General Method for the Synthesis of Chiral 2,3-Bisarylmethoxy-1,4-Butanediols from L-(+)-Tartrate

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Abstract: Various (2*S*,3*S*)-2,3-bisarylmethoxy-1,4-butanediols **3a**–**h** were synthesized from L-(+)-tartrate through bisallylether **12**. Protection of the primary alcohol as an allyl ether was essential for selective deprotection in the presence of reactive arylmethyl ethers.

Key words: tartaric acid, allyl ether, catalyst, palladium, deprotection

Tartaric acid is one of the most useful and readily available chiral building blocks for asymmetric synthesis.[1] In fact, **3a** derived from **1** has been used as an intermediate in the synthesis of natural products,[2] chiral ligands,[3] and catalysts.[4] Recently, we developed a catalytic asymmetric Michael reaction of glycine Schiff base **5** using novel chiral quaternary salts **4** derived from **3a**.[4a] In this reaction, Michael adduct of glycine derivative **6** was isolated in up to 77% ee using **4b** as a chiral catalyst (Scheme 1).[4a] We also found that **4b** catalyzed enantioselective alkylation of **5** to give phenylalanine derivative **7** in up to 57% ee.[4b] The substituent on the aromatic rings of **4** dramatically influenced the reaction time and ee in these reactions.

However, despite its utility, only two methods have been reported for the preparation of **3a**. Seebach reported the use of thallium alkoxide as a base for the O-alkylation of **2**, though its high toxicity is problematic.[5a] Yamamoto described the preparation of **3a** using sodium hydroxide in the presence of Bu_4NI and 18-crown-6.[5b] Although, this method seemed to be quite practical, these conditions were not shown to be applicable to other substrates. We prepared **3a** from **2** according to Yamamoto's procedure for the synthesis of novel PTCs.[4a] Although this method is facile and efficient, the reaction is highly dependent on the structure of the alkylating agents, and attempts to produce **3b** and **3c** were unsuccessful, and gave either a messy or no reaction. Moreover, forced conditions would promote undesired racemization or β-elimination. Therefore, a facile and general method for the preparation of **3** is required. We report here a new method for the synthesis of chiral **3** from **2**.

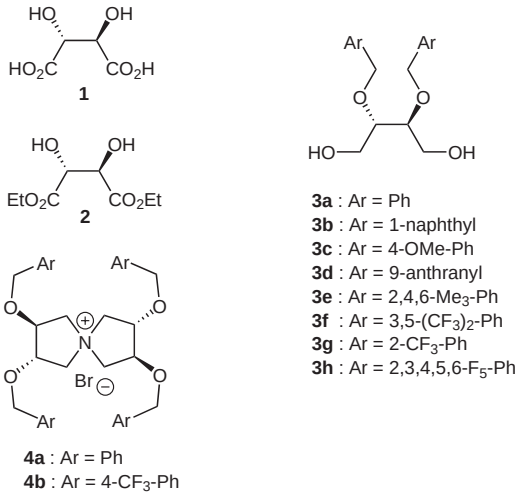
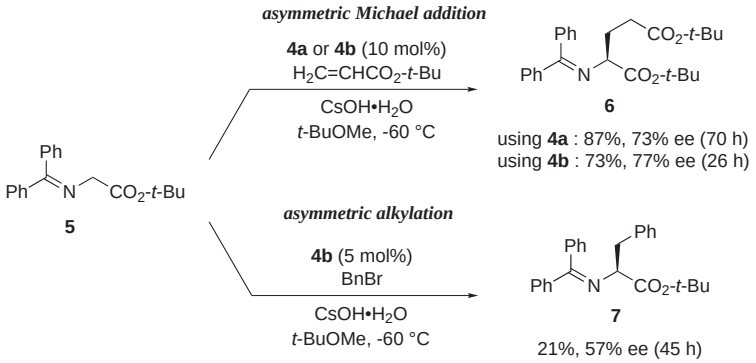


Figure 1



Scheme 1

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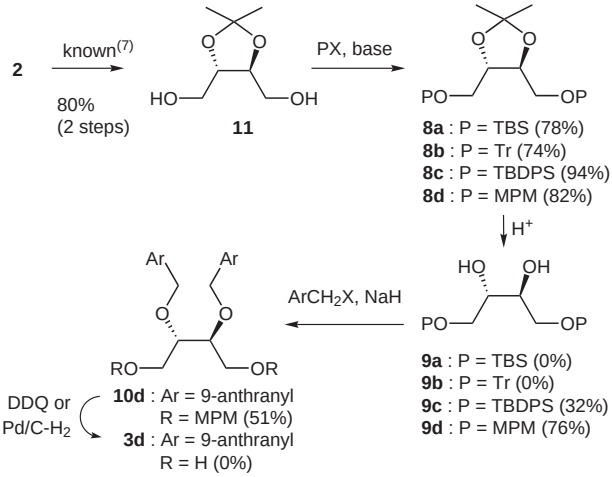
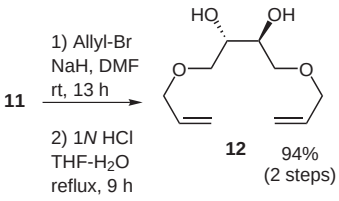


