=2 : 1, which gave 50 mg (20%) of **16**: mp 186.5-186.9 ℃; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.90 (t, J=12.0 Hz, 6H, CH_3), 0.99 (t, J=12.0 Hz, 6H, CH_3), 1.15-1.70 (m, 24H, $(CH_2)_3CH_3$), 2.00-2.15 (m, 4H, $CHCH_2$), 2.30 (d, J=12.0 Hz, 4H, SCH_2), 2.30-2.40 (m, 4H, $CHCH_2$), 4.13 (d, J=12.0 Hz, 4H, SCH_2), 4.17 (d, J=8.1 Hz, 2H, H-C-H_{in}), 4.67 (t, J=18.0 Hz, 2H, $CHCH_2$), 4.86 (d, J=8.0 Hz, 2H, H-C-H_{in}), 5.40 (t, J=20.0 Hz, 2H, $CHCH_2$), 5.50 (d, J=8.1 Hz, 2H, H-C-H_{out}), 6.20 (d, J=8.0 Hz, 2H, H-C-H_{out}), 7.16 (s, 4H, ArH), 7.15-7.25 (m, 8H, ArH); FAB MS m/z 1149 (M^+, 100%).

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A Synthetic Route to a C_2-Symmetrical Alkoxyketone

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Asymmetric induction is one of the most tackling targets in the area of organic synthesis. For this purpose, chiral auxiliaries have been frequently employed and are being developed increasingly.[1] Among various classes of auxiliaries, C_2-symmetry chiral ligands,[2] whether natural or synthetic, play a critical role in the scenario, providing exceedingly high levels of absolute stereochemical control.[3] Therefore, searching for better ligands is an unabating endeavor in terms of better economy as well as higher efficiency.

For this purpose, we became interested in C_2-symmetrical ketones.[4] C_2-Symmetric ketones have been quite rarely utilized in the area, probably because those compounds are not naturally abundant or have not been elaborated enough for useful reactions.[4f] However, we envisioned that chiral C_2-symmetric ketones could be served as distinctive chiral auxiliaries, and designed a simple dialkoxyketone derivative **1** as a trial entrant. First we decided to secure a potentially divergent pathway to this class. In this note, we briefly describe a reliable route to **1** from a natural chiral source.

Initial attempts to differentiate hydroxy groups of **2**[5] *via* selective protections proved to be impractical (Scheme 1).[6] 6-Membered benzylidene **3** was formed as a major product over **4** in *ca.* 4 : 1 to 6 : 1 ratios,[7] however, difficulties in separation of the two made us seek an alternative pathway.

We counted that diepoxide **7** should be an appropriate precursor for the ketone **1**. Selective epoxide opening from the less hindered site would provide the desired hydroxy groups at the proper positions. Amberite resin treatment of bischloride **5** and the corresponding regioisomers formed

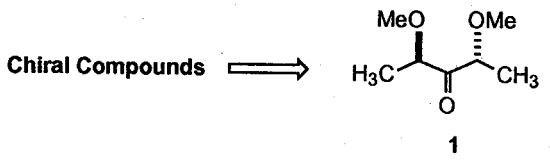

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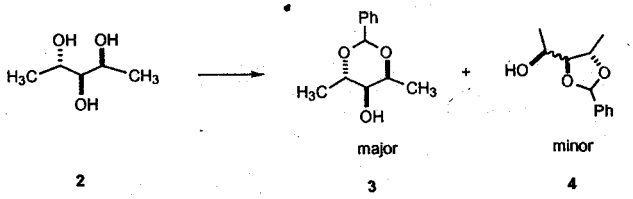
Figure 1.



2 **3** **4**

Scheme 1.

