Tetraaryl-1,3-dioxolane-4,5-dimethanols as catalysts for the addition of trimethylsilyl cyanide to benzaldehyde and the oxirane ring

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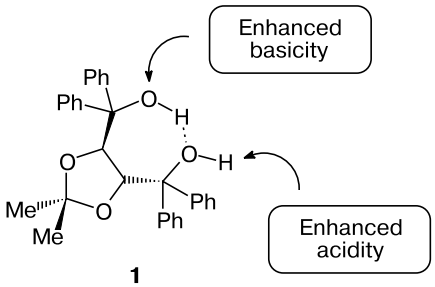
The synthesis of 1,2-, 1,3-, and 1,4-phenylene-bis[(4*R*,5*R*)-4,5-di(hydroxydiphenylmethyl)-1,3-dioxolane]s (*ortho*-, *meta*-, and *para*-bis-(*R*,*R*)-TADDOLs) and bis[4-{[(4*R*,5*R*)-4,5-di(hydroxydiphenylmethyl)]-1,3-dioxolan-2-yl}phenyl]methane was carried out. The possibilities of the use of these compounds as catalysts for the C—C bond formation in the addition of Me_3SiCN to benzaldehyde and the oxirane ring opening in cyclohexene oxide by Me_3SiCN were investigated. The catalytic activity of different bis-(*R*,*R*)-TADDOLs in this series depends on their structure.

Key words: organic catalysis, Brønsted acids, bis-(*R*,*R*)-α,α,α´,α´-tetraaryl-1,3-dioxolane-4,5-dimethanols, mandelonitrile, trimethylsilyl cyanide.

Asymmetric organocatalysis with chiral organic Brønsted acids and bases is an important field of investigation in modern asymmetric synthesis.[1—3] This approach is very attractive due to the conceptual and experimental simplicity, the absence of hazardous heavy metal salts in reaction mixtures, and extremely high efficiency of catalysis.[4] This class of catalysts includes chiral polyfunctional Brønsted acids, α,α,α´,α´-tetraaryl-1,3-dioxolane-4,5-dimethanols ((*R*,*R*)-TADDOLs),[5] in which the acidity of one hydroxy group increases due to the presence of another hydroxy group as a result of intramolecular hydrogen bonding. The structure of (4*R*,5*R*)-2,2-dimethyl-4,5-di(hydroxydiphenylmethyl)-1,3-dioxolane (**1**) is given below.



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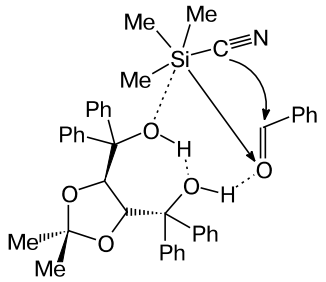
This type of catalysts activated by Brønsted acids is called Brønsted acid assisted Brønsted acid catalysts.[6] The asymmetric Diels—Alder reactions,[7] the Mukaiyama reaction,[8] and the TADDOL-promoted condensation of nitroso compounds with enamines[9] provide examples of this catalysis.

Evidently, an increase in the acidity of one hydroxy group leads to an increase in the basicity of another hydroxy group, in which the hydrogen atom is involved in hydrogen bonding.[6] Hence, TADDOLs would be expected to act as chiral bifunctional catalysts by activating both the electrophilic and nucleophilic components of the reaction, as exemplified by the hypothetical transition state (TS**1**) of the addition reaction[10] of Me_3SiCN to aldehydes.



TS**1**

Presumably, the presence of two (*R*,*R*)-TADDOL fragments in a single molecule can increase the efficiency of such catalysts due to the spatially favorable arrangement of several acidic groups capable of activating substrates.

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The use of cyclohexanedione-based bis-TADDOLs[11,12] in photochemical reactions was documented.[13] However, these compounds were used in equimolar amounts with respect to substrates.

In the present study, we synthesized bis-(*R*,*R*)-TADDOLs and investigated their catalytic activity in the addition reactions of Me_3SiCN with benzaldehyde and the oxirane ring opening in cyclohexene oxide. The known examples of the addition of Me_3SiCN to benzaldehyde in the presence of organic catalysts are few in number and involve the use of bases and carbenes.[14,15]

