Tetrahedron: *Asymmetry* 20 (2009) 2474–2478

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

# Convenient access to sterically hindered $C_2$ chiral 2,2,5,5-tetraphenyltetrahydrofuran-3,4-diols: intramolecular selective 1,4-cyclocondensation of (2*R*,3*R*)- and (2*S*,3*S*)-1,1,4,4-tetraphenylbutanetetraols

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ARTICLE INFO

*Article history:*
Received 16 July 2009
Accepted 30 September 2009
Available online 2 November 2009

ABSTRACT

Sterically hindered $C_2$ chiral (3*R*,4*R*)- and (3*S*,4*S*)-2,2,5,5-tetraphenyltetrahydrofuran-3,4-diols have been conveniently prepared in a very high yield via heterogeneous intramolecular selective 1,4-cyclocondensation of (2*R*,3*R*)- and (2*S*,3*S*)-1,1,4,4-tetraphenylbutanetetraol in concentrated hydrohalic acids, respectively. Preliminary examination of additives for the Barbas–List reaction showed that in certain cases, the hindered $C_2$ chiral tetrahydrofuran-3,4-diols were better chiral auxiliaries than enantiopure (*R*)- and (*S*)-1,1′-bi-2-naphthols.



## 1. Introduction

The hydroxyl group composition of enantiomerically pure 1,1,4,4-tetrasubstituted butanetetraols determines that they must have rich reaction chemistry. In order to prepare sterically hindered $C_2$ chiral 1,1,4,4-tetrasubstituted bifunctional dihydroxy, diamino or diphosphino compounds, which are considered to be candidates of highly useful chiral ligands or auxiliaries for asymmetric synthesis, selective functional group transformation of enantiomerically pure 1,1,4,4-tetrasubstituted butanetetraols was investigated. A short time ago, we[1] reported the selective 1,3-cycloboration of enantiomerically pure 1,1,4,4-tetraphenylbutanetetraol.[2] Herein we report a convenient procedure for preparing $C_2$ chiral (3*R*,4*R*)- and (3*S*,4*S*)-2,2,5,5-tetraphenyltetrahydro-furan-3,4-diols via intramolecular and selective 1,4-cyclocondensation of (2*R*,3*R*)- and (2*S*,3*S*)-1,1,4,4-tetraphenylbutanetetraols under heterogeneous conditions and preliminary examination of the chiral-inducing action of these sterically hindered chiral vicinal diols.

## 2. Results and discussion

### 2.1. Preparation of (3*R*,4*R*)- and (3*S*,4*S*)-2,2,5,5-tetraphenyltetrahydrofuran-3,4-diols (TTFOL)

The reaction behavior of (2*R*,3*R*)- and (2*S*,3*S*)-1,1,4,4-tetraphenylbutanetetraols (**TBTOL**) in hydrohalic acids was examined. Solid (2*R*,3*R*)-**TBTOL** was allowed to stir in concentrated hydrochloric acid or 48% hydrobromic acid at room temperature for 12 h to furnish a white solid. The solid was recrystallized in ethanol to give colorless crystals with mp 120–122 °C, $[\alpha]_D^{25} = -208$ (*c* 0.87, $CHCl_3$). The $^1H$ NMR spectra shows that there are three sets of aromatic proton resonances (the integral intensity for the singlet at 7.11 ppm equals the sum for the other two sets) and two sets of non-aromatic proton resonances (the one at 1.87 ppm disappeared after the addition of $D_2O$) in an intensity ratio of 2:3:5:1:1 from 7.7 to 1.8 ppm, meaning that the two benzene rings bound to the same carbon atom are in different environments; namely, the five protons in one benzene ring are near equivalent, while the ones in another benzene ring experience in a more complicated coupling; for the non-aromatic protons, two hydroxyl groups of the tetraol were reacted via halogenation or dehydration. Furthermore, the $^{13}C$ NMR spectra exhibited two kinds of aliphatic carbons bound to oxygen at 85.2 and 79.5 ppm (the chemical shift of the carbon in the C–X bond for the *sec*- or *tert*-alkyl halides is generally less than 60 ppm[3]). These spectroscopic characteristics reveal that the product must have a symmetric molecular structure. The ESMS (−) display an ionic peak of 407 (100%), corresponding to a dehydration product of (2*R*,3*R*)-**TBTOL** ($[M_{426}-18]^+$). Based on the above facts, it may be thought that the compound is (3*R*,4*R*)-**TTFOL**. The X-ray crystallographic analysis[4] is in good agreement with the above estimation. As seen in Figure 1, recrystallization from ethanol afforded a solvate of (3*R*,4*R*)-**TTFOL** with ethanol, while in the molecular system, there is no intramolecular H bonding; both the hydroxyl groups of the **TTFOL** were separated in the hydrogen bonding environment with ethanol and one hydroxyl group of another **TTFOL** molecule. Based on (3*R*,4*R*)-**TTFOL**·EtOH, the yield of (3*R*,4*R*)-**TTFOL** is over 90%.