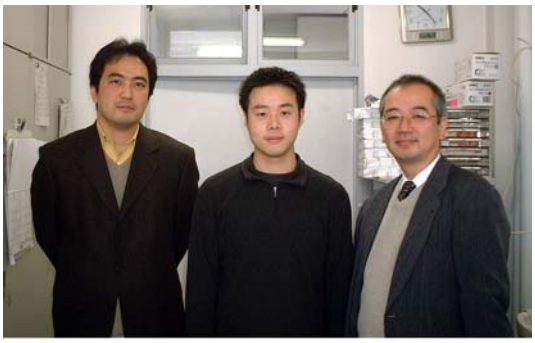
Scheme 2



Scheme 3

Initially, we chose chiral bis O-protected ethers (**8**) as a common intermediate, which we prepared from **2** in 3 steps (Scheme 2). Unfortunately, the selective removal of acetonide in **8a** and **8b** was unsuccessful under all of the conditions tested. In the case of bis-TBDPS ether **8c**, deprotected **9c** was obtained in 32% yield, but was found to be unstable under subsequent alkylation conditions, resulting in decomposition. Moreover, bis-MPM ether **10d** was found to be problematic with regard to the removal of MPM groups because of the high reactivity of anthranyl

Biographical Sketches



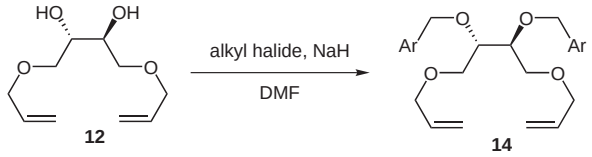
from left to right: Shigeru Arai, Riichiro Tsuji, Atsushi Nishida

Riichiro Tsuji was born in Tokyo, Japan, in 1975. He received his B.S. from the Science University of Tokyo (1999) and his M.S. from Chiba University (2001), working with Prof. Masako Nakagawa. He is now a graduate student of Pharmaceutical Sciences, Chiba University and will finish in March 2004. His scientific interests include synthetic organic chemistry using organocatalysts and transition metal catalysts.

Shigeru Arai was born in Sapporo, Japan, in 1968. He received his B.S. at Hokkaido University (1992), where he worked with Prof. Masakatsu Shibasaki. He moved to graduate school of the University of Tokyo to start rare earth metal chemistry under the direction of Prof. Shibasaki and then received his PhD degree in 1998. In 1996, he started his academic career with Prof. Takayuki Shioiri at Nagoya City University and became an associate professor at Chiba University (Prof. Atsushi Nishida) in December 2001. He also spent time in the chemistry department at MIT (Prof. G. C. Fu) as a postdoctral fellow (JSPS) during 1999–2000. His research interests are concentrated on design and synthesis of a new phase-transfer catalysts and its application to the synthesis of biologically active compounds.

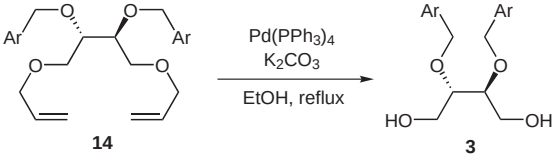
Atsushi Nishida was born in Muroran, Japan in 1954 and received B.S. in 1976 and M.S. in 1978 from Hokkaido University. He joined Prof. Ikegami's group at Teikyo University and received his PhD in 1985 from Hokkaido University. Then he moved to MIT (Prof. Rick L. Danheiser) as a postdoctoral fellow in 1985. After spending one year, he moved back to Hokkaido University as an Assistant Professor in the Faculty of Pharmaceutical Sciences. He moved to Hokkaido College of Pharmacy in 1990 as an Associate Professor. He joined Professor Nakagawa's group in Chiba University in1996 and was promoted to Full Professor at the Graduate School of Pharmaceutical Sciences in 2001. His research interests concern the total synthesis of biologically active natural products, development of useful radical reactions, and asymmetric reactions.

substituents with DDQ or Pd/C under H_2. Finally, we found that bis-allylether was quite stable under acidic and basic conditions, and **11**[6] was successfully converted to **12** in 94% yield (2 steps), as shown in Scheme 3. Next, we examined the synthesis of **14** from **12** with various alkylating agents **13**. After testing different solvents and temperatures, we found that the reaction proceeded well in DMF at room temperature. Under these mild conditions, the alkylation reaction occurred to give **14** in excellent yield without any side products. For example, benzylation proceeded within 1.5 hours to give **14a** in 95% yield (entry 1). Other arylmethyl halides such as **14b** and **14c** were also converted into the corresponding bis-O-alkylated products in yields of 94% and 92% respectively (entries 2 and 3). In particular, we were pleased to find that bulkier reagents such as **13d** and **13e**, which were ineffective in Yamamoto's method, smoothly converted to give the desired products **14d** and **14e**, at 50 °C. Electron-withdrawing groups in the aromatic ring had no effect, and gave the corresponding ethers in good to high yields (entries 6 and 7) except that pentafluorobenzylether (**14h**) was extremely unstable. These results are summarized in Table 1.