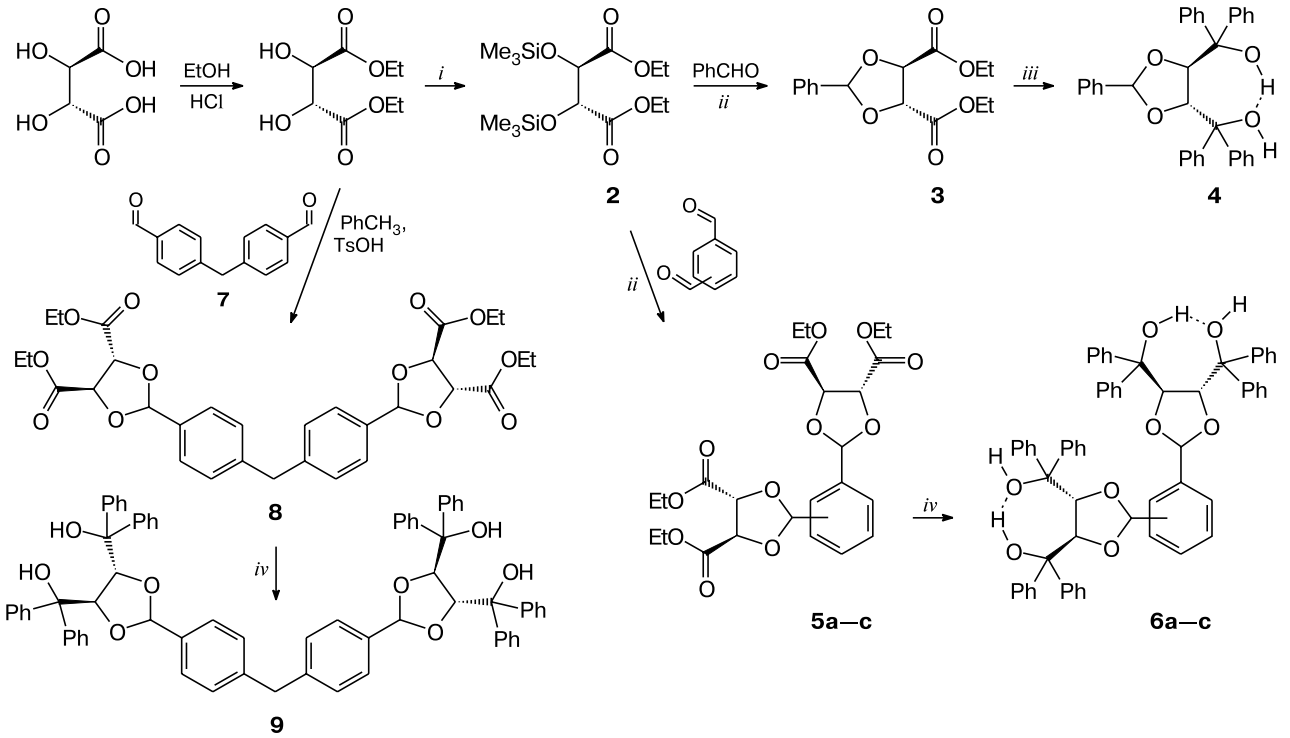
Results and Discussion

Mono-(*R*,*R*)-TADDOL and bis-(*R*,*R*)-TADDOLs were synthesized starting from diethyl ester of natural L-tartaric acid, benzaldehyde, the corresponding diformylbenzenes, and bis(4-formylphenyl)methane (Scheme 1). 2,2´-(Phenylene)bis[(4*R*,5*R*)-4,5-di(hydroxydiphenylmethyl)-1,3-dioxolane)]s and bis[4-{[(4*R*,5*R*)-4,5-di(hydroxydiphenylmethyl)]-1,3-dioxolan-2-yl}phenyl]methane were synthesized according to a procedure analogous to that used earlier[16] for the preparation of mono-(*R*,*R*)-TADDOL. The first step affords diethyl tartrate, and the treatment of the latter with trimethylchlorosilane in the presence of triethylamine gives bis-*O*-silyl derivative **2** (see Scheme 1). The condensation of **2** with 1,2-, 1,3-, or 1,4-phthalaldehyde or benzaldehyde in the presence of boron trifluoride diethyl etherate and trifluoromethanesulfonic acid affords acetals, whose treatment with phenylmagnesium bromide yields the corresponding bis-(*R*,*R*)-TADDOLs. In the case of the diphenylmethane derivative, acetal **8** was prepared by refluxing the corresponding dialdehyde and diethyl tartrate in toluene in the presence of toluenesulfonic acid with azeotropic distillation of water.

The structures of the resulting bis-(*R*,*R*)-TADDOLs were confirmed by elemental analysis, ^1H NMR spectroscopy, and mass spectrometry, as well as by the results of X-ray diffraction study of tetramethyl ester **5a´**, which is a related compound of intermediate compound **5a** (Fig. 1) and for which crystals suitable for X-ray diffraction were grown (crystals of **5a** were not obtained), and *para*-bis-TADDOL **6c** (Fig. 2).

The X-ray diffraction study showed that the crystals of compound **5a´** contain two independent molecules per asymmetric unit. The main geometric parameters of two molecules are virtually identical. The dioxolane rings adopt an envelope conformation with the C(7) and C(14) atoms deviating from the plane through the other atoms

Scheme 1



1,2- (**5a**, **6a**), 1,3- (**5b**, **6b**), 1,4-phenylene-bis[(4*R*,5*R*)-4,5-di(hydroxydiphenylmethyl)-1,3-dioxolane] (**5c**, **6c**).