A similar reaction of (2*S*,3*S*)-1,1,4,4-tetraphenylbutanetetraol afforded (3*S*,4*S*)-2,2,5,5-tetraphenyltetrahydrofuran-3,4-diol; after

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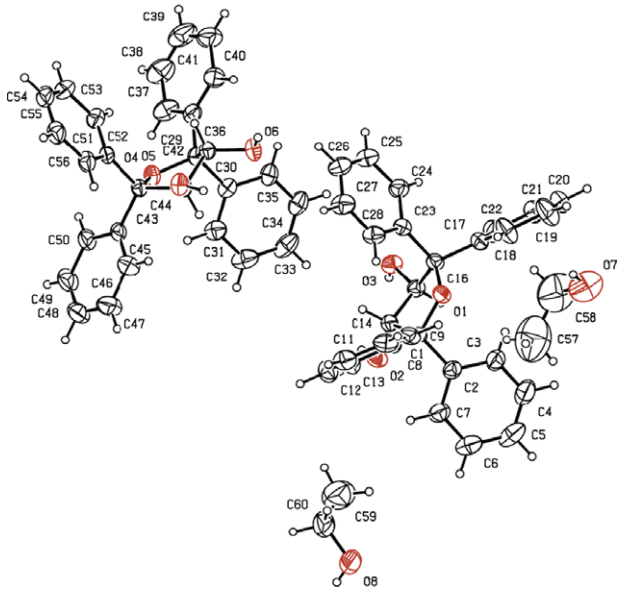
doi:10.1016/j.tetasy.2009.10.005




Hydrogen bonding: O6 H6A O3 0.82 1.96 2.776(3) 178.4
O7 H7A O2 0.82 2.03 2.725(4) 142.8

**Figure 1.** ORTEP of (3*R*,4*R*)-2,2,5,5-tetraphenyltetrahydrofuran-3,4-diol (**TTFOL**) bearing one ethanol molecule.

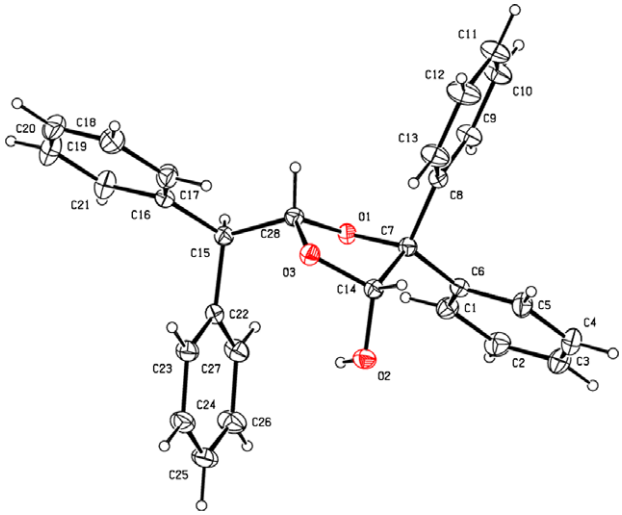



**Figure 2.** Molecular structure of 5,5-diphenyl-2-diphenylmethyl-4-hydroxy-1,3-dioxolane (**DDHDA**).

recrystallization in ethanol, a solvate of (3*S*,4*S*)-**TTFOL** with ethanol was obtained, mp 119–121 °C; $[\alpha]_D^{25} = +207.5$ (*c* 0.5, $CHCl_3$).

Compound (3*R*,4*R*)-**TTFOL** has previously been reported by Seebach et al.[5] as a by-product of chlorination of 4,5-bis(diphenylhydroxymethyl)-2,2-dimethyl-1,3-dioxolane with $CH_3SO_2Cl$ in the presence of triethylamine, but with a yield of only 17%. The synthesis and electron spectra of racemic **TTFOL** have also been reported.[6]

