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DIASTEREO-DIFFERENTIATING CYCLOPROPANATION OF A CHIRAL ENOL ETHER: A SIMPLE METHOD FOR THE PREPARATION OF OPTICALLY PURE CYCLOPROPYL ETHERS

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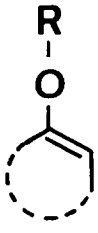
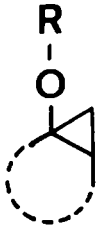
Enol ether of cyclohexanone carrying 2,4-pentanediol(PD) or 2,6-dimethyl-3,5-heptanediol(DMHD) as a chiral auxiliary was subjected to diastereo-differentiating cyclopropanation. The highest diastereomer excess(d.e.) of the product was found to be 95.2% in the case of PD and over 99.5% in the case of DMHD. The enol ethers prepared from various ketones and DMHD were also cyclopropanated in giving cyclopropyl ethers in almost 100 % d.e..

Cyclopropyl ethers are reactive under the acidic and the oxidative conditions to give various ketone derivatives.[1] Although an optically active 1,2-disubstituted cyclopropyl ether is expected to be a useful chiral C_3 synthon, synthetic studies have not yet been carried out.[2] A simple and straightforward method to obtain an optically active cyclopropyl ether is a diastereo-differentiating cyclopropanation of prochiral enol ether carrying a chiral auxiliary. In this paper, we wish to report our results to optimize the reaction system for the diastereo-differentiating cyclopropanation of enol ether of cyclohexanone, by changing a reagent and a solvent of the cyclopropanation, and a chiral auxiliary built in the substrate, together with the applicability of the established system to enol ethers of various ketones.[3]



enol ether



cyclopropyl ether

Results and Discussion

Optically pure (2R,4R)-2,4-pentanediol(**1**)(PD) whose synthetic procedure was established by our group[4] was a useful compound as a chiral auxiliary of the present studies. It reacted smoothly with cyclohexanone to give a cyclic ketal(**2**). The ketal was easily isomerized to an enol ether(**3**) by treatment with trialkylaluminum in an almost quantitative yield.[5] Furthermore, the chiral auxiliary was easily removed from the reaction product by the well established method.[6] In these respects, we employed 3 as a substrate in the series of studies.

The results of the reactions between 3 and Simmons-Smith reagent(Zn-Cu/diiodomethane) under the various conditions are summarized in Table I. In all cases, the reaction proceeded in giving a mixture of diastereomers(**4**) with good chemical yield, while the d.e. did not exceed 90 %. The separation of the diastereomers with a preparative chromatography was in failure. Although a major diastereomer could be isolated from the mixture by recrystallization, the yield of the pure material was insufficient. These facts implied that the reaction system was hard to utilize as a practical synthetic method for optically pure product unless its d.e. could be improved to be more than 95% d.e.

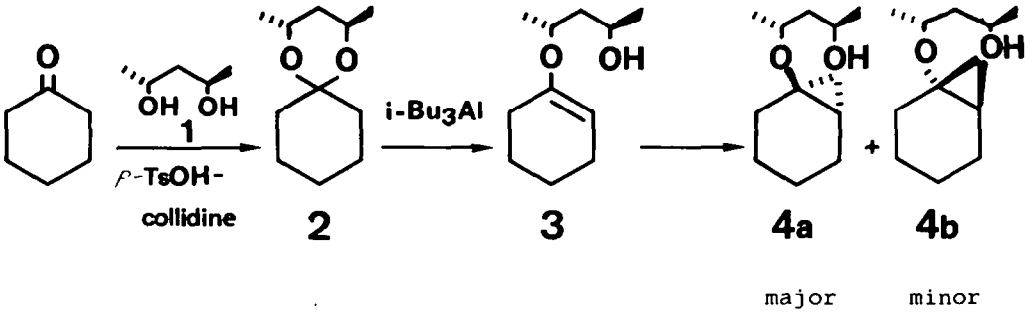


Table I. Cyclopropanations of 3 with Zn-Cu and CH_2I_2

No.	Solvent	Bath temp.(°C)	Yield(%)[a]	d.e.(%)[b]
1	ether	50	52.5	87.4
2	ether[c]	38	62.6	81.4
3	ether+DME	50	68.5	89.6
4	THF	60	64.9	80.6

a) Isolated yield by MPLC on SiO_2 as a mixture of **4a** and **4b**.
b) The ratio was determined by peak integration of capillary GLC.
c) Simmons-Smith reagent was performed before addition of **3**.

The diethylzinc/diiodomethane system is a more active reagent for cyclopropanation than the Zn-Cu/diiodomethane and is known to undergo the reaction in variety of solvents and at low temperatures. With this reagent, the investigations to improve the d.e. of the reaction system were carried out. The representative results are shown in Table II.

As is found in Table II, the d.e. and chemical yield of this reaction were considerably influenced by a solvent and an additive.

The reaction of 3 in conventional solvents proceeded smoothly and was completed within a few hours, when excess amounts of reagents(5 eq. of diethylzinc and 10 eq. of diiodomethane) was employed. The resulting d.e.'s stayed below 60 %(Table II, No.1, 3, 7, 8). In these reactions, an existence of week Lewis acid, zinc iodide, in the reaction system was found to change the product d.e. as shown in Table II.