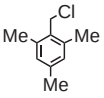
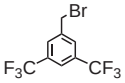
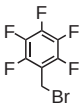
Scheme 4

Finally, the deprotection of allyl groups was investigated. To remove them clearly, it is essential to keep the reaction media either neutral or basic because some arylmethyl ethers are quite unstable under acidic conditions. An initial trial using $NaBH_4/I_2$[7] resulted in none of the desired product.[8] However, the deallylation **14a** catalyzed by Pd in the presence of K_2CO_3, as reported by Thayumanavan,[9] proceeded to give exclusively **3a** in 89% yield (entry 1). No racemization was observed when the optical rotation was compared to the previously reported value {$[\alpha]_D^{23}$ +13.1 (EtOH, *c* 1.30)}.[5a] Encouraged by these results, we next studied the deallylation of other bisallylethers. As expected, allyl groups were smoothly removed to give the corresponding 1,4-diols in excellent yields. Although greater catalyst loading was required in the reaction of **14d**, **14f**, and **14g**, two allylgroups were removed to give **3d**, **3f**, and **3g** in yields of 96%, 76%, and 83%, respectively. These results are summarized in Table 2.



Scheme 5

Table 1 Alkylation of Diol **12** with Various Alkyl Halides

Entry	Alkyl Halide	Time (h)	Temp	Product	Yield (%)[a]
1	BnBr **13a**	1.5	r.t.	**14a**	95
2	 **13b**	11	r.t.	**14b**	94
3	 **13c**	5	r.t.	**14c**	92
4	 **13d**	4	50 °C	**14d**	84
5	 **13e**	7	50 °C	**14e**	99
6	 **13f**	11	r.t.	**14f**	75
7[b]	 **13g**	1	50 °C	**14g**	70
8	 **13h**	24	r.t.	**14h**	27

[a] Isolated yield.
[b] THF–DMF (2:1) was used as a solvent.

In conclusion, we have succeeded in establishing a general and efficient method for preparing various chiral diols **3a**–**h** through bis-allylether **12** as a common intermediate. The mildness and overall feasibility make this process suitable for synthesizing a variety of 2,3-dialkoxy-1,4-butanediols. We have recently found that one of the novel quaternary salts derived from **3g** catalyzed enantioselective Michael reaction with more than 90% ee. The details of these results will be reported in due course.

(2*S*,3*S*)-1,4-Bis(*tert*-butyldimethylsiloxy)-2,3-*O*-isopropylidenedioxybutane (8a)

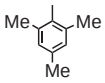
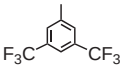
$[\alpha]_D^{23}$ +0.84 (*c* 1.67, $CHCl_3$).

IR (neat): 2930, 1254, 1085, 837 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.06 (12 H, s), 0.89 (18 H, s), 1.39 (6 H, s), 3.74–3.78 (4 H, m), 3.91–3.97 (2 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.3, 25.9, 27.1, 63.8, 78.6, 109.0.

Table 2 Deprotection of Allyl Function of **14**

Entry	Ar	Pd Cat. (mol%)	Time (h)	Product	Yield (%)[a]
1	Ph	5	16	**3a**	89
2		5	4	**3b**	95
3		5	2.5	**3c**	99
4		20	8	**3d**	96
5		5	5	**3e**	76
6		10	2	**3f**	96
7		10	12	**3g**	83
8		10	13	**3h**	52

[a] Isolated yield.

(2*S*,3*S*)-1,4-Bis(triphenylmethoxy)-2,3-*O*-isopropylidenedioxybutane (8b)
Mp 126–129 °C; $[\alpha]_D^{23}$ –17.2 (*c* 1.27, $CHCl_3$).

IR (KBr) 1448, 1078, 700 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.41 (6 H, s), 3.21 (4 H, dd, *J* = 6.0, 10.4 Hz), 3.99–4.04 (2 H, m), 7.16–7.40 (30 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.2, 64.8, 77.6, 86.7, 109.3, 126.9, 127.7, 128.6, 143.8.

MS (FAB): *m*/*z* = 403 (M^+ – Tr).

HRMS (FAB): *m*/*z* calcd for $C_{26}H_{27}O_4$ (M^+– Tr), 403.1909; found, 403.1891.

(2*S*,3*S*)-1,4-Bis(*tert*-butyldiphenylsiloxy)-2,3-*O*-isopropylidenedioxybutane (8c)
$[\alpha]_D^{23}$ –11.05 (*c* 1.72, $CHCl_3$).

IR (neat): 2930, 1428, 1112, 701 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.03 (18 H, s), 1.41 (6 H, s), 3.72–3.83 (4 H, m), 4.12 (2 H, s), 7.24–7.70 (20 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 26.8, 27.1, 64.2, 78.3, 109.1, 127.6, 129.6, 133.2, 135.6.