### 2.2. Influence of the reaction system on the formation of (3*R*,4*R*)- and (3*S*,4*S*)-TTFOL

The formation of (3*R*,4*R*)- and (3*S*,4*S*)-**TTFOL** is in close relationship with the reaction system. In the aforementioned two concentrated hydrohalic acids, the heterogeneous reactions of solid (2*R*,3*R*)- or (2*S*,3*S*)-**TBTOL** afforded nearly quantitatively (3*R*,4*R*)- or (3*S*,4*S*)-**TTFOL**. While a similar reaction in hydriodic acid gave some floccule, except (3*R*,4*R*)- or (3*S*,4*S*)-**TTFOL**. The floccue was recrystallized from ethyl acetate to afford a colorless crystal with mp 164–166 °C. The $^1H$ and $^{13}C$ NMR spectra, and mass spectra as well as single crystal X-ray diffraction analysis[7] showed the compound to be 5,5-diphenyl-2-diphenylmethyl-4-hydroxy-1,3-dioxolane (**DDHDA**, Fig. 2). The specific rotation indicates that **DDHDA** is a racemate. This result may be attributed to its complicated formation process (see Section 2.3).

Solid (2*R*,3*R*)-**TBTOL** was stirred in hydriodic acid at room temperate for 48 h to offer (3*R*,4*R*)-**TTFOL** in 47% yield and **DDHDA** in 42% yield. It seems that the reaction of (2*R*,3*R*)-**TBTOL** in hydriodic acid is more complicated than in concentrated hydrochloric acid or hydrobromic acid.

It has been observed that the homogeneous reaction product of (2*R*,3*R*)- or (2*S*,3*S*)-**TBTOL** in the hydrohalic acids is dependent on the reaction time. When a homogeneous mixture of a dilute THF or MeOH solution of (2*R*,3*R*)- or (2*S*,3*S*)-**TBTOL** with hydrohalic acid was stirred for several hours, most of the (2*R*,3*R*)- or (2*S*,3*S*)-**TBTOL** was recovered; however, if it was stirred overnight (more than 12 h), **DDHDA** was obtained in very high yield, and little (3*R*,4*R*)- or (3*S*,4*S*)-**TTFOL** was isolated. It appears that under the catalysis of hydrohalic acids, there is competition between the formation reactions of **DDHDA** and **TTFOL**.

The reaction of (2*R*,3*R*)- and (2*S*,3*S*)-1,1,4,4-tetraphenylbutanetetraols in hydrohalic acids is summarized in Scheme 1.

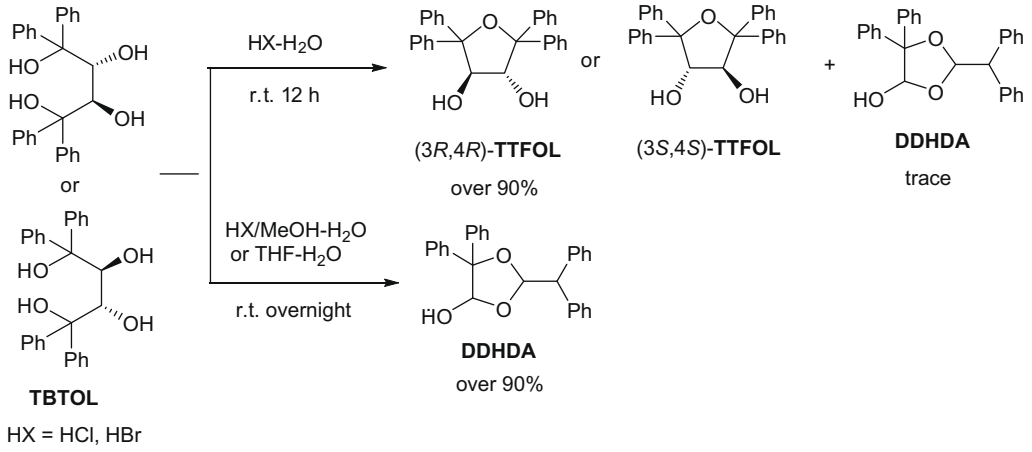
The above facts reveal that (2*R*,3*R*)- and (2*S*,3*S*)-1,1,4,4-tetraphenylbutanetetraol cannot be halogenated by dilute or concentrated hydrohalic acids HX (X = Cl, Br or I) under the experimental conditions.