Reagents and conditions: *i*. Me_3SiCl/Et_3N, $PhCH_3$, 0 °C; *ii*. 1) $BF_3 \cdot OEt_2$, 2) CF_3SO_3H; *iii*. 4 PhMgBr, THF; *iv*. 8 PhMgBr, THF.

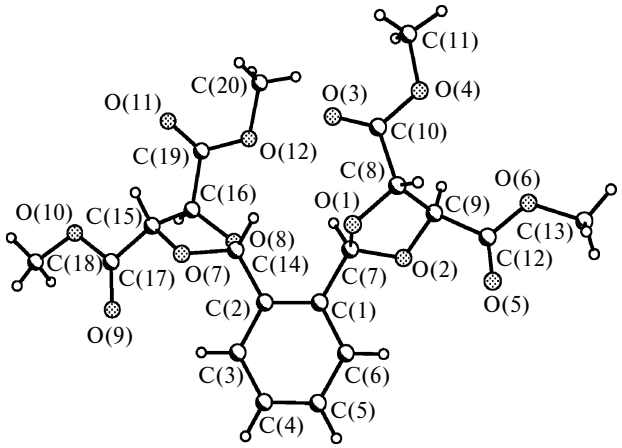


Fig. 1. Overall view of tetramethyl ester **5a´** related to compound **5a**.

of the ring (see Fig. 1). The carboxy substituents in the dioxolane rings are in the axial positions and have *trans* orientations with respect to each other. Slight differences in the geometry of the independent molecules in the crystal structure of **5a´** are associated with the mutual arrangement of the dioxolane substituents with respect to the aromatic ring. The torsion angles characterizing the rotation of the rings in two independent molecules vary in a rather narrow range from 25.7° to 54.8°. In turn, this fact allows the conclusion that the rotation of one dioxolane ring with respect to another ring is hindered by steric factors. The steric strain can substantially influence the catalytic properties of bis-(*R*,*R*)-TADDOLs prepared from compounds **5**.

The X-ray diffraction data for *para*-bis-(*R*,*R*)-TADDOL **6c** (see Fig. 2) show that the crystals of **6c**, like those of **5a´**, contain two crystallographically independent molecules. Compound **6c** crystallizes as a solvate with two methanol molecules per independent *para*-bis-(*R*,*R*)-TADDOL molecule. The geometry of two independent molecules in the crystal structure of **6c** is virtually identical. Slight differences are observed only in the conformations, to be more precise, in the orientation of the dioxolane ring with respect to the central aromatic ring. In compound **6c**, one of the hydroxy groups in both TADDOL fragments is involved in an intramolecular O—H...O bond (O...O, 2.686(4)—2.791(4) Å), whereas another OH group forms an intermolecular hydrogen bond with the methanol solvent molecules (O...O, 2.670(4)—2.850(4) Å) (see Fig. 2). The bis-(*R*,*R*)-TADDOL molecules are linked to each other by these interactions to form H-bonded chains (Fig. 3).

Initially, we studied the catalytic activity of bis-TADDOLs **6a—c** based on three isomeric diformyl-