MS: *m*/*z* = 637 (M^+ – H).

HRMS (FAB): *m*/*z* calcd for $C_{39}H_{49}O_4Si_2$ (M^+ – H), 637.3169; found, 637.3182.

(2*S*,3*S*)-1,4-Bis(4-methoxyphenylmethoxy)-2,3-*O*-isopropylidenedioxybutane (8d)
$[\alpha]_D^{23}$ –7.09 (*c* 0.53, $CHCl_3$).

IR (neat): 2934, 2862, 1513, 1247, 819 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.41 (6 H, s), 3.53–3.57 (4 H, m), 3.79 (6 H, s), 3.96–4.02 (2 H, m), 4.47 (2 H, d, *J* = 12.0 Hz), 4.51 (2 H, d, *J* = 11.6 Hz), 6.83–6.87 (4 H, m), 7.20–7.24 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.2, 54.4, 69.5, 72.3, 76.7, 108.8, 112.9, 128.4, 129.2, 158.3.

MS (FAB): *m*/*z* = 401 (M^+–H).

HRMS (FAB): *m*/*z* calcd for $C_{23}H_{29}O_6$ (M^+ – H), 401.1964; found, 401.1930.

(2*S*,3*S*)-1,4-Bis(*tert*-butyldiphenylsiloxy)butane-2,3-diol (9c)
$[\alpha]_D^{23}$ +3.28 (*c* 0.85, $CHCl_3$).

IR (neat): 3440, 2930, 1428, 1112 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.04 (18 H, s), 2.73 (2 H, d, *J* = 4.4 Hz), 3.70–3.85 (6 H, m), 7.34–7.44 (12 H, m), 7.62–7.66 (8 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ 19.1, 26.8, 65.4, 71.2, 127.7, 129.8, 132.9, 133.0, 135.4, 135.5.

MS (FAB): *m*/*z* = 637 (M^+ + K).

HRMS (FAB): *m*/*z* calcd for $C_{36}H_{46}O_4Si_2K$ (M^+ + K), 637.2572; found, 637.2537.

(2*S*,3*S*)-1,4-Bis(4-methoxyphenylmethoxy)butane-2,3-diol (9d)
Mp 59–60 °C; $[\alpha]_D^{23}$ –8.10 (*c* 0.32, $CHCl_3$).

IR (KBr) 3262, 2862, 1514, 1253, 817 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.03 (2 H, br s), 3.50 (2 H, dd, *J* = 5.8, 9.8 Hz), 3.54 (2 H, dd, *J* = 4.4, 6.0 Hz), 3.73–3.81 (2 H, m), 3.77 (6 H, s), 4.43 (4 H, dd, *J* = 11.4, 16.4 Hz), 6.82–6.84 (4 H, m), 7.20–7.24 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.1, 70.4, 71.4, 73.0, 113.7, 129.3, 129.7, 159.1.

MS (FAB): *m*/*z* = 401 (M^+ + K).

HRMS (FAB): *m*/*z* calcd for $C_{20}H_{26}O_6K$ (M^+ + K), 401.1366; found, 401.1335.

(2*S*,3*S*)-2,3-Bis(anthracen-9-ylmethoxy)-1,4-bis(4-methoxyphenylmethoxy)butane (10d)
Mp 172–175 °C; $[\alpha]_D^{23}$ +20.14 (*c* 0.57, $CHCl_3$).

IR (KBr) 2903, 1512, 1240, 1092, 730 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.32 (2 H, dd, *J* = 3.4, 5.8 Hz), 3.54 (2 H, dd, *J* = 2.4, 10.0 Hz), 3.74–3.89 (8 H, m), 4.14 (4 H, dd, *J* = 11.6, 15.6 Hz), 5.53 (2 H, d, *J* = 11.6 Hz), 5.60 (2 H, d, *J* = 12.0 Hz), 6.80–6.83 (4 H, m), 7.08–7.10 (4 H, m), 7.33–7.43 (8 H, m), 7.96 (4 H, d, *J* = 8.4 Hz), 8.34–8.40 (6 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.1, 64.6, 70.5, 72.7, 77.3, 113.5, 124.7, 125.8, 128.7, 129.0, 129.1, 130.2, 131.1, 131.2, 158.9.

MS (FAB): *m*/*z* = 742 (M^+).

HRMS (FAB): *m*/*z* calcd for $C_{50}H_{46}O_6$ (M^+), 742.3294; found, 742.3296.

(2*S*,3*S*)-1,4-Bis(allyloxy)-2,3-dihydroxybutane (12)
To a solution of **11** (1.62 g, 10 mmol) in THF (30 mL) was added a suspension of 60% NaH (1.20 g, 30 mmol) in oil at 0 °C. After vigorous stirring for 20 min at r.t., allyl bromide (2.5 mL, 30 mmol) was added and the mixture was stirred vigorously for 13 h at r.t. The reaction was quenched by addition of sat. NH_4Cl aqueous solution (20 mL) and extracted with EtOAc. Combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo.