### 2.3. Mechanism of the formation of TTFOL and DDHDA

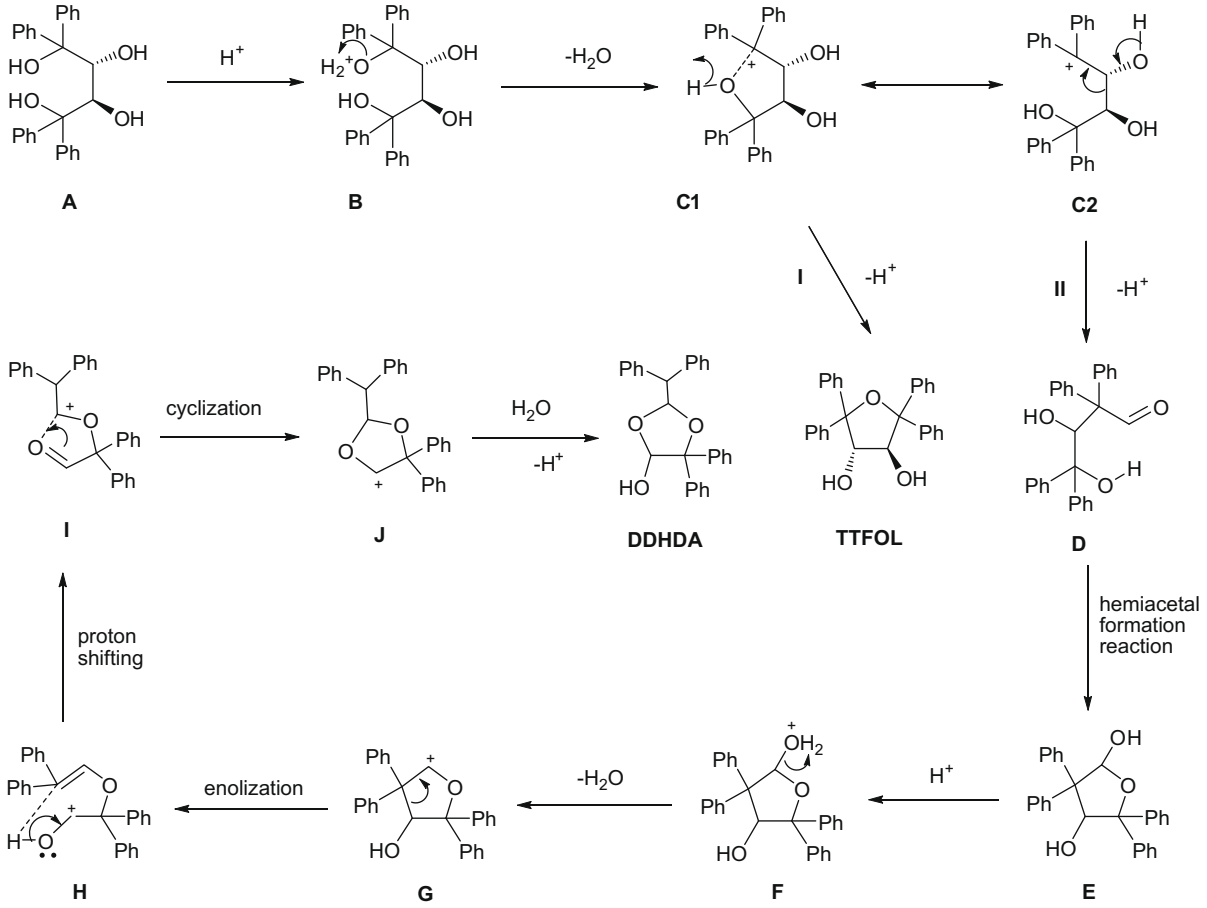
As aforementioned, (3*R*,4*R*)- and (3*S*,4*S*)-**TTFOL**s as well as **DDHDA** are isomers possessing the same composition. How is **DDHDA** generated from (2*R*,3*R*)- or (2*S*,2*S*)-**TBTOL,** via the isomerization of (3*R*,4*R*)- or (2*S*,3*S*)-**TTFOL** or via other routes? To understand the reactions of (2*R*,3*R*)- and (2*S*,3*S*)-**TBTOL**s in the hydrohalic acids, some experiments were performed. The results indicated that when solid (2*R*,3*R*)- and (2*S*,3*S*)-**TBTOL**s were worked-up in dilute hydrochloric acid or hydrobromic acid (ca. 2 mol $L^{-1}$) for 12 h, no cyclization product (3*R*,4*R*)-**TTFOL**, (3*S*,4*S*)-**TTFOL** or **DDHDA** could be separated, and (2*R*,3*R*)- or (2*S*,3*S*)-**TBTOL** was recovered almost quantitatively; (3*R*,4*R*)- and (3*S*,4*S*)-**TTFOL**s, whether they were solids or in solution, were sufficiently stable to the hydrohalic acids, and were not isomerized to **DDHDA** at ambient temperatures. These facts reveal that (3*R*,4*R*)- or (3*S*,4*S*)-**TTFOL** was not an intermediate for **DDHDA**, that is, **DDHDA** must be generated from (2*R*,3*R*)- or (2*S*,3*S*)-**TBTOL** via a complicated process under the catalysis of the appropriate concentration of hydrohalic acids.