The reactions in a little basic solvents, THF, dioxane, and DME, did not proceed as fast as those in the solvents as mentioned above but gave good d.e.'s.(Table II, No.11, 12, 16.). Especially in the case of DME, the d.e. reached to more than 95 %. An addition of zinc iodide in the system using THF as a solvent resulted in no significant change in the d.e.. Except for the requirement of long reaction time(more than 20 hr) and unsatisfactory chemical yield (55%), the reaction system, diethylzinc/diiodomethane in DME, was the most favorable one so long as 3 was used as the substrate.

Table II. Cyclopropanations of 3 with Et_2Zn and CH_2I_2

No.	Solvent[a)]	Temp.(°C)	Time(hr)	ZnI_2(% vs 3)	d.e.(Yield, %)
1	hexane	0	1.0	0	40.8 (51.8)
2		0	0.9	10[b]	69.2 (66.0)
3	benzene	20	2.5	0	49.2 (67.9)
4	CH_2Cl_2	0	2.0	0	14.2 (72.7)
5		0	1.5	10	61.0 (59.0)
6		0	1.2	100[b]	93.0 (14.8)
7	isopropyl ether	0	1.9	0	56.8 (77.3)
8	ethyl ether	0	1.9	0	-7.8 (72.5)
9		0	2.4	10	49.0 (-)
10		0	4.4	100[b]	67.6 (64.9)
11	dioxane	20	20.2	0	92.0 (58.8)
12	THF	20	2.5	0	93.6 (64.7)
13		20	2.5	10	87.4 (57.5)
14		20	2.4	100	89.6 (56.0)
15		20	4.7	500[b]	92.2 (31.0)
16	DME	20	20.5	0	95.2 (55.7)
17	diglyme	20	-	0	- (0)

a) The reaction solvent contained 40 %(v/v) of hexane.
b) Zinc iodide was saturated in the solution of 3.

The effects of solvent and zinc iodide on the d.e. and the chemical yield of the reaction were suggestive of the involvement of not a single reaction species but several substrate/solvent/reagent complexes of different activities and diastereo-differentiating abilities as reaction species. To exclude these effects and to improve d.e., the use of a substrate carrying stereochemically congested reaction center is a promising alternative approach. On the basis of this presumption, a new chiral auxiliary, 2,6-dimethyl-3,5-heptanediol(**5**)(DMHD) was designed as a bulky analogue of PD. The preparation of a practical amount of optically pure DMHD was achieved by the method established by our group.[7]

Enol ether carrying (3S,5S)-DMHD moiety(**7**) was easily prepared from cyclohexanone by the procedure employed for the preparation of **3**. The cyclopropanation of **7** with Zn-Cu/diiodomethane and diethylzinc/diiodomethane proceeded smoothly in the conventional solvent. The results were listed in Table III. As was expected, d.e.'s in all cases were excellent and chemical yields were reasonable. Especially the case employing ether as a solvent and diethylzinc/diiodomethane as a reagent gave essentially a single diastereomer with more than 80 % of chemical yield(Table III, No.4). Thus, the substitution of chiral auxiliary from PD to DMHD enabled us to establish the reaction system for the synthesis of a diastereomerically pure the [4.1.0]bicycloheptane system(**8**).

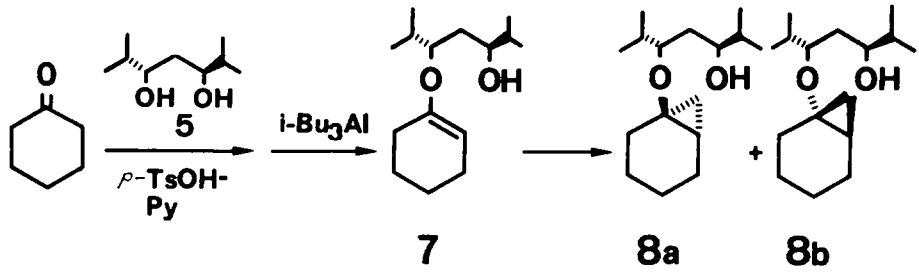


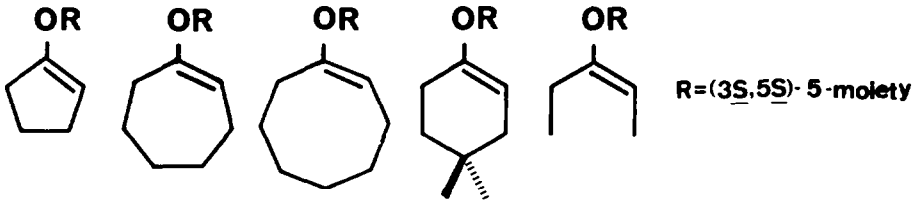
Table III. Cyclopropanations of **7**

No.	Reagent	Solvent	Bath Temp.(°C)	Yield(%)	d.e.(%)
1	Zn-Cu	ether	50	50.5	93.8
2	Et_2Zn	hexane	0	54.3	98.8
3	Et_2Zn	hexane	-40 to 0[a]	75.3	98.8
4	Et_2Zn	ether	20	86.4	>99.5
5	Et_2Zn	ether	0	72.0	99.4
6	Et_2Zn	ether	-40	59.3	95.0
7	Et_2Zn	THF	20	69.0	95.8

a) The mixture was kept for 0.5 hr at -40°C, warmed up to 0°C over 1.5 hr, and then kept for 0.5 hr at 0°C.