The residue was dissolved in a mixture of THF (100 mL) and 1 N aqueous solution HCl (1 mL), the mixture was heated under reflux for 9 h. Then the resulting mixture was concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane–EtOAc, 1:2) to furnish **12** [1.89 g, 94% yield (2 steps)].

(2*S*,3*S*)-1,4-Bis(allyloxy)-2,3-*O*-isopropylidenedioxybutane
$[\alpha]_D^{23}$ –10.43 (*c* 1.80, $CHCl_3$).

IR (KBr): 2986, 1370, 1086 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.42 (6 H, s), 3.57–3.60 (4 H, m), 3.99–4.08 (6 H, m), 5.17–5.30 (4 H, m), 5.85–5.95 (2 H, m).

^{13}C NMR (100 MHz, $CDCl_3$) δ 26.9, 70.7, 72.4, 77.4, 109.6, 117.1, 134.4.

MS (FAB): *m*/*z* = 243 (M^+ + H).

HRMS (FAB): *m*/*z* calcd for $C_{13}H_{23}O_4$ (M^+ + H), 243.1596; found, 243.1607.

(2*S*,3*S*)-1,4-Bis(allyloxy)-2,3-dihydroxybutane (12)
$[\alpha]_D^{23}$ –3.65 (*c* 1.05, $CHCl_3$).

IR (KBr) 3194, 2866, 1429, 1103, 995 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.87 (2 H, br s), 3.55–3.62 (4 H, m), 3.85 (2 H, br s), 3.99–4.07 (4 H, m), 5.18–5.30 (4 H, m), 5.85–5.95 (2 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 70.4, 71.9, 72.4, 117.4, 134.2.

MS (FAB): *m*/*z* = 203 (M^+ + H).

HRMS (FAB): *m*/*z* calcd for $C_{10}H_{19}O_4$ (M^+ + H), 203.1283; found, 203.1269.

(2*S*,3*S*)-2,3-Bis(phenylmethoxy)-1,4-bis(allyloxy)butane (14a);Typical Procedure
To a stirred suspension of 60% NaH (96 mg, 2.4 mmol) in DMF (2 mL) was added a solution of **12** (202 mg, 1.0 mmol), in DMF (3 mL), and the mixture was stirred at r.t. After 20 min, BnBr (0.28 mL, 2.4 mmol) was added slowly and the mixture was stirred at r.t. for an additional 1.5 h. The mixture was cooled to 0 °C and sat. NH_4Cl aqueous solution (5 mL) was carefully added. The separated aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The crude residue was purified by flash column chromatography (silica gel, hexane–EtOAc, 10:1) to furnish **14a** (362 mg, 95% yield).

$[\alpha]_D^{23}$ +18.40 (*c* 1.35, $CHCl_3$).

IR (neat): 2864, 1454, 1097, 698 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.53–3.63 (4 H, m), 3.73–3.77 (2 H, m), 3.93 (4 H, dd, *J* = 1.2, 5.6 Hz), 4.60 (2 H, d, *J* = 11.6 Hz), 4.70 (2 H, d, *J* = 11.6 Hz), 5.14–5.27 (4 H, m), 5.82–5.91 (2 H, m), 5.82–5.91 (2 H, m), 7.24–7.34 (10 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 69.8, 72.1, 73.1, 77.8, 116.7, 127.5, 128.0, 128.2, 134.7, 138.6

MS (FAB): *m*/*z* = 383 (M^+ + H).

HRMS (FAB): *m*/*z* calcd for $C_{24}H_{31}O_4$ (M^+ + H), 383.2222; found, 383.2200.

(2*S*,3*S*)-2,3-Bis(naphthalene-1-ylmethoxy)-1,4-bis(allyloxy)butane (14b)
$[\alpha]_D^{23}$ +44.54 (*c* 2.27, $CHCl_3$).

IR (neat): 2863, 1509, 1094, 777 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.45 (2 H, dd, *J* = 4.0, 10.0 Hz), 3.50 (2 H, dd, *J* = 5.6, 10.0 Hz), 3.69–3.81 (6 H, m), 4.96 (2 H, d, *J* = 12.0 Hz), 5.08–5.18 (4 H, m), 5.17 (2 H, d, *J* = 12.0 Hz), 5.72–5.82 (2 H, m), 7.31–7.48 (8 H, m), 7.75–7.83 (4 H, m), 8.15–8.18 (2 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 69.9, 71.2, 71.9, 77.3, 116.5, 124.4, 125.0, 125.5, 125.9, 126.9, 128.2, 128.5, 131.9, 133.6, 133.8, 134.6.

MS (FAB): *m*/*z* = 483 (M^+ + H).

HRMS (FAB): *m*/*z* calcd for $C_{32}H_{35}O_4$ (M^+ + H), 483.2535; found, 483.2522.

(2*S*,3*S*)-2,3-Bis(4-methoxyphenylmethoxy)-1,4-bis(allyloxy)butane (14c)
$[\alpha]_D^{23}$ +21.41 (*c* 1.11, $CHCl_3$).