For the reaction system, it may be thought that the dehydration reaction of (2*R*,3*R*)- or (2*S*,3*S*)-**TBTOL** is essential and sequentially competition between the cyclization and rearrangement reaction takes place. Under heterogeneous condition, the intermediate generated by dehydration was quickly cyclized into stable (3*R*,4*R*)- or (3*S*,4*S*)-**TTFOL** and isolated out of the reaction system. However, under homogeneous conditions, the intermediate is readily attacked in situ by the hydrohalic acids to form **DDHDA** via a complicated process involving C–C bond cleavage.

A possible mechanism for the formation of (3*R*,4*R*)- or (3*S*,4*S*)-**TTFOL** and **DDHDA** from (2*R*,3*R*)- or (2*S*,3*S*)-**TBTOL** is shown in Scheme 2. As can be seen in Scheme 2, (2*R*,3*R*)-**TBTOL** (**A**) is dehydrated under catalysis of hydrohalic acids to generate a tertiary carbonium ion **C** (**C1** or **C2**) via dehydration. The carbonium ion undergoes deprotonation to form




**Scheme 1.** Reaction of (2*R*,3*R*)- or (2*S*,3*S*)-1,1,4,4-tetraphenylbutanetetraol in hydrohalic acid.




**Scheme 2.** A possible mechanism for the formation of (3*R*,4*R*)-**TTFOL** and **DDHDA** from (2*R*,3*R*)-1,1,4,4-tetraphenylbutanetetraol.

(3*R*,4*R*)-**TTFOL** from **C1** via Route **I** or a dihydroxyaldehyde **D** from **C2** via Route **II**. It can be anticipated, that **D** would undergo intramolecular hemiacetal formation reaction to produce a 2,4-dihydroxytetrahydrofuran **E**. Compound **E** is not stable under acidic conditions, and would undergo further dehydration, enolization, rearrangement, cyclization and hydration to give **DDHDA**.

It is well known that the C–C bond of a vicinal diol is readily broken by periodic acid[8] or lead tetreacetate[9] via oxidation. The cleavage reaction of the C–C bond by a hydrohalic acid seems to have been seldom observed.

## 2.4. Preliminary examination on the chiral induction activity of (3*R*,4*R*)- and (3*S*,4*S*)-TTFOL*s*

Compounds (3*R*,4*R*)- and (3*S*,4*S*)-**TTFOL***s* are sterically hindered, $C_2$ chiral diols and can be conveniently transformed into diamine, diphosphine, and cyclophosphoric ester. according to similar procedures for transformation of hydroxyl group to other functional groups reported previously. However, the chemistry of the sterically hindered $C_2$ chiral diols has been seldom investigated before, although unsubstituted optically active *cis*- and *trans*-tetrahydrofuran-3,4-diols have been synthesized via a variety of routes[10]

and their derivatives applied in asymmetric epoxidations,[11] asymmetric hydrogenation[10f], etc.[12] Considering that chiral diols[13] are highly effective chiral induction auxiliary agents for the (*S*)-proline-catalyzed asymmetric direct aldol reaction, we decided to examine the action of (3*R*,4*R*)- and (3*S*,4*S*)-**TTFOL**s in this type of reaction; we found that they displayed an excellent chiral assistant function. The addition of 1 mol % (3*R*,4*R*)- or (3*S*,4*S*)-**TTFOL**, in the direct (*S*)-proline-catalyzed addition of acetone to 4-chlorobenzaldehyde, 4-bromobenzaldehyde, or 2,6-dichlorobenaldehyde, increased the enantiomeric purity of the desired products up to 9%, 11%, and 26%, respectively, and in the cases of the reactions with 4-chlorobenaldehyde and 2,6-dichlorobenzaldehyde, (3*R*,4*R*)- and (3*S*,4*S*)-**TTFOL**s were stronger asymmetric induction auxiliary agents than enantiopure (*R*)- and (*S*)-1,1′-bi-2-naphthols (Table 1).