The optimized reaction conditions for **7** (Table III, No.4) was successfully applied to the cyclopropanation of various enol ethers listed below.

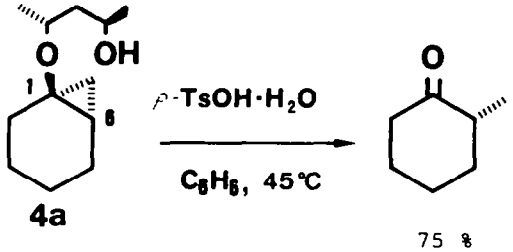
All compounds except for **13** were prepared by the method employed for the synthesis of **7**. To obtain pure (E)-**13**, the ketal of 3-pentanone had to be isomerized at -50°C, otherwise a mixture of E and Z isomers were produced. The results of cyclopropanations of **9** to **13** were summarized in Table IV. In all cases, the produced homo enol ethers, **14** to **18**, were essentially freed from the corresponding epimer.



9 **10** **11** **12** **13**

Table IV. Cyclopropanations of various enol ethers

Original ketone	Substrate	Yield(%)	d.e.(%)	Configuration
Cyclopentanone	**9**	80.7	>99	
Cycloheptanone	**10**	77.2	>99	(1S,7S)
Cyclooctanone	**11**	58.2	>99	(1S,8S)
4,4-Dimethylcyclohexanone	**12**	80.0	>99	
3-Pentanone	**13**	57.1	>99	

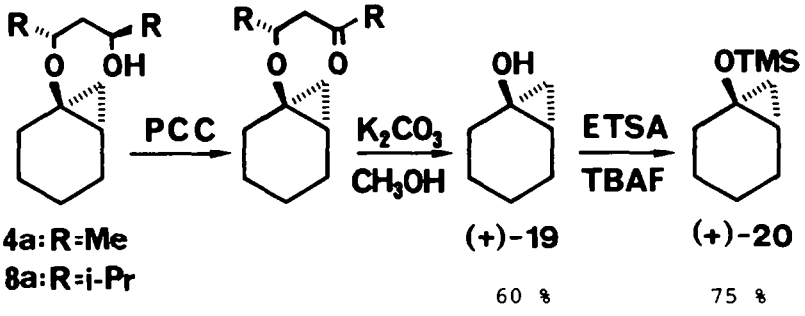


4a 75 %

The configurations of cyclopropane ring of a major diastereomer, **4a**, were determined to be (1S,6S) by the chemical correlation with (-)-(R)-2-methylcyclohexanone[8] as shown in the above equation. Those of **8a** were also determined to be (1S,6S) because **8a** as well as **4a** was transformed to an optically active cyclopropanol, (+)-**19**, as is depicted below. The configurations of **15** and **16** were also determined to be (1S,7S) and (1S,8S)

by the correlation with (-)-(R)-2-methylcycloheptanone[9] and (-)-(R)-2-methylcyclooctanone,[10] respectively, while those of **14**, **17**, and **18** were not yet determined owing to the lack of stereochemical data of the corresponding 2-methyl ketones. On the basis of the configuration of the products so long as confirmed, diastereo-differentiating cyclopropanation was conducted by the attack of reagent from si-re face of the substrates when (2R,4R)-PD or (3S,5S)-DMHD was employed as a chiral auxiliary.

From **4a** and **8a**, the chiral auxiliaries were removed by an ordinary method. That is, oxidation of **4a** or **8a** with pyridinium chlorochromate followed by the treatment with potassium carbonate in methanol gave an optically active cyclopropanol(**19**) and 4-methoxy-2-pentanone or 2,6-dimethyl-5-methoxy-3-heptanone. An optically active siloxycyclopropane(**20**), a more synthetically useful intermediate than **19**, could be obtained by the treatment of **19** with ethyl trimethylsilylacetate and tetrabutylammonium fluoride.



Besides the finding of excellent diastereo-differentiating cyclopropanation, present result demonstrated that PD and DMHD could be utilized as excellent chiral auxiliaries not only as cyclic ketal or acetal derivatives already documented, but also as acyclic mono ether derivatives.