IR (neat): 2909, 2864, 1513, 1248 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.51 (2 H, dd, *J* = 6.0, 10.0 Hz), 3.56 (2 H, dd, *J* = 4.0, 10.0 Hz), 3.68–3.72 (4 H, m), 3.79 (6 H, s), 3.91–3.93 (2 H, m), 4.53 (2 H, d, *J* = 12.0 Hz), 4.62 (2 H, d, *J* = 11.2 Hz), 5.13–5.27 (4 H, m), 5.82–5.91 (2 H, m), 6.82–6.88 (4 H, m), 7.23–7.27 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.2, 69.9, 72.1, 72.6, 77.3, 113.6, 116.6, 129.6, 130.7, 134.8, 159.1.

MS (FAB): *m*/*z* = 481 (M^+ + K).

HRMS (FAB): *m*/*z* calcd for $C_{26}H_{34}O_6K$ (M^+ + K), 481.1992; found, 481.2002.

(2*S*,3*S*)-2,3-Bis(anthracen-9-ylmethoxy)-1,4-bis(allyloxy)butane (14d)
Mp 71–72 °C; $[\alpha]_D^{23}$ +40.97 (*c* 0.62, $CHCl_3$).

IR (KBr): 2853, 1062, 888, 730 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.37 (2 H, dd, *J* = 3.6, 10.0 Hz), 3.54 (2 H, dd, *J* = 6.4, 10.0 Hz), 3.70–3.83 (6 H, m), 5.09–5.20 (4 H, m), 5.51 (2 H, d, *J* = 11.6 Hz), 5.61 (2 H, d, *J* = 11.6 Hz), 5.76–5.85 (2 H, m), 7.39–7.44 (8 H, m), 7.92–7.97 (4 H, m), 8.36–8.39 (6 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 64.8, 70.6, 72.0, 77.4, 116.7, 124.7, 124.8, 125.9, 128.1, 128.7, 129.0, 131.1, 131.3, 134.6.

MS (FAB): *m*/*z* = 582 (M^+).

HRMS (FAB): *m*/*z* calcd for $C_{40}H_{38}O_4$ (M^+), 582.2770; found, 582.2750.

(2*S*,3*S*)-2,3-Bis(2,4,6-trimethyl-phenylmethoxy)-1,4-bis(allyloxy)butane (14e)
$[\alpha]_D^{23}$ –7.36 (*c* 0.42, $CHCl_3$).

IR (neat): 2915, 1614, 1087, 849 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.24 (6 H, s), 2.34 (12 H, s), 3.48 (2 H, dd, J = 6.4, 9.6 Hz), 3.63 (2 H, dd, *J* = 2.8, 9.6 Hz), 3.71–3.75 (2 H, m), 3.92 (4 H, d, *J* = 5.6 Hz), 4.57 (2 H, d, *J* = 10.0 Hz), 4.68 (2 H, d, *J* = 10.0 Hz), 5.12–5.26 (4 H, m), 5.82–5.92 (2 H, m), 6.81 (4 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.5, 20.9, 67.0, 70.0, 72.1, 77.7, 116.6, 128.7, 131.5, 134.8, 137.4, 137.9.

MS (FAB): *m*/*z* = 466 (M^+).

HRMS (FAB): *m*/*z* calcd for $C_{30}H_{42}O_4$ (M^+) 466.3083; found, 466.3074.

(2*S*,3*S*)-2,3-Bis(3,5-bis-trifluoromethylphenylmethoxy)-1,4-bis(allyloxy)butane (14f)
Mp 56.5–57.5 °C; $[\alpha]_D^{23}$ +5.69 (*c* 1.62, $CHCl_3$).

IR (KBr): 2904, 1376, 1283, 1129, 886 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.62 (2 H, dd, *J* = 5.6, 10.0 Hz), 3.67 (2 H, dd, *J* = 3.6, 10.4 Hz), 3.80–3.85 (2 H, m), 3.97–3.99 (4 H, m), 4.75 (2 H, d, *J* = 12.8 Hz), 4.87 (2 H, d, *J* = 12.8 Hz), 5.17–5.28 (4 H, m), 5.82–5.92 (2 H, m), 7.78–7.82 (6 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 69.8, 71.8, 72.4, 79.4, 117.4, 121.4 (q, *J* = 4.1 Hz), 123.3 (q, *J* = 272 Hz), 127.3, 131.5 (q, *J* = 33 Hz), 134.2, 141.2.

MS (FAB): *m*/*z* = 655 (M^+ + H).

HRMS (FAB): *m*/*z* calcd for $C_{28}H_{27}O_4F_{12}$ (M^+ + H), 655.1718; found, 655.1691.

(2*S*,3*S*)-2,3-Bis(2-trifluoromethylphenylmethoxy)-1,4-bis(allyloxy)butane (14g)
$[\alpha]_D^{23}$ +3.03 (*c* 1.35, $CHCl_3$).