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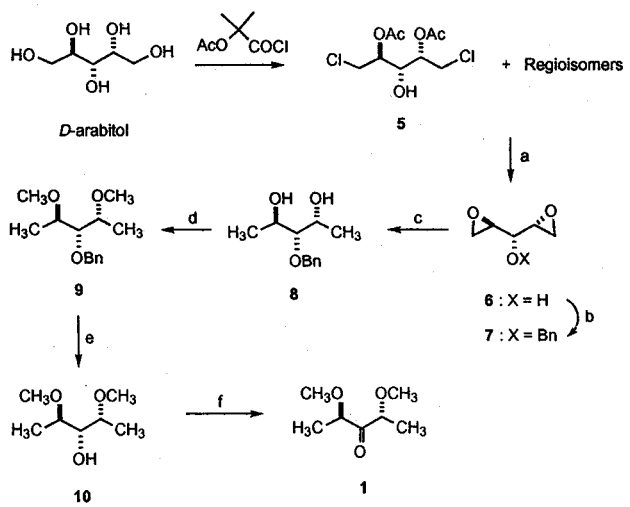

Reagents : (a) Amberite IRA 400(- OH), MeOH (b) NaH, BnBr, TBAI, THF (c) LAH, Et_2O (d) CH_3I, NaH, THF (e) $Pd(OH)_2/C$, EtOH, Cyclohexene (f) TPAP, TMNO, 4A° Sieves, CH_2Cl_2

Scheme 2.

from *D*-arabitol with Moffatt reagent yielded diepoxide **6** in 84% yield reproducibly.[8,9] The hydroxy group of compound **6** was converted upon reaction with benzyl bromide in THF in the presence of NaH to diepoxybenzyl ether **7** in 41% yield. Conversion of **7** to diol **8** was performed by a reductive opening of epoxide using LAH in ether (87% yield). The corresponding dimethyl ether **9** was readily provided by treating the diol **8** with MeI in THF in 87% yield. And debenzylation of **9** to the precursor **10** was carried out in refluxing EtOH containing palladium hydroxide on carbon and cyclohexene as a hydrogen source in quantitative yield. At this stage, oxidation of **10** would afford the desired ketone **1** finally. The most reliable condition found so far was treating **10** with 5 mol % of tetrapropylammonium perruthenate (TPAP) using trimethyl *N*-oxide as an oxidant in methylene chloride,[9] providing **1** in 65% yield.

According to this practical sequence, many analogous derivatives could be prepared by employing different nucleophiles for the epoxide opening and electrophiles for the protection of the corresponding diol intermediates. Antipodes would be also available from *L*-arabitol. And as we have the ketone in hand, an investigation of its utility for chiral induction will be pursued.

Experimental

General. All commercial chemicals were used as obtained without further purification, and all solvents were carefully dried and distilled by standard methods prior to use. Column chromatography was carried out on silica gel 60 (E. Merck, 230-400 mesh) with the flash technique. Melting points were determined on a Thomas-Hoover melting point apparatus and uncorrected. Nuclear magnetic resonance spectra were determined on a Bruker ARX 300 spectrometer. Chemical shifts are reported in δ ppm relative to $(CH_3)_4Si$ for ^1H and ^{13}C NMR. Coupling constants, J are reported in Hz. Infrared spectra (cm^{-1}) were obtained on a Nicolet 710 FT-IR spectrometer. GC-mass analysis was performed on a Hewlet -Packard 5890- MSD 5971 series equipped with a capillary column(HP 1, 25 m).

(2*R*,4*R*)-1,2;4,5-Diepoxy-3-pentanol (6). To a solution of bischloride **5** (4.01 g, 14.68 mmol) in methanol was added Amberite IRA 400 (OH^-) ion exchange resin (10 g) at 0 ℃. The solution was stirred for 30 min at 0 ℃ and 40 min more after removing ice bath. After filtering the resin, the solution was concentrated under reduced pressure at 0 ℃ and the resulting oil was chromatographed (pentane : ether=2 : 3 and then 1 : 3) to afford 1.44 g (84% yield) of diepoxide **6**: ^1H NMR ($CDCl_3$) δ 3.55 (t, J=4.6 Hz, 1H), 3.20-3.05 (m, 2H), 2.89-2.78 (m, 4H), 2.3 (br. s, 1H).