Experimental Section

General

All melting points are uncorrected. ^{1}H-NMR(400 MHz) and ^{13}C-NMR(100 MHz) were recorded on a JEOL GX-400 spectrometer in $CDCl_3$ or C_6D_6 as solvents and as internal standards(7.26 ppm or 7.20 ppm). IR spectra were obtained on a JASCO IR-810 spectrometer. Optical rotations were measured on a JASCO DIP-360 or Perkin-Elmer 243B polarimeter. Analytical GLC was conducted with a Hitachi gas chromatograph G-3000 using PEG-20M capillary column(50m-0.25 mm i.d.). MPLC was carried out by using a FMI pump(10 ml/min) and a Lobar column(MERCK Si-60 type B). Dry diethyl ether and THF were distilled from sodium-benzophenone ketyl and the other dry solvents

were distilled from calcium hydride. Diiodomethane was purified by passing aluminum column before use. Diethylzinc was obtained from commercial source(Kanto Kagaku, Co.). All reactions were carried out under dry nitrogen atmosphere.

Preparation of 2

A solution of cyclohexanone(9.60 ml, 92.6 mmol), 1(10.52g, 101.0 mmol) and collidinium tosylate(100 mg) in benzene(250 ml) was azeotropically refluxed for two days. A mixture after extraction was fractionally distilled to give 2(14.15 g, 82.9 % yield). b.p. 72.0-73.2 °C/7mmHg; $[\alpha]_D^{20}$=-29.4(c 1.0, CH_2Cl_2); Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.25; H, 11.20%; ^{1}H-NMR($CDCl_3$) δ 3.98(m, J=7.3, 6.4 Hz, 2H), 1.67-1.50(m, 10H), 1.41-1.35(m, 2H), 1.19(d, J=6.4 Hz, 6H).

Preparation of 3

To a solution of 2(4.42 g, 24.0 mmol) in dry dichloromethane(240 ml) was added a hexane solution of triisobutylaluminum(120 ml, 120 mmol) for 25 minutes at 0°C. The mixture was stirred for 2 hours and poured into 1N aqueous sodium hydroxide(400 ml) followed by extraction with dichloromethane(4 times) and drying over sodium sulfate. Evaporation of the solvent gave 5.2 g of 3(96.7 % yield). $[\alpha]_D^{20}$=-54.78(c 1.2, CH_2Cl_2); ^{1}H-NMR(C_6D_6) δ 4.70(t, J=3,9 Hz, 1H), 4.35(m, 1H), 4.00(m, 1H), 2.12-2.04(m, 4H), 1.62-1.44(m, 7H), 1.17(d, J=6.3 Hz, 3H), 1.08(d, J=6.3 Hz, 3H); IR(neat, cm^{-1}) 3360(OH).

Cyclopropanation of 3 with Zn-Cu

A mixture of 3(1.88 g, 10.2 mmol) and diiodomethane(1.8 ml, 2.2 eq.) in ether (4 ml) was added to a stirred suspension of zinc-copper couple(2.77 g) prepared from zinc dust and copper acetate in ether(6.6 ml) at room temperature. Reflux occurred in ten minutes and the moderate refluxing was kept for 2.5 hours by heating. The reaction mixture was quenched with water(20 ml) and filtered through celite to remove excess zinc followed by extraction. The crude product was purified by MPLC on silica gel(elution with 20% ethyl acetate in hexane) to give a mixture of **4a** and **4b**(1.02g, 50.7 % yield). The reactions in the other solvents stated in Table II in the text were carried out the same procedure except the solvent and the reaction time. The ratio of **4a** and **4b** was determined to be 93.2 : 6.8 by capillary GLC analysis(110 °C, retention time 30.6 min and 32.2 min, respectively). The ^{13}C-NMR of **4** showed twelve pairs of signals which were assigned as follows by comparison with the spectrum of pure **4a**. ^{13}C-NMR($CDCl_3$) for **4a**: δ 70.45, 64.48, 59.65, 45.27, 29.29, 24.36, 23.66, 21.73, 21.44, 21.08, 18.44, 17.79.; for **4b**: δ 70.91, 64.42, 60.09, 45.52, 29.90, 24.40, 23.75, 21.95, 21.66, 21.23, 19.79, 16.82.

Purification of **4a**

A mixture(1.75 g) of **4a** and **4b** obtained above was dissolved in minimum amount of ether and cooled to -20 °C. The resulting crystals was subjected to recrystallization five times to give 741 mg of pure **4a**. m.p. 32.8 °C; $[\alpha]_D^{20}$=-23.5(C 1.0, methanol); Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.38; H, 11.25%. ^{1}H-NMR($CDCl_3$) δ 4.10-4.03(m, 2H), 3.10(d, J=2.9

Hz, 1H), 2.12(dt, J=8.3, 4.9 Hz, 1H), 2.00-1.93(m, 2H), 1.63-1.59(m, 1H), 1.51-1.38(m, 3H), 1.27-1.04(m, 4H), 1.20(d, J=6.4 Hz, 3H), 1.16(d, J=6.4 Hz, 3H), 0.88(ddd, J=10.7, 5.4, 1.5 Hz, 1H), 0.29(dd, J=6.4, 5.4 Hz, 1H); IR(neat, cm^{-1}) 3450(OH).

Cyclopropanation of 3 with diethylzinc and diiodomethane

To a solution of **3** in the solvent shown in Table II in the text was added a listed amount of zinc iodide and stirred for 30 minutes, and then 5 eq. of diethylzinc was added at 0 °C except in the case of THF(20 °C). To this solution 10 eq. of diiodomethane was added dropwise and the mixture was stirred at the same temperature until **3a** disappeared. The mixture of **4a** and **4b** was isolated by MPLC and analyzed by capillary GLC.