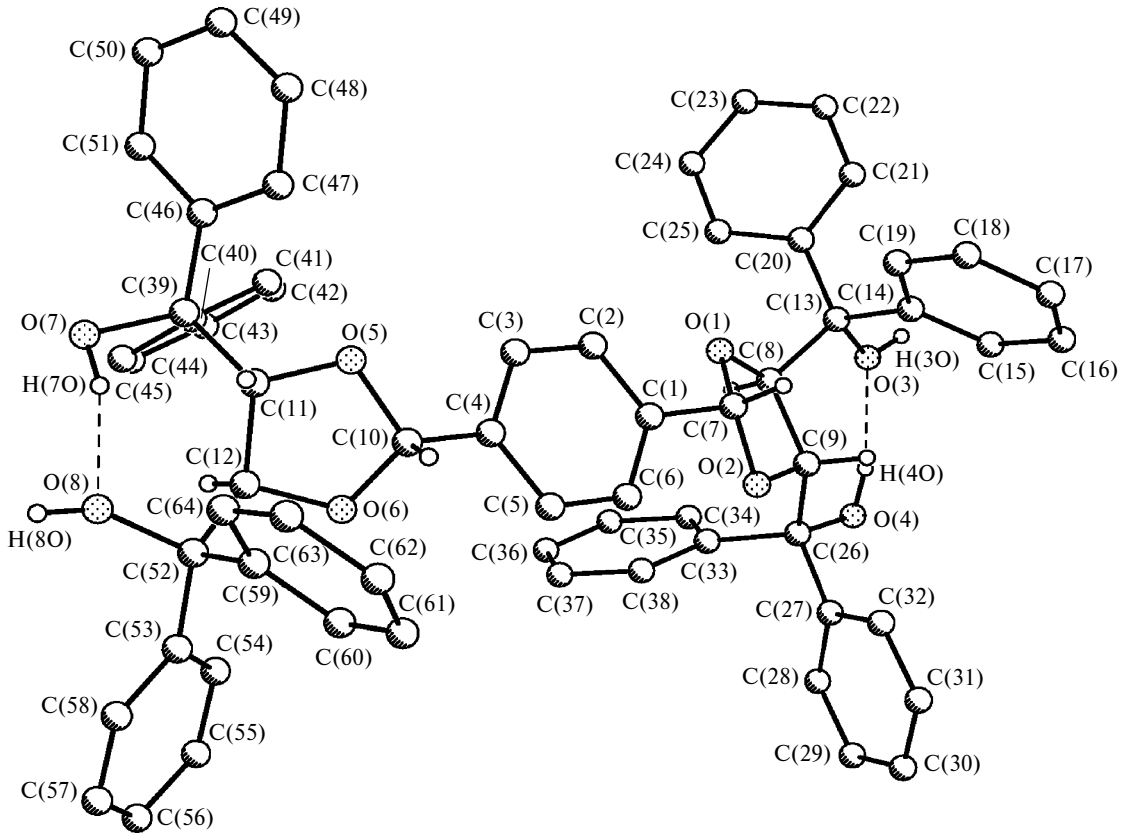


Fig. 2. Overall view of *para*-bis-(*R*,*R*)-TADDOL **6c**.

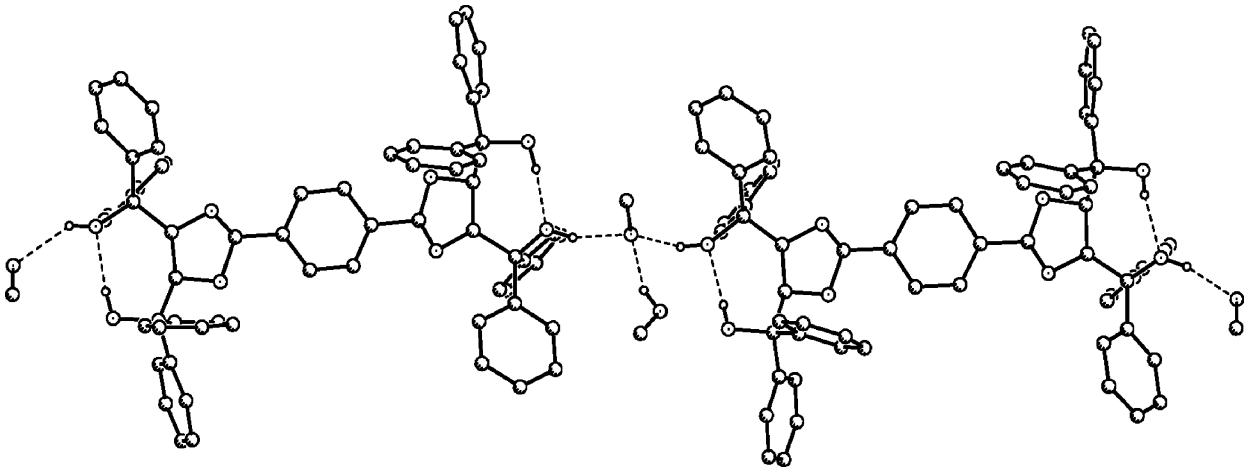
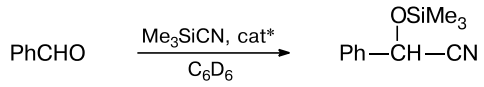


Fig. 3. Fragment of the H-bonded chain of *para*-bis-(*R*,*R*)-TADDOL and the methanol molecules of solvation in the crystal structure of **6c**.

benzenes and mono-TADDOL **4** in the addition of Me_3SiCN to benzaldehyde and cyclohexene oxide.

The addition of trimethylsilyl cyanide to benzaldehyde (Scheme 2) was monitored by ^1H NMR spectroscopy. The reaction was carried out in deuterated benzene in an NMR tube. It was found that the reaction does not proceed in the absence of a catalyst. In the presence of both mono-(*R*,*R*)-TADDOL (10 mol.%) and bis-(*R*,*R*)-TADDOLs (5 mol.%),* the reaction produces the *O*-silyl derivative of mandelonitrile. The course of the reaction can easily be followed based on the disappearance of the signal for the proton at the carbonyl group of benzaldehyde at δ 9.78 and the appearance of the signal for the α proton of the trimethylsilyl derivative of mandelonitrile at δ 5.36. According to the ^1H NMR specta of the reaction mixture recorded at certain intervals, no by-products were formed even after 48 h.

Scheme 2



It could not be sure that the reaction was not accompanied by leaching of sodium ions from the glass surface to form the corresponding sodium derivatives of TADDOL, which can serve as catalysts for the reaction. To exclude this possibility, we carried out kinetic studies in a quartz tube with the use of 10 mol.% of compound **6c**. It appeared that, both in quartz and glass tubes, the reactions proceed at the same rate (within the experimental error). Hence, it can be concluded that the reaction is catalyzed by free (*R*,*R*)-TADDOLs.