(2*R*,4*R*)-1,2;4,5-Diepoxy-3-benzyloxy-pentane (7). To a THF solution (20 mL) of hydroxy diepoxide **6** (1.44 g, 12.40 mmol) at 0 ℃ was added NaH (95%, 1.3 eq.). After 5 min, the solution became homogeneous, ice bath was removed and tetrabutylammonium iodide (0.2 eq.) and benzyl bromide (1.5 eq) was added. After 3 hr, saturated aqueous $NaHCO_3$ was added and the solution was extracted with 1 : 1 mixture of hexane : ethyl acetate. The extracts were dried over Na_2SO_4, and the solvent was removed on the rotatory evaporator. Purification of the mixture by column chromatography on silica gel using hexane-ethyl acetate (5 : 1) gave diepoxy benzyl ether **7** (1.65 g, 41% yield): ^1H NMR ($CDCl_3$) δ 7.5-7.2 (m, 5H), 4.78, 4.67 (2d, J=11.9 Hz, 2H), 3.18 (m, 1H), 3.08 (m, 1H), 2.99 (t, J=5.7 Hz, 1H), 2.83 (m, 2H), 2.67 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 137.9, 128.4, 127.8, 79.7, 72.2, 52.7, 50.0, 45.4, 43.2.

1,5-Dideoxy-3-benzyl-*D*-arabitol (8). $LiAlH_4$ (0.65 g, 3eq.) was slowly added to an Et_2O solution of diepoxide **7** (1.07 g, 5.19 mmol) at 0 ℃. After 1 hr at 0 ℃, the reaction mixture was allowed to come to room temperature over 2 hr and then was quenched by sequential addition of H_2O (5 mL), 15% NaOH (5 mL), and additional H_2O (15 mL). After stirring 2 hr at room temperature, the precipitates were separated by filteration and washed with ethyl acetate. The resulting filtrate was washed with saturated aqueous solution and dried over $MgSO_4$. Removal of solvent provided an oil which was chromatographed (hexane : ethyl acetate=3 : 2) to afford diol **8** (0.95 g, 86% yield): ^1H NMR ($CDCl_3$) δ 7.4-7.2 (m, 5H), 4.74, 4.64 (2d, J=11.5 Hz, 2H), 4.2-3.8 (m, 2H), 3.16 (dd, J=4.4, 3.9 Hz, 1H), 2.71 (d, J=5.8 Hz, 1H), 2.49 (d, J=5.1 Hz, 1H), 1.27 (d, J=5.1 Hz, 3H), 1.25 (d, J=5.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 138.3, 28.8, 128.2, 85.1, 74.0, 68.2, 67.5, 19.9, 19.5.

1,5-Dideoxy-2,4-dimethyl-3-benzyl-*D*-arabitol (9). To a solution of diol **8** (0.94 g, 4.4 mmol) in THF was added NaH (95%, 0.54 g, 3eq.) at 0 ℃ and methyl iodide (0.84 mL, 3eq.) after 10 min. After stirring at room temperature for 2 hr, the reaction mixture was diluted with ethyl acetate and washed with saturated aqueous $NaHCO_3$ solution. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on silica gel with hexane-ethyl acetate (10 : 1) to afford 0.93 g (87% yield) of **9**: ^1H NMR ($CDCl_3$) δ 7.4-7.2 (m, 5H), 4.74, 4.64 (2d, J=11.4 Hz, 2H), 3.55-3.42 (m, 2H), 3.36, 3.34 (2s, 6H), 3.4-3.25 (m, 1H), 1.24 (d, J=6.2 Hz, 3H), 1.15 (d, J=6.5 Hz, 3H).

1,5-Dideoxy-2,4-dimethyl-*D*-arabitol (10). A solu-

tion of 0.93 g (3.90 mmol) of compound **9** and 0.23 g of $Pd(OH)_2/C$ (20 wt %) in 20 mL of EtOH and 10 mL of cyclohexene was heated at reflux for 1 hr. The resulting solution was filtered through a pad of Celite, and the solvent was removed under reduced pressure to yield 0.58 g (99% yield) of alcohol **10**: $[\alpha]_D^{28} = -37.00$ (C=1.00, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 3.6-3.2 (m, 3H), 3.39, 3.36 (2s, 6H), 2.29 (br. s, 1H), 1.20 (d, J=6.0 Hz, 3H), 1.17 (d, J=6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 77.4, 77.2, 76.3, 56.9, 56.6, 15.6, 14.8.