Preparation of 6

A benzene solution of cyclohexanone(3.1 ml, 29.9 mmol) and (3S,5S)-**5**(5.21 g, 32.5 mmol) in the presence of pyridinium tosylate was azeotropically refluxed for three days. The extracted and concentrated mixture was purified by MPLC on silica gel(elution with 20 % ethyl acetate in hexane) to give 6.27 g of **6**(87.3 % yield). $[\alpha]_D^{20}$=-31.7(c 1.0, $CHCl_3$); Anal. Calcd for $C_{15}H_{28}O_2$: C, 74.95; H, 11.74. Found: C, 74.76; H, 11.61%. ^{1}H-NMR($CDCl_3$) δ 3.37(q, J=7.8Hz, 2H), 1.70-1.50(m, 12H), 1.41-1.37(m, 2H), 0.94(d, J=6.4 Hz, 6H), 0.85(d, J=6.4 Hz, 6H).

Ketalization of ketones with 5

From the cyclopentanone, cycloheptanone, cyclooctanone, 4,4-dimethylcyclohexanone, and 3-pentanone, the corresponding ketals were obtained by the same method as those of **6** in yields of 80-90 %.

Cyclopentanone ketal: $[\alpha]_D^{20}$=-16.0(c 1.0, CH_2Cl_2); Anal. Calcd for $C_{14}H_{26}O_2$: C, 74.29; H, 11.58. Found: C, 73.45; H, 11.66 %.; ^{1}H-NMR($CDCl_3$) δ 3.30(td, J=8.0, 7.8 Hz, 2H), 1.79(m, 2H), 1.70-1.52(m, 10H), 0.93(d, J=6.6 Hz, 6H), 0.85(d, J=6.6 Hz, 6H).

Cycloheptanone ketal: $[\alpha]_D^{20}$=-19.4(c 1.2, CH_2Cl_2); Anal. Calcd for $C_{16}H_{30}O_2$: C, 75.54; H, 11.89. Found: C, 75.48; H, 11.54 %.^{1}H-NMR($CDCl_3$) δ 3.34(q, J=8.1 Hz, 2H), 2.00-1.94(m, 2H), 1.71-1.42(m, 14H), 0.93(d, J=6.5 Hz, 6H), 0.85(d, J=6.7 Hz, 6H).

Cyclooctanone ketal: $[\alpha]_D^{20}$=-12.6(c 1.1, CH_2Cl_2); Anal. Calcd for $C_{17}H_{32}O_2$: C, 76.06 ; H, 12.02. Found: C, 75.76; H, 11.89.; ^{1}H-NMR($CDCl_3$) δ 3.32(q, J=7.8 Hz, 2H), 1.92(m, 2H), 1.69(m, 2H), 1.67-1.45(m, 14H), 0.93(d, J=6.6 Hz, 6H), 0.84(d, J=6.6 Hz, 6H).

4,4-Dimethylcyclohexanone ketal: $[\alpha]_D^{20}$=-21.5(c 1.1, CH_2Cl_2); Anal. Calcd for $C_{17}H_{32}O_2$: C, 76.06;H, 12.01. Found: C, 75.64; H, 12.14 %.; ^{1}H-NMR($CDCl_3$) δ 3.38(td, J=8.0, 7.8 Hz, 2H), 1.71-1.55(m, 8H), 1.35(t, J=6.5, 4H), 0.94(d, J=6.6 Hz, 6H), 0.92(s, 6H), 0.85(d, J=6.8 Hz, 6H).

3-Pentanone ketal: $[\alpha]_D^{20}$=-20.9(c 1.1, CH_2Cl_2); Anal. Calcd for $C_{14}H_{28}O_2$: C, 73.63 ;H, 12.36. Found: C, 71.56;H, 12.13 %.^{1}H-NMR($CDCl_3$) δ 3.35(q, J=7.8 Hz, 2H), 1.70(m, 2H), 1.64-1.45(m, 6H), 0.94(d, J=6.8 Hz, 6H), 0.85(d, J=6.8 Hz, 6H), 0.84(t, J=7.4 Hz, 6H).

Preparation of 7

To a solution of **6**(2.75 g, 11.5 mmol) in dry dichloromethane(110 ml)

was added a hexane solution of triisobutylaluminum(58 ml, 58 mmol) for 25 minutes at 0°C. The mixture was stirred for 2 hours and poured into 1N sodium hydroxide aqueous solution(200 ml) followed by extraction with dichloromethane(3 times) and drying over sodium sulfate. Evaporation of the solvent gave 2.69 g of **7**(97.7 % yield). $[\alpha]_D^{20}$=-27.5(c 1.1, CH_2Cl_2); ^{1}H-NMR(C_6D_6) δ 4.86(t, J=3.9 Hz, 1H), 4.26(m, 1H), 3.62(m, 1H), 2.18-2.06(m 5H), 1.70-1.44(m, 8H), 0.97(d, J=6.8 Hz, 3H), 0.96(d, J=6.8 Hz, 3H), 0.92(d, J=6.8 Hz, 3H), 0.89(d, J=6.8 Hz, 3H); IR(neat, cm^{-1}) 3450(OH).