IR (neat): 2865, 1314, 1118, 769 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.64 (2 H, dd, *J* = 5.6, 10.4 Hz), 3.74 (2 H, dd, *J* = 3.6, 10.0 Hz), 3.86–3.90 (2 H, m), 3.97–3.99 (4 H, m), 4.82 (2 H, d, *J* = 13.2 Hz), 4.95 (2 H, d, *J* = 13.2 Hz), 5.14–5.18 (2 H, m), 5.23–5.29 (2 H, m), 5.83–5.93 (2 H, m), 7.34 (2 H, t, *J* = 7.6 Hz), 7.50 (2 H, t, *J* = 7.6 Hz), 7.60 (2 H, d, *J* = 7.6 Hz), 7.76 (2 H, d, *J* = 8.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 68.9 (dd, *J* = 2.5, 3.3 Hz), 69.6, 72.2, 79.0, 116.9, 124.3 (q, *J* = 272 Hz), 125.4 (q, *J* = 5.8 Hz), 127.1, 127.1 (q, *J* = 30.4 Hz), 129.1, 131.7, 134.5, 137.4.

MS (FAB): *m*/*z* = 519 (M^+ + H).

HRMS (FAB): *m*/*z* calcd for $C_{26}H_{29}O_4F_6$ (M^+ + H), 519.1970; found, 519.1960.

(2*S*,3*S*)-2,3-Bis(2,3,4,5,6-pentafluorophenylmethoxy)- 1,4-bis(allyloxy)butane (14h)
$[\alpha]_D^{23}$ +9.79 (*c* 1.50, $CHCl_3$).

IR (neat): 2917, 1505, 1125 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.53–3.62 (4 H, m), 3.71–3.75 (2 H, m), 3.95–3.97 (4 H, m), 4.68 (2 H, d, *J* = 11.2 Hz), 4.80 (2 H, d, *J* = 11.2 Hz), 5.16–5.27 (4 H, m), 5.82–5.91 (2 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 59.9, 69.0, 72.3, 78.4, 111.3 (m), 116.9, 134.3, 137.3 (br d, *J* = 250 Hz), 141.3 (br d, *J* = 205 Hz), 145.6 (br d, *J* = 251 Hz).

MS (FAB): *m*/*z* = 563 (M^+ + H).

HRMS (FAB): *m*/*z* calcd for $C_{24}H_{21}O_4F_{10}$ (M^+ + H), 563.1280; found: 563.1262.

(2*S*,3*S*)-2,3-Bis(phenylmethoxy)-1,4-butanediol (3a)[5a]; Typical Procedure
To a stirred solution of allyl compound **14a** (38.2 mg, 0.1 mmol) in EtOH (1.0 mL) was added catalytic amounts of $Pd(PPh_3)_4$ (5.7 mg, 5 μmol, 5 mol%) under an argon atmosphere. The slightly yellow solution was stirred for 5 min, K_2CO_3 (82.8 mg, 0.6 mmol, 6 equiv) was added. After 16 h, the starting material and mono allyl compound were completely consumed (monitoring by TLC. The reaction mixture was cooled to 0 °C, and quenched by addition of 1 N HCl and CH_2Cl_2. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The crude residue was purified by flash column chromatography (silica gel, EtOAc) to furnish **3a** (27 mg, 89% yield).

(2*S*,3*S*)-2,3-Bis(naphthalene-1-ylmethoxy)-1,4-butanediol (3b)
$[\alpha]_D^{23}$ +11.60 (*c* 1.82, $CHCl_3$).

IR (neat): 3409, 2878, 1101, 793, 776 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.33 (2 H, br s), 3.65–3.75 (6 H, m), 5.03 (4 H, dd, *J* = 12.0, 16.4 Hz), 7.36–7.49 (8 H, m), 7.78–7.87 (4 H, m), 8.07–8.10 (2 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 60.6, 70.8, 78.6, 123.7, 125.1, 125.8, 126.4, 126.8, 128.6, 128.9, 131.6, 133.3, 133.7.

MS (FAB): *m*/*z* = 441 (M^+ + K).

HRMS (FAB): *m*/*z* calcd for $C_{26}H_{26}O_4K$ (M^+ + K), 441.1468; found, 441.1443.

(2*S*,3*S*)-2,3-Bis(4-methoxyphenylmethoxy)-1,4-butanediol (3c)
$[\alpha]_D^{23}$ +13.92 (*c* 1.60, $CHCl_3$).

IR (neat): 3416, 2935, 1513, 1248 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.53 (2 H, br s), 3.61–3.68 (4 H, m), 3.75–3.79 (8 H, m), 4.55 (4 H, s), 6.85–6.88 (4 H, m), 7.22–7.25 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.2, 60.7, 72.1, 78.4, 113.8, 129.5, 129.9, 159.3.

MS (FAB): *m*/*z* = 401 (M^+ + K).

HRMS (FAB): *m*/*z* calcd for $C_{20}H_{26}O_6K$ (M^+ + K), 401.1366; found, 401.1345.

(2*S*,3*S*)-2,3-Bis(anthracene-9-ylmethoxy)-1,4-butanediol (3d)
Mp 174–175 °C; $[\alpha]_D^{24}$ +21.58 (*c* 1.00, $CHCl_3$).