* The ratio PhCHO : TMSCN = 1 : 1.5 at benzaldehyde concentrations of 0.94 mol L^{-1}.

The NMR monitoring of the reaction allowed us also to refute the possibility of silylation (complete or partial) of alcohol groups in the catalysts. In the course of the reaction, the signals for the hydroxy protons of mono-TADDOL and all bis-(*R*,*R*)-TADDOLs (at δ 3.94 and 3.59) became slightly broader, but their integral intensities remained unchanged, which is evidence that the catalysts undergo no substantial changes in the course of the reaction.

The dependence of the yield of *O*-silylmandelonitrile on the reaction time of the addition reaction in the presence of bis-(*R*,*R*)-TADDOLs as the catalysts is presented in Fig. 4. This figure also shows the accumulation of the product in the reaction catalyzed by mono-TADDOL **4** taken in a double amount with respect to bis-(*R*,*R*)-TADDOLs. As can be seen from these data,

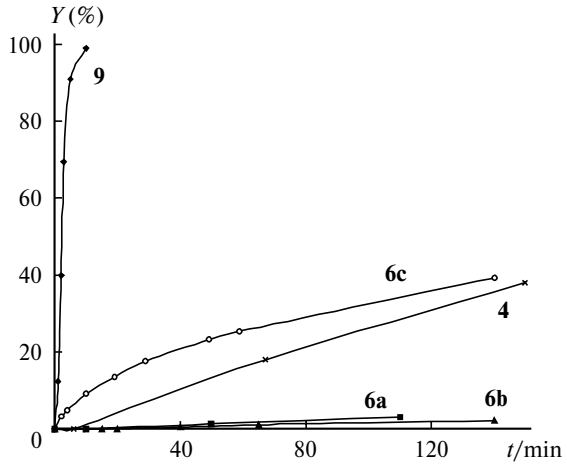


Fig. 4. Plot of the yield (*Y*) of the reaction product *vs.* the time (*t*) of the addition of trimethylsilyl cyanide to benzaldehyde in C_6D_6 in the presence of 5 mol.% of **6a—c** or **9** and 10 mol.% of **4** as the catalyst at 20 °C; [PhCHO] = 0.94 mol L^{-1}, [Me_3SiCN] = 1.41 mol L^{-1}.

Table 1. Reaction of benzaldehyde with trimethylsilyl cyanide catalyzed by (*R*,*R*)-TADDOLs in C_6D_6 and CH_2Cl_2[a]

TADDOL	Yield of the product[b] (%)	
	CH_2Cl_2	C_6D_6
4	10	8
6a	0	0
6b	5	1
6c	85	18

[a] The reaction conditions: benzaldehyde (1 mmol), trimethylsilyl cyanide (1.5 mmol), the catalysts (5 mol.% in the case of **6a—c** and 10 mol.% in the case of **4**), CH_2Cl_2 (1 mL) or C_6D_6, argon atmosphere, 25 °C, 30 min.
[b] The yield of *O*-silylmandelonitrile was determined by ^{1}H NMR spectroscopy.

terephthalaldehyde-based *para*-(*R*,*R*)-TADDOL **6c** is the most efficient catalyst superior to *ortho* (**6a**) and *meta* isomers (**6b**), as well as to mono-(*R*,*R*)-TADDOL **4**.

Our studies showed that the catalytic activity of bis-TADDOLs remains unchanged in going from deuterobenzene to toluene or dichloromethane. The reaction in dichloromethane in the presence of 5 mol.% of catalyst **6c** is completed in 30 min to give the product in 85% yield, whereas other bis-(*R*,*R*)-TADDOLs and mono-(*R*,*R*)-TADDOL **4** appeared to be inefficient (Table 1).

The reaction rate substantially increases as the amount of the catalyst increases from 1 mol.% to 10 mol.% (Fig. 5).

The linearization of the kinetic curves in logarithmic coordinates allows the calculation of the reaction order with respect to the catalyst (Fig. 6). The slope is 1.89 (the correlation coefficient is 0.9989), which is indicative of the second reaction order with respect to the catalyst (calculated for **6c**).

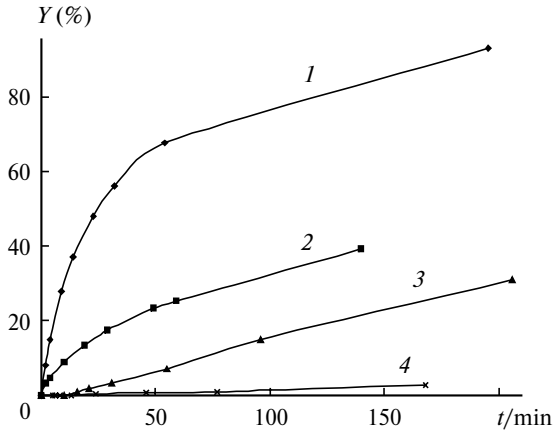


Fig. 5. Plot of the yield (*Y*) of the reaction product *vs*. the reaction time (*t*) of the trimethylsilylcyanation of benzaldehyde in C_6D_6 in the presence of 10 (*1*), 5 (*2*), 2 (*3*), and 1 mol.% (*4*) of *para*-bis-(*R*,*R*)-TADDOL **6c** at 20 °C; [PhCHO] = 0.94 mol L^{-1}, [Me_3SiCN] = 1.41 mol L^{-1}.