Preparations of **9**, **10**, **11**, **12**, and **13**

These compounds were obtained from corresponding ketals by the same method as above except **13**, which was prepared at -50 °C(6 hour). The product yields are shown in parentheses.

9(74.7%): ^{1}H-NMR(C_6D_6) δ 4.59(m, 1H), 4.20(m, 1H), 3.61(m, 1H), 2.44-2.35(m, 4H), 2.07(m, 1H), 1.92-1.51(m, 6H), 0.96(d, J=6.9 Hz, 3H), 0.94(d, J=6.9 Hz, 3H), 0.93(d, J=6.9 Hz, 3H), 0.88(d, J=6.9 Hz, 3H); IR(neat, cm^{-1}) 3460(OH).

10(100%): ^{1}H-NMR(C_6D_6) δ 4.98(t, J=6.8 Hz, 1H), 4.13(m, 1H), 3.63(m, 1H), 2.35(dd, J=6.8, 2.9 Hz, 2H), 2.12-2.06(m 3H), 1.69-1.48(m, 10H), 0.98(d, J=6.8 Hz, 3H), 0.96(d, J=6.8 Hz, 3H), 0.92(d, J=6.8 Hz, 3H), 0.91(d, J=6.8 Hz, 3H); IR(neat, cm^{-1}) 3480(OH).

11(58.9%): ^{1}H-NMR(C_6D_6) δ 4.68(t, J=8.1 Hz, 1H), 4.19(m, 1H), 3.64(m, 1H), 2.31-2.24(m, 2H), 2.15-2.09(m, 3H), 1.71-1.52(m, 12H), 0.98(d, J=6.8 Hz, 3H), 0.96(d, J=6.8 Hz, 3H), 0.92(d, J=6.8 Hz, 3H), 0.91(d, J=6.8 Hz, 3H); IR(neat, cm^{-1}) 3480(OH).

12(87.9%): ^{1}H-NMR(C_6D_6) δ 4.79(t, J=3.4 Hz, 1H), 4.24(m, 1H), 3.64(m, 1H), 2.19(tm, J=6.6 Hz, 2H), 2.06(m, 1H), 1.92-1.90(m, 2H), 1.70-1.54(m, 4H), 1.35(t, J=6.6 Hz, 2H), 0.97(d, J=6.8 Hz, 6H), 0.96(s, 3H), 0.95(s, 3H), 0.93(d, J=6.8 Hz, 3H), 0.90(d, J=6.8 Hz, 3H); IR(neat, cm^{-1}) 3480(OH).

13(73.9%): ^{1}H-NMR(C_6D_6) δ 4.56(q, J=6.8 Hz, 1H), 4.19(m, 1H), 3.60(m, 1H), 2.21-2.06(m, 4H), 1.69-1.52(m, 3H), 1.60(d, J=6.8 Hz, 3H), 1.14(t, J=7.6 Hz, 3H), 0.96(d, J=6.8 Hz, 3H), 0.94(d, J=6.8 Hz, 3H), 0.92(d, J=6.8 Hz, 3H), 0.90(d, J=6.8 Hz, 3H); IR(neat, cm^{-1}) 3450(OH).

Cyclopropanation of **7**

To a solution of **7**(333 mg, 1.39 mmol) in dry ether(10.3 ml) was added diethylzinc(10.3 ml, 1M in hexane) at 24 °C and stirred for a minute. To this mixture diiodomethane(1.2 ml, 14.9 mmol) was added dropwise for ten minutes, and then allowed to stand for two hours at the same temperature. The reaction mixture was poured into aqueous ammonium chloride, extracted with ether(twice), dried over magnesium sulfate, and purified by MPLC on silica gel(elution with 6% ethyl acetate in hexane) to give 304.4 mg as colorless oil(86.3 % yield, >99.5 % d.e.). Anal. Calcd for $C_{16}H_{30}O_2$: C, 75.54; H, 11.89. Found: C, 75.26; H, 11.92 %. ^{1}H-NMR($CDCl_3$) δ 3.61-3.55(m, 2H), 3.10(brs, 1H), 2.12(dt, J=13.2, 5.4 Hz, 1H), 2.07-1.95(m, 3H), 1.67-1.36(m, 5H), 1.31-1.15(m, 4H), 1.05(m, 1H), 0.93(d, J=6.8 Hz, 3H), 0.89(d, J=6.8 Hz, 3H), 0.87(d, J=6.8 Hz, 3H), 0.82(d, J=6.8 Hz, 3H), 0.26(dd, J=6.4, 5.4 Hz, 1H); ^{13}C-NMR($CDCl_3$) δ 80.29, 73.43, 60.46, 34.06, 33.05, 30.22, 30.10, 24.46, 21.88, 21.51, 19.78, 18.55, 17.87, 17.78, 17.56; IR(neat, cm^{-1}) 3500(OH).

