ. Chem. Lab., Lensfield Road, Cambridge, CB2 1EW, U.K.

9) Lewis acid-catalyzed cyclization of 7-methyl-6-octen-1-als affords the trans-alcohol. Y.Nakatani, K.Kawashima, Synthesis, 1978, 147; S.Sakane, K.Maruoka, and H.Yamamoto, Tetrahedron, 42, 2203 (1986).

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