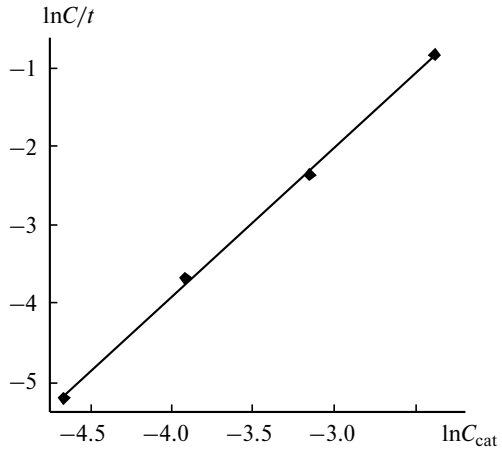
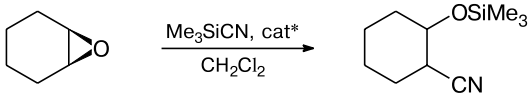


Fig. 6. Plot of the logarithm of the initial rate of the reaction PhCHO with Me_3SiCN *vs*. the logarithm of the concentration of **6c**: $y = 1.8901x + 3.6504$; $R^2 = 0.9989$.

Taking into account the data on the catalytic activity of bis-TADDOLs, it can be concluded that the distance between the dioxolane fragments in the molecules of these compounds is of considerable importance. This dependence is additionally exemplified by the use of bis-(*R*,*R*)-TADDOL **9** as the catalyst for the addition of trimethylsilyl cyanide to benzaldehyde, whose catalytic activity is substantially higher than that of compounds **6a—c** (see Fig. 4). The quantitative conversion of benzaldehyde in the presence of 5 mol.% of catalyst **9** was achieved within 15 min, as opposed to compound **6c**, in the presence of which the analogous result was attained only within 8 h.

The epoxide ring opening with Me_3SiCN is another reaction, which would be catalyzed by Brønsted acids (Scheme 3). Like the addition of Me_3SiCN to aldehydes, the epoxide cleavage does not proceed in the absence of catalysts. The asymmetric epoxide cleavage catalyzed by chiral Lewis acids,[17,18] including the reaction with Me_3SiCN,[19,20] was studied in detail. However, to our knowledge, there are no examples of the asymmetric catalysis of the epoxide ring opening with Me_3SiCN promoted by chiral Brønsted acids.

Scheme 3



It appeared that, of all (*R*,*R*)-TADDOLs, only bis-(*R*,*R*)-TADDOL **6c** (5 mol.%) catalyzes this reaction, which proceeds at room temperature for 4 days and produces the racemic product in quantitative yield. This product was detected by ^{1}H NMR spectroscopy (no by-products were observed in the reaction mixture). The

concentration of cyclohexene oxide in dichloromethane was 0.25 mol L^{-1}.

Therefore, the fixation of two (*R*,*R*)-TADDOL fragments at a particular distance in a single organic molecule is an efficient approach to the design of new organic chiral BBA catalysts.[6] The further modification of the bridge between two (*R*,*R*)-TADDOL fragments, in particular, an increase in its flexibility, would be expected to result in even higher activity of the catalysts. Although we prepared racemic products, the replacement of the phenyl groups in the bis-(*R*,*R*)-TADDOL fragment by bulkier substituents would be expected to increase the enantioselectivity of the reactions.[21]

Experimental

The ^{1}H NMR spectra were recorded on Bruker Avance 300 (300.13 MHz), Bruker Avance 400 (400.13 MHz), and Bruker Avance 600 (600.22 MHz) spectrometers; the chemical shifts were measured relative to the residual protons of the deuterated solvent ($CDCl_3$ or C_6D_6). The optical rotation was measured on a Perkin—Elmer 241 polarimeter in a 5-cm cell temperature-stabilized at 25 °C. The column chromatography was performed with the use of silica gel Kieselgel 60 (Merck). The catalysts were prepared from the following commercial reagents: phthalaldehyde, isophthalaldehyde, terephthalaldehyde (Aldrich), and trifluoromethanesulfonic acid (Acros). The elemental analysis was carried out in the Laboratory of Microanalysis of the A. N. Nesmeyanov Institute of Organoelement Compounds of the Russian Academy of Sciences. All solvents were purified according to standard procedures. Benzaldehyde and trimethylsilyl cyanide were freshly distilled.