Cyclopropanations of **9**, **10**, **11**, **12**, and **13**

The reaction conditions and purification methods were the same as above. The product yields are shown in parentheses.

Cyclopropane(14) from 9(80.7%). ^{1}H-NMR($CDCl_3$) δ 3.63(m, 1H), 3.54(m, 1H), 3.05(bs, 1H), 2.08-1.95(m, 3H), 1.82(m, 1H), 1.69-1.56(m, 4H), 1.51-1.42(m, 2H), 1.10(m, 1H), 0.94(d, J=6.8 Hz, 3H), 0.90(d, J=6.8 Hz, 3H), 0.89(d, J=6.8 Hz, 3H), 0.83(d, J=6.8 Hz, 3H), 0.83(m, 1H), 0.55(t, J=5.1 Hz, 1H); ^{13}C-NMR($CDCl_3$) 82.23, 73.34, 69.35, 34.02, 32.86, 31.79, 30.02, 26.18, 23.54, 21.34, 19.69, 18.52, 17.84, 17.60, 13.97; IR(neat, cm^{-1}) 3500(OH); MS,m/z(M+) calcd for $C_{15}H_{28}O_2$ 240.2.89, obsd 240.2101.

Cyclopropane(15) from 10(77.2%). ^{1}H-NMR($CDCl_3$) δ 3.64-3.57(m, 2H), 3.06(d, J=3.7 Hz, 1H), 2.53(dd, J=15.1, 7.1 Hz, 1H), 2.15-1.98(m, 2H), 1.84-1.37(m, 9H), 1.24-1.04(m, 4H), 0.94(d, J=6.8 Hz, 3H), 0.90(d, J=6.8 Hz, 3H), 0.86(d, J=6.8 Hz, 3H), 0.81(d, J=6.8 Hz, 3H), 0.24(m, 1H); ^{13}C-NMR($CDCl_3$) 79.17, 73.21, 65.05, 33.93, 33.60, 33.00, 31.99, 31.47, 29.90, 28.91, 25.69, 24.27, 21.96, 19.71, 18.44, 17.72, 17.06; IR(neat, cm^{-1}) 3500(OH); MS,m/z(M+) calcd for $C_{17}H_{32}O_2$ 270.2559, obsd 270.2553.

Cyclopropane(16) from 11(58.2%). ^{1}H-NMR($CDCl_3$) δ 3.66(m, 1H), 3.58(m, 1H), 3.16(d, J=2.9Hz, 1H), 2.35(dt, J=15.4, 3.7 Hz, 1H), 2.09(m, 1H), 1.98-1.83(m, 2H), 1.71-1.27(m, 12H), 1.04(ddd, J=16.8, 13.2, 3.7 Hz, 1H), 0.93(d, J=6.6 Hz, 3H), 0.90(d, J=6.8 Hz, 3H), 0.86(d, J=6.8 Hz, 3H), 0.80(d, J=6.6 Hz, 3H), 0.86(m, 1H), -0.09(m, 1H); ^{13}C-NMR($CDCl_3$) 79.41, 73.50, 62.47, 34.00, 33.19, 29.24, 29.05, 28.69, 26.57, 26.15, 25.35, 24.17, 19.74, 18.52, 17.85, 17.49, 17.42; IR(neat, cm^{-1}) 3500(OH); MS,m/z(M+1) calcd for $C_{18}H_{35}O_2$ 283.2637, obsd 283.2669.

Cyclopropane(17) from 12(80.0%). ^{1}H-NMR($CDCl_3$) δ 3.64-3.57(m, 2H), 3.26(d, J=2.9 Hz, 1H), 2.15-1.95(m, 3H), 1.77(ddd, J=14.2, 9.3, 2.4 Hz, 1H), 1.69-1.56(m, 4H), 1.30-1.15(m, 2H), 1.04-0.84(m, 2H), 0.94(d, J=6.8 Hz, 3H), 0.93(s, 3H), 0.89(d, J=6.8 Hz, 3H), 0.88(d, J=6.8 Hz, 3H), 0.82(d, J=6.8 Hz, 3H), 0.79(s, 3H), 0.14(t, J=6.1 Hz, 1H); ^{13}C-NMR($CDCl_3$) 80.26, 73.32, 59.67, 39.28, 34.19, 33.94, 32.94, 31.56, 30.03, 28.11, 25.84, 25.33, 19.79, 18.42, 17.88, 17.55, 16.95; IR(neat, cm^{-1}) 3500(OH); MS,m/z(M+) calcd for $C_{18}H_{34}O_2$ 282.2559, obsd 282.2541.

Cyclopropane(18) from 13(57.1%). ^{1}H-NMR($CDCl_3$) δ 3.57-3.52(m, 2H), 2.70(d, J=3.9 Hz, 1H), 2.02(m, 1H), 1.71-1.43(m, 5H), 1.18(m, 1H), 1.09(t, J=7.3 Hz, 3H), 1.04(d, J=6.4 Hz, 3H), 0.92(d, J=6.8 Hz, 3H), 0.91(m, 1H), 0.89(d, J=7.1 Hz, 3H), 0.87(d, J=7.3 Hz, 3H), 0.85(d, J=6.8 Hz, 3H), -0.03(dd, J=6.6, 5,4 Hz, 1H); ^{13}C-NMR($CDCl_3$) 79.48, 73.47, 65.38, 34.13, 33.04, 30.52, 24.59, 19.83, 19.66, 18.68, 18.27, 17.77, 17.27, 14.28, 10.35; IR(neat, cm^{-1}) 3500(OH); MS,m/z(M+1) calcd for $C_{15}H_{31}O_2$ 243.2324, obsd 243.2334.