(2*R*,4*R*)-2,4-Dimethoxy-3-Pentanone (11). Alcohol **11** (0.58 g, 3.89 mmol) was dissolved in CH_2Cl_2 containing both 4 Å molecular sieves (2 g) and trimethyl *N*-oxide (0.44 g, 1.5eq). After stirring the mixture for 10 min, tetrapropylammonium perruthenate (TPAP, 70 mg, 5 mol %) was added and stirred for 1 hr. The reaction mixture was filtered through a pad of silica gel, eluting with ethyl acetate. The filtrate was evaporated and chromatographed on silica gel (Pentane : Ether=3 : 1) to give 0.37 g (65% yield) of C_2 symmetric ketone **11**: $[\alpha]_D^{28} = +16.7$ (C=1.00, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 4.09 (q, J=6.8 Hz, 2H), 3.38 (s, 6H), 1.35 (d, J=6.9 Hz, 6H); ^{13}C NMR ($CDCl_3$) δ 212.0, 80.3, 57.7, 17.3; MS (M^+-1): 145; IR (film) ν 1730 cm^{-1}.

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5. Compound **2** was prepared from *L*-arabitol according to the following literatue and by further transformations. Bestmann, H. J.; Heid, H. A. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 336.
6. We have tried three conditions; PhCHO, *p*-TsOH in benzene or $PhCH(OMe)_2$, *p*-TsOH in CH_2Cl_2 or PhCHO, H_2SO_4 in DMF.
7. The ratios were determined by ^1H NMR after oxidation of the liberated alcohol to ketone. The epimers of the ketones were 1 : 1 mixtures.
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Orthocyclophanes. 5.[1] Functionalization of [1$_6$] Starand on the Aromatic Ring

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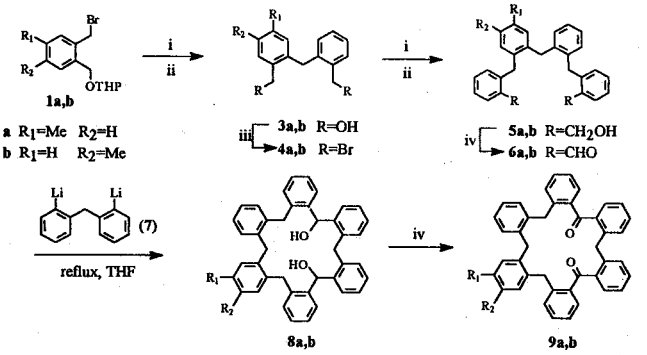
Since the first starand, [1$_6$]orthocyclophano-12-crown-6 ([1$_6$]starand)[2] has the up-down-up arrangement of the six oxygen atoms which forms a preorganized spherical cavity, it is expected to have an unusual cation binding properties.[2] In order to improve the binding ability of [1$_6$]starand towards cations, we planned to attach side arm donor functional groups on the benzene ring which could provide internal solvation to the starand-bound cation.[3] Herein, we report the first synthesis of the functionalized [1$_6$]starands-methyl[1$_6$] orthocyclophano-12-crown-6 (**10**) and acetoxymethyl[1$_6$]orthocyclophano-12-crown-6 (**11**).

Reaction of the isomeric mixture of **1a** and **1b**[4] with Grignard reagent **2** in the presence of catalytic amounts of CuI, followed by removal of the THP protecting group gave benzylic diols **3a** and **3b**, which upon treatment with dry HBr gas in CH_2Cl_2 furnished the corresponding dibromides **4a** and **4b** in 82% overall yield. Benzylic diols **5a** and **5b** were obtained in 55% yield by the same method as the synthesis of **3a** and **3b**. Oxidation of **5a** and **5b** with PCC to give the aromatic dialdehydes **6a** and **6b** followed by condensation with 1 molar equivalent of dilithio reagent **7**[5] gave the cyclic diols **8a** and **8b**. Oxidation of **8a** and **8b** with PCC gave



Scheme 1. Reagents and conditions: i) CuI, (**2**), THF; ii) TsOH, MeOH; iii) HBr, CH_2Cl_2; iv) PCC, CH_2Cl_2.