## 3. Conclusion

In conclusion, a convenient access to sterically hindered $C_2$ chiral (3*R*,4*R*)- and (3*S*,4*S*)-**TTFOL**s has been developed. Solid (2*R*,3*R*)- or (2*S*,3*S*)-**TBTOL** have been worked-up in concentrated hydrochloric acid or 48% hydrobrominic acid at ambient temperature for 12 h under heterogeneous condition to form nearly quantitatively (3*R*,4*R*)- or (3*S*,4*S*)-**TTFOL**. However, under homogeneous condition (such as in a THF–$H_2O$ or MeOH–$H_2O$ solution), the 1,1,4,4-tetraphenylbutanetetraols reacted with the hydrohalic acids overnight to offer 5,5-diphenyl-2-diphenylmethyl-4-hydroxy-1,3-dioxolane in high yield. Preliminary examination of their asymmetric induction ability shows that (3*R*,4*R*)- or (3*S*,4*S*)-**TTFOL** is a promising chiral auxiliary agent for asymmetric synthesis.

## 4. Experimental

### 4.1. General

Enantiopure (2*R*,3*R*)- and (2*S*,3*S*)-1,1,4,4-tetraphenylbutanetetraols were synthesized from diethyl (2*R*,3*R*)- and (2*S*,3*S*)-tartrate and PhMgBr in THF in a conventional Grignard reaction procedure. L-Proline was purchased from commercial suppliers, and oven-dried at ca. 120 °C and ground finely prior to use. Acetone was dried over anhydrous $K_2CO_3$ and redistilled from $KMnO_4$. Other commercially available starting materials were used without further purification unless specified.

IR spectra were recorded on a Nicolet 170 SX FT-IR spectrophotometer, in KBr, in $cm^{-1}$. NMR spectra were recorded at 300 or 400 MHz for $^1H$, and 75 MHz for $^{13}C$ on a Varian Mercury VS 300 or Bruker AV 400; $\delta$ in (ppm) relative to TMS. Optical rotations were measured on a Perkin–Elmer 341 Mc polarimeter. Mp: VEB Wägetechnik Rapido PHMK 05; uncorrected.

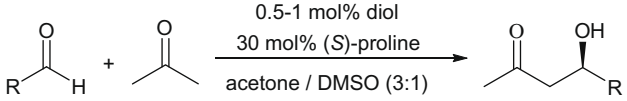
The single crystal X-ray diffraction analysis was performed on Bruker SMART 1 K CCD diffractometer using graphite-monochromated Mo K$\alpha$ radiation ($\lambda$ = 0.71073 Å). The structure was solved by direct methods (SHELXS-97)[16] and refined[17] on $F^2$ values by full-matrix least squares for all unique data.

### 4.2. Preparation of (3*R*,4*R*)- and (3*S*,4*S*)-2,2,5,5-tetraphenyltetrahydrofuran-3,4-diols (TTFOL)

*A representative procedure*: A mixture of 0.396 g (0.93 mmol) of (2*R*,3*R*)-1,1,4,4-tetraphenyl- butanetetraol and 12 mL concentrated hydrochloric acid was stirred at ambient temperature for 12 h, filtered, and a white solid was collected. The solid was crystallized in ethanol to afford 0.361 g of colorless needle crystals of (3*R*,4*R*)-2,2,5,5-tetraphenyltetrahydrofuran-3,4-diol bearing one ethanol molecule, mp: 120–122 °C, 95% yield. $[\alpha]_D^{25} = -208$ (*c* 0.87, $CHCl_3$). IR (KBr, $cm^{-1}$): *v* 3414 s br, 1637 s, 1618 s, 1017 ms. $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.68 (d, *J* = 6.9 Hz, 4H, Ph-H), 7.45–7.33 (m, 6H, Ph-H), 7.11 (s, 10H, Ph-H), 4.51 (d, *J* = 6.9 Hz, 1H, C(3)–H or C(4)–H), 4.50 (d, *J* = 7.8 Hz, 1H, C(4)–H or C(3)–H), 3.71 (q, *J* = 6.9 Hz, 2H, $CH_2$ of EtOH); 1.87 (s, 2H, OH, disappeared after adding $D_2O$), 1.23 (*t*, *J* = 6.9 Hz, 3H, Me of EtOH). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 145.9, 142.1, 128.5, 128.0, 127.8, 127.6, 127.3, 126.6, 85.1, 79.3, 58.7, 18.6. ES-MS (MeOH, ES+): 431(100, $[M_{408}+Na]^+$).