Conversion of **4a** to 2-methylcyclohexanone

A solution of **4a**(208 mg) and p-toluenesulfonic acid monohydrate(2.01 g, 10.58 mmol) in benzene(18 ml) was stirred at 45 °C for 1.5 hours. The mixture was extracted and purified by preparative GLC(OV-101, 3m, 110 °C) to give 2-methylcyclohexanone(62.8 mg, 53.3 % yield). $[\alpha]_D^{20}$=-2.07(c 0.63, methanol, 15 %e.e.).

(+)-(1S,6S)-1-bicyclo[4.1.0]heptanol(**19**) from **4a**

To a solution of **4a**(100.2 mg) in dry dichloromethane(10 ml) was added pyridinium chlorochromate(164.5 mg, 1.5 eq.) at one portion at room temperature and the mixture was stirred for four hours. The mixture was worked up by an ordinary method and purified by MPLC on silica gel(elution with 20 % ethyl acetate in hexane) to give 66.5 mg of a ketone(67 % yield). $[\alpha]_D^{20}$=6.94(c 0.66, CH_2Cl_2), ^{1}H-NMR($CDCl_3$) δ 4.19(qt, J=6.4, 6.4 Hz, 1H), 2.70(dd, J=16.1, 6.4 Hz, 1H), 2.41(dd, J=16.1, 6.4 Hz, 1H), 2.15(s, 3H), 2.08(dt, J=13.2, 5.4 Hz, 1H), 2.00(m, 2H), 1.51-1.38(m, 2H), 1.30-1.03(m, 4H), 1.17(d, J=6.4 Hz, 3H), 0.86(ddd, J=10.7, 4.9, 1.0 Hz, 1H), 0.28(dd, J=6.4, 4.9 Hz, 1H); IR(neat, cm^{-1}) 1720(C=O). A solution of the ketone(61.1 mg) given above in methanol(2.3 ml) was stirred with potassium carbonate(334.4 mg) at room temperature for two hours. The resulting mixture was extracted and purified on preparative GLC(OV-101, 3 m, 110 °C) to give **19** as colorless oil(19.9 mg, 57.1 % yield), of which NMR and IR spectra were identical with those of racemic **19**. $[\alpha]_D^{20}$=12.0(c 0.2, methanol).

Preparation of (+)-**19** from **8**

To a solution of **8**(149 mg, 0.59 mmol) in dry dichloromethane(7 ml) was added pyridinium chlorochromate(190.7 mg, 1.5 eq.) at one portion at room temperature and the mixture was stirred for 3.5 hours. The mixture was worked up by ordinary method and purified by MPLC on silica gel(elution with 20 % ethyl acetate in hexane) to give 123 mg of a ketone(83.2 % yield). ^{1}H-NMR($CDCl_3$) δ 3.99(m, 1H), 2.68(dd, J=16.6, 6.8 Hz, 1H), 2.59(heptet, J=6.8 Hz, 1H), 2.44(dd, J=16.6, 5.4 Hz, 1H), 2.03(dt, J=13.7, 5.4 Hz, 1H), 1.99-1.80(m, 3H), 1.48-1.35(m, 2H), 1.28-0.93(m, 5H), 1.09(d, J=6.8 Hz, 3H), 1.08(d, J=6.8 Hz, 3H), 0.84(d, J=6.8 Hz, 3H), 0.81(d, J=6.8Hz, 3H), 0.24(dd, J=6.4, 5.4 Hz, 1H); IR(neat, cm-1) 1720(C=O). A solution of the ketone(123 mg) given above in methanol(3.6 ml) was stirred with potassium carbonate(533 mg) at room temperature for four hours. The resulting solution was extracted and purified by MPLC on silica gel(elution with 20 % ethyl acetate in hexane) to give **19** as colorless oil. $[\alpha]_D^{20}$=16.6(c 1.0, methanol).

(+)-(1S,6S)-1-trimethylsiloxybicyclo[4.1.0]heptane(**20**)

A solution of **19**(123 mg, 1.10 mmol) and ethyl trimethylsilylacetate(0.23 ml, 1.32 mmol) in THF(1 ml) was added to pre-dried tetrabutylammonium fluoride(6.2 mg, 0.02 eq.) at 0 °C, and allowed to stand for one hour at the same temperature. The mixture was diluted with hexane(5 ml) and filtered through silica gel column. After evaporation of the solvent, the residue was purified by MPLC on silica gel(elution with 10 % ethyl acetate in hexane) to give 138 mg of **20**, whose NMR and IR spectra were identical with those of racemic **20**. $[\alpha]_D^{20}$=26.0(c 1.0, methanol).

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