The X-ray diffraction study of compounds **5a´** and **6c** was carried out on Syntex $P2_1$ (Mo-Kα radiation, graphite monochromator, θ/2θ-scanning technique) and SMART 1000 CCD (Mo-Kα radiation, graphite monochromator, ω-scanning technique) diffractometers, respectively. The structures were solved by direct methods and refined anisotropically by the full-matrix least-squared method based on F^2_{hkl}. The hydrogen atoms of the hydroxy groups were located in difference Fourier maps. Other hydrogen atoms were positioned geometrically. The hydrogen atoms of three methanol molecules in the crystal structure of **6c** were not located. Principal crystallographic data and the refinement statistics are given in Table 2. All calculations were carried out with the use of the SHELXTL PLUS program package.[22]

The positive ion MALDI-TOF mass spectra were obtained on a Reflex III instrument (Bruker Daltonics) in the linear mode; the target voltage was set to 20 kV. 2,5-Dihydroxybenzoic acid was used as the matrix. Samples were prepared by dissolving the compounds in chloroform ($c = 10^{-4}$—10^{-6} mol L^{-1}) and mixing with a solution of the matrix in 30% aqueous acetonitrile (30 mg mL^{-1}) in a ratio of 1 : 1.

Diethyl L-tartrate (1) was synthesized according to a standard procedure[23] in 95% yield, b.p. 133—135 °C (1 Torr) (*cf.* lit. data[23]: b.p. 113 °C (0.5 Torr)).

Diethyl (*R*,*R*)-2,3-bis(*O*-trimethylsilyl)tartrate (2). Trimethylchlorosilane (16 g, 0.147 mol) was added dropwise to a solution of diethyl L-tartrate (**1**) (11.6 g, 0.066 mol) and triethylamine (17.5 mL) in toluene (100 mL) under argon with cooling to −5 °C. The white reaction mixture was stirred at ~20 °C for 4 h. Then an aqueous saturated sodium bicarbonate solution (50 mL) was added, the organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3×30 mL). The combined organic layers were washed with a saturated $NaHCO_3$ solution (2×50 mL), dried over $MgSO_4$, and filtered. The solvent was removed by evaporation. The yield was 15.4 g (78%), b.p. 142—145 °C (1 Torr). ^{1}H NMR ($CDCl_3$), δ: 4.59—4.61 (m, 2 H, CH); 4.12—4.24 (m, 4 H, CH_2); 1.23—1.32 (m, 6 H, Me); 0.10 (s, 18 H, Me).

Table 2. Principal crystallographic data and the refinement statistics for **5a´** and **6c**

Parameter	**5a´**	**6c**
Molecular formula	$C_{20}H_{22}O_{12}$	$C_{66}H_{62}O_{10}$
Molecular weight	454.38	1015.16
T/K	193	100
Crystal system	Triclinic	Monoclinic
Space group	*P*1	$P2_1$
Z (*Z´*)	2 (2)	4 (2)
a/Å	8.5511(17)	20.023(3)
b/Å	10.887(2)	9.0490(11)
c/Å	13.157(3)	29.047(4)
α/deg	67.79(3)	—
β/deg	74.92(3)	100.020(6)
γ/deg	70.09(3)	—
V/Å	1054.0(5)	5182.7(13)
d_{calc}/g cm^{-3}	1.432	1.301
μ/cm^{-3}	1.20	0.87
F(000)	476	2152
$2\theta_{max}$/deg	58	54
Number of measured reflections	5909	34679
Number of independent reflections	5909	22163
Number of reflections with $I > 2\sigma(I)$	4111	11127
Number of variables	585	—
R_1	0.0505	0.0842
wR_2	0.1081	0.1949
GOOF	1.005	0.999
Residual electron density/e $Å^3$ (d_{min}/d_{max})	0.273/−0.229	0.492/−0.361

2,2´-(Phenylene)bis[(4*R*,5*R*)-4,5-di(ethoxycarbonyl)-1,3-dioxolanes] 5a—c (general procedure). Boron trifluoride diethyl etherate (0.14 mL, 0.1 mmol) was added to a solution of the corresponding diformylbenzene (1 g, 0.94 mmol) and diethyl (*R*,*R*)-2,3-bis(trimethylsilyl)tartrate (6.2 g, 1.9 mmol) in CH_2Cl_2 (25 mL) under argon at 0 °C. The reaction mixture was stirred for 15 min, and then trifluoromethanesulfonic acid (0.06 mL, 0.4 mmol) was added dropwise. The mixture was stirred at 0 °C for 30 min, kept at ~20 °C for 16 h, and again cooled to 0 °C. A saturated sodium carbonate solution (25 mL) was added. The reaction mixture was allowed to warm to ~20 °C and stirred for 15 min. The organic layer was separated, and the aqueous layer

was extracted with dichloromethane (2×25 mL). The combined organic layers were washed with water (2×100 mL), dried over $MgSO_4$, and concentrated. The product was recrystallized from a 1 : 1 hexane—ethyl acetate mixture.