According to a similar procedure, (3*S*,4*S*)-2,2,5,5-tetraphenyltetrahydrofuran-3,4-diol was obtained via intramolecular

**Table 1**
Comparison of (3*R*,4*R*)- and (3*S*,4*S*)-**TTFOL**s with enantiopure **BINOL**s in chiral assistant activity in asymmetric aldol additions catalyzed by a (*S*)-proline-diol system[a]




| Entry | R in aldehyde | Chiral diol additive | Yield (%) | $[\alpha]_D^{20}$ (in $CHCl_3$) | ee (%) | Config. |
|---|---|---|---|---|---|---|
| 1 | 2,6-$Cl_2C_6H_3$ | (*R*,*R*)-**TTFOL** | 80 | $[\alpha]_D^{27} = -53.3$ (*c* 0.6) | 98 | (*R*) |
| 2 | 2,6-$Cl_2C_6H_3$ | (*S*,*S*)-**TTFOL** | 83 | $[\alpha]_D^{25} = -52.8$ (*c* 0.7) | 97 | (*R*) |
| 3 | 2,6-$Cl_2C_6H_3$ | (*R*)-**BINOL** | 89 | $[\alpha]_D^{20} = -51$ (*c* 0.9) | 96 | (*R*) |
| 4 | 2,6-$Cl_2C_6H_3$ | (*S*)-**BINOL** | 90 | $[\alpha]_D^{20} = -51.7$ (*c* 1.3) | 96 | (*R*) |
| 5 | 2,6-$Cl_2C_6H_3$ | 0 | 80 | $[\alpha]_D^{25} = -48.4$ (*c* 1.0) | 89 | (*R*) |
| 6 | 4-$ClC_6H_4$ | (*R*,*R*)-**TTFOL** | 78 | $[\alpha]_D^{27} = +55.4$ (*c* 0.8) | 86 | (*R*) |
| 7 | 4-$ClC_6H_4$ | (*S*,*S*)-**TTFOL** | 79 | $[\alpha]_D^{25} = +54.7$ (*c* 0.9) | 85 | (*R*) |
| 8 | 4-$ClC_6H_4$ | (*R*)-**BINOL** | 78 | $[\alpha]_D^{27} = +53.5$ (*c* 1.0) | 83 | (*R*) |
| 9 | 4-$ClC_6H_4$ | (*S*)-**BINOL** | 79 | $[\alpha]_D^{27} = +52.9$ (*c* 1.3) | 83 | (*R*) |
| 10 | 4-$ClC_6H_4$ | 0 | 76 | $[\alpha]_D^{20} = +48.3$ (*c* 1.0) | 75 | (*R*) |
| 11 | 4-$BrC_6H_4$ | (*R*,*R*)-**TTFOL** | 83 | $[\alpha]_D^{27} = +44.3$ (*c* 0.9) | 89 | (*R*) |
| 12 | 4-$BrC_6H_4$ | (*S*,*S*)-**TTFOL** | 87 | $[\alpha]_D^{25} = +45.3$ (*c* 0.9) | 91 | (*R*) |
| 13 | 4-$BrC_6H_4$ | (*R*)-**BINOL** | 74 | $[\alpha]_D^{27} = +48.3$ (*c* 0.8) | 97 | (*R*) |
| 14 | 4-$BrC_6H_4$ | (*S*)-**BINOL** | 76 | $[\alpha]_D^{27} = +47.1$ (*c* 0.8) | 97 | (*R*) |
| 15 | 4-$BrC_6H_4$ | 0 | 82 | $[\alpha]_D^{20} = +35.3$ (*c* 1.0) | 65[b] | (*R*) |

[a] The reactions were carried out in acetone/DMSO (3:1) at 0 °C for 48 h, where 1 mol % (3*R*,4*R*)- or (3*S*,4*S*)-**TTFOL**, 0.5 mol % (*R*)-**BINOL** and 1 mol % (*S*)-**BINOL** were used as chiral additives, respectively. Entries 5 and 10 are abstracted from the literature.[14] The ee was obtained by comparison with the maximum of specific rotation.
[b] Entry 15 is cited from the literature.[15]

cyclocondensation of (2*S*,3*S*)-1,1,4,4-tetraphenylbutanetetraol. mp: 119–121 °C, 92% yield. $[\alpha]_D^{25} = -207.8$ (*c* 0.7, $CHCl_3$). $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$ 7.70 (d, *J* = 8.0 Hz, 4H, Ph-H), 7.47–7.36 (m, 6H, Ph-H), 7.13–7.09 (s, 10H, Ph-H), 4.49 (s, 2H, C(4)–H and C(3)–H), 3.69 (q *J* = 6.8 Hz, 2H, $CH_2$ of EtOH), 2.26 (s, 2H, OH, disappeared after adding $D_2O$), 1.40 (s, 1H, OH, disappeared after adding $D_2O$), 1.24 (*t*, *J* = 6.8 Hz, 3H, Me of EtOH). $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 145.6, 141.9, 128.3, 127.8, 127.4, 127.1, 126.4, 85.0, 79.2, 58.5, 18.4.