IR (KBr): 3371, 1286, 1118, 888 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.11 (2 H, br s), 3.65 (2 H, d, *J* = 11.6 Hz), 3.76 (2 H, d, *J* = 12.0 Hz), 3.84–3.88 (2 H, m), 5.56 (2 H, d, *J* = 11.6 Hz), 5.61 (2 H, d, *J* = 11.6 Hz), 7.43–7.49 (8 H, m), 7.98–8.02 (4 H, m), 8.30–8.33 (4 H, m) 8.46 (2 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 61.0, 64.4, 79.1, 123.9, 125.0, 126.49, 128.3, 128.6, 129.1, 130.8, 131.3.

MS (FAB): *m*/*z* = 502 (M^+).

HRMS (FAB): *m*/*z* calcd for $C_{34}H_{30}O_4$ (M^+), 502.2144; found, 502.2100.

(2*S*,3*S*)-2,3-Bis(2,4,6-trimethylbenzyloxy)-1,4-butanediol (3e)
Mp 154–155 °C; $[\alpha]_D^{23}$ +1.67 (*c* 1.00, $CHCl_3$).

IR (KBr): 3418, 2913, 1613, 1034, 849 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.26 (6 H, s), 2.35 (12 H, s), 3.70–3.73 (4 H, m), 3.82 (2 H, dd, *J* = 4.8, 12.8 Hz), 4.63 (4 H, s), 6.85 (4 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ =19.5, 20.9, 60.6, 66.4, 78.7, 129.0, 130.9, 137.7, 138.0.

MS (FAB): *m*/*z* = 388 (M^+ + H).

HRMS (FAB): *m*/*z* calcd for $C_{24}H_{35}O_4$ (M^+ + H), 387.2535; found 387.2517.

(2*S*,3*S*)-2,3-Bis(3,5-bistrifluoromethylphenylmethoxy)-1,4-butanediol (3h)
Mp 84–84.5 °C; $[\alpha]_D^{24}$ +17.67 (*c* 1.00, $CHCl_3$).

IR (KBr): 3468, 1076, 730 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.28 (2 H, br s), 3.79 (2 H, d, *J* = 2.4 Hz), 3.83 (2 H, d, *J* = 13.6 Hz), 3.94 (2 H, d, *J* = 12.0 Hz), 4.76 (2 H, d, *J* = 12.4 Hz), 4.86 (2 H, d, *J* = 12.8 Hz), 7.77–7.82 (6 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 60.8, 71.2, 80.4, 121.5–121.7 (m), 123.1 (q, *J* = 271 Hz), 127.0 (d, *J* = 3.0 Hz), 131.7 (q, *J* = 33 Hz), 140.6.

MS (FAB): *m*/*z* = 575 (M^+ + H).

HRMS (FAB): *m*/*z* calcd for $C_{22}H_{19}O_4F_{12}$ (M^+ + H), 575.1092; found, 575.1108.

(2*S*,3*S*)-2,3-Bis(2-trifluoromethylphenylmethoxy)-1,4-butanediol (3g)
Mp 97–98 °C; $[\alpha]_D^{23}$ +14.82 (*c* 1.00, $CHCl_3$).

IR (KBr): 3354, 1320, 1160, 1108, 768 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.34 (2 H, br s), 3.79–3.92 (6 H, m), 4.82 (2 H, d, *J* = 12.8 Hz), 4.88 (2 H, d, *J* = 12.8 Hz), 7.37–7.41 (2 H, m), 7.51–7.54 (2 H, m), 7.63–7.67 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 60.4, 68.5 (d, *J* = 2.4 Hz), 80.0, 124.2 (q, *J* = 272 Hz), 125.7 (q, *J* = 5.8 Hz), 127.4 (q, *J* = 30 Hz), 127.5, 129.3, 131.9, 136.6.

MS (FAB): *m*/*z* = 439 (M^+ + H).

HRMS (FAB): *m*/*z* calcd for $C_{20}H_{21}O_4F_6$ (M^+ + H), 439.1344; found, 439.1359.

(2*S*,3*S*)-2,3-Bis(2,3,4,5,6-pentafluorophenylmethoxy)-1,4-butanediol (3f)

Mp 89–91 °C; $[\alpha]_D^{23}$ +15.18 (*c* 1.50, $CHCl_3$).

IR (KBr) 3306, 1500, 940 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.21 (2 H, br s), 3.67–3.70 (4 H, m), 3.82 (2 H, d, *J* = 9.2 Hz), 4.76 (4 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 59.6, 60.8, 80.4, 111.0 (m) 137.4 (br d, *J* = 249 Hz), 141.4 (br d, *J* = 254 Hz), 145.5 (br d, *J* = 247 Hz).

MS (FAB): *m*/*z* = 483 (M^+ + H).

HRMS (FAB): *m*/*z* calcd for $C_{18}H_{13}O_4F_{10}$ (M^+ + H), 483.0654; found, 483.0680.

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