### 4.3. Crystallographic data of (3*R*,4*R*)-TTFOL

Empirical formula, $C_{30}H_{30}O_4$ ($C_{28}H_{24}O_3 \cdot C_2H_5OH$); formula weight, 454.54; calculated density, 1.149 g/cm$^3$; volume (V), 5257(2) Å$^3$; crystal system, orthorhombic; *Z* = 8; space group, *P*2(1)2(1)2(1); unit cell dimensions, *a* = 10.120 (3), *b* = 14.658 (4), *c* = 35.440 (9); $\mu$, 0.075 mm$^{-1}$; $-12 < h < 12$, $-13 < k < 18$, $-43 < l < 37$; *F*(0 0 0): 1936; GOF, 1.028; *T* = 273(2) K; radiation type, Mo K$\alpha$; *R*(reflections) = 0.0558 (7317); $wR_2$ (reflections) = 0.1727 (10296).

### 4.4. Formation of 2-diphenylmethyl-4-hydroxy-5,5-diphenyl-1,3-dioxolane (DDHDA)

In a similar reaction to the above, a THF solution of (2*R*,3*R*)-1,1,4,4-tetraphenylbutanetetraol was allowed to stir with hydrochloric or hydrobromic acid under homogeneous conditions overnight to afford a solid. The solid was recrystallized in AcOEt to give 2-diphenylmethyl-4-hydroxy-5,5-diphenyl-1,3-dioxolane, 90% yield, mp 164–166 °C. $[\alpha]_D^{25} = 0$ (*c* 1, $CHCl_3$). IR (KBr, cm$^{-1}$): 2027 w, 1650 br, 1435, 1360, 1102, 1026; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 7.51–7.45 (m, 8H, Ph-H), 7.38–7.19 (m, 12H, Ph-H), 5.91 (d, *J* = 12.6 Hz, 1H, C–H), 5.55 (d, *J* = 2.1 Hz, 1H, C–H), 4.54 (s, 1H, C–H), 1.11 (d, *J* = 11.7 Hz, 1H, OH, disappeared after adding $D_2O$). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 136.9, 136.8, 127.6, 126.4, 126.0, 125.8, 125.1, 124.8, 124.0, 101.1, 95.3, 88.2, 52.8. ES-MS (MeOH, ES+): 431 (58, $[M_{408}+Na]^+$).

### 4.5. Crystallographic data of DDHDA

Empirical formula, $C_{28}H_{24}O_3$; formula weight, 408.47; calculated density, 1.257 g/cm$^3$; volume (V), 4316 (4) Å$^3$; crystal system, monoclinic; *Z* = 8; space group, *C*2/*c*; unit cell dimensions, *a* = 39.95 (2), *b* = 5.622 (3), *c* = 22.604 (12); $\beta$ = 121.784 (8); $\mu$, 0.081 mm$^{-1}$; $-28 < h < 50$, $-6 < k < 7$, $-28 < l < 17$; *F*(0 0 0): 1728; GOF, 1.049. *T* = 273(2) K, radiation type, Mo K$\alpha$; *R* (reflections) = 0.0394 (3306); $wR_2$ (reflections) = 0.1041 (4443).

### 4.6. Asymmetric direct aldol reaction catalyzed by a (*S*)-proline-enantiopure TTFOL system

*A representative procedure*: In a test tube fitted with a magnetic bar, (*S*)-proline (1.5 mmol) and (3*R*,4*R*)-2,2,5,5-tetraphenyltetrahydrofuran-3,4-diol (0.05 mmol) were charged, and followed by injection of acetone (3 mL) and DMSO (1 mL). After stirring for 15 min at 0–5 °C, an aromatic aldehyde (5 mmol) was added and stirred continuously at the same temperature for 48 h. The reaction was quenched with saturated aqueous ammonium chloride and extracted with ethyl acetate (10 mL × 3). The combined organic phase was dried over anhydrous $Na_2SO_4$, filtered, concentrated, and purified through flash column chromatography on a silica gel (200–300 mesh, eluent: petroleum ether/acetate 2:1) to give the desired product. The results are summarized in Table 1.

### Acknowledgments

We thank the National Natural Science Foundation of China (20672083 and 20872115) for financial support. We also thank associate professor Zhongxing Jing for beneficial discussion on the formation mechanism of 2-diphenylmethyl-4-hydroxy-5,5-diphenyl-1,3-dioxolane.

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