2,2´-(1,2-Phenylene)bis[(4*R*,5*R*)-4,5-di(ethoxycarbonyl)-1,3-dioxolane] (5a). The yield was 3.3 g (87%), m.p. 70 °C, $[\alpha]_D^{25}$ −16.0 (*c* 1, $CHCl_3$). Found (%): C, 52.78; H, 5.07. $C_{24}H_{30}O_{12}$. Calculated (%): C, 52.86; H, 4.85. ^{1}H NMR ($CDCl_3$), δ: 7.88—7.85 (m, 2 H, H arom.); 7.51—7.48 (m, 2 H, H arom.); 6.54 (s, 2 H, CH); 5.03 (d, 2 H, CH, *J* = 4.23 Hz); 4.89 (d, 2 H, CH, *J* = 4.26 Hz); 4.39—4.29 (m, 8 H, CH_2); 1.43—1.32 (m, 12 H, Me).

2,2´-(1,3-Phenylene)bis[(4*R*,5*R*)-4,5-di(ethoxycarbonyl)-1,3-dioxolane] (5b) was prepared as oil in a yield of 2.5 g (68%), $[\alpha]_D^{25}$ −24.6 (*c* 1, $CHCl_3$). Found (%): C, 52.81; H, 4.84. $C_{24}H_{30}O_{12}$. Calculated (%): C, 52.86; H, 4.85. ^{1}H NMR ($CDCl_3$), δ: 7.78 (s, 1 H, H arom.); 7.70 (d, 1 H, H arom., *J* = 7.47 Hz); 7.69 (d, 1 H, H arom., *J* = 7.47 Hz); 7.48 (t, 1 H, H arom., *J* = 7.4 Hz); 6.21 (s, 2 H, CH); 4.98 (d, 2 H, CH, *J* = 3.9 Hz); 4.87 (d, 2 H, CH, *J* = 4.1 Hz); 4.39—4.26 (m, 8 H, CH_2); 1.41—1.30 (m, 12 H, Me).

2,2´-(1,4-Phenylene)bis[(4*R*,5*R*)-4,5-di(ethoxycarbonyl)-1,3-dioxolane] (5c). The yield was 2.9 g (77%), m.p. 78 °C, $[\alpha]_D^{25}$ −17.3 (*c* 1, $CHCl_3$). Found (%): C, 52.80; H, 4.79. $C_{24}H_{30}O_{12}$. Calculated (%): C, 52.86; H, 4.85. ^{1}H NMR ($CDCl_3$), δ: 7.67 (s, 4 H, H arom.); 6.23 (s, 2 H, CH); 4.99 (d, 2 H, CH, *J* = 4.0 Hz); 4.87 (d, 2 H, CH, *J* = 3.8 Hz); 4.42—4.29 (m, 8 H, CH_2); 1.44—1.33 (m, 12 H, Me).

2,2´-(1,2-Phenylene)bis[(4*R*,5*R*)-4,5-di(methoxycarbonyl)-1,3-dioxolane] (5a´) was synthesized analogously to acetals **5a—c** with the use of dimethyl 2,3-bis(*o*-trimethylsilyl) tartrate according to the above-described procedure. The yield was 1.5 g (77%), m.p. 53 °C, $[\alpha]_D^{25}$ −43 (*c* 1, $CHCl_3$). Found (%): C, 52.80; H, 4.91. $C_{20}H_{22}O_{12}$. Calculated (%): C, 52.87; H, 4.88. ^{1}H NMR ($CDCl_3$), δ: 7.86—7.83 (m, 2 H, H arom.); 7.50—7.47 (m, 2 H, H arom.); 6.44 (s, 2 H, CH); 4.87 (d, 2 H, CH, *J* = 3.02 Hz); 4.77 (d, 2 H, CH, *J* = 3.04 Hz); 3.74, 3.75, 3.77, 3.78 (all s, 12 H, OMe).

2,2´-(1,4-Phenylene)bis[(4*R*,5*R*)-4,5-di(hydroxydiphenylmethyl)-1,3-dioxolane] (6c). The synthesis was carried out under argon. A solution of compound **5c** (0.3 g, 0.59 mmol) was added at 5 °C to a solution of PhMgBr, which was prepared from magnesium metal (0.5 g) and PhBr (1.57 g, 10 mmol) in THF (20 mL). The reaction mixture was heated to boiling, refluxed for 2 h, and kept at ~20 °C for 16 h. Then the reaction mixture was quenched with a saturated NH_4Cl solution (50 mL). The organic layer was separated, washed with a saturated $NaHCO_3$ solution (50 mL), and dried over $MgSO_4$. The solvent was removed *in vacuo*. The resulting oil was recrystallized from acetone. The yield of the product was 0.44 g (79%), m.p. 271 °C (with decomp.), $[\alpha]_D^{25}$ +68° (*c* 1, $CHCl_3$). Found (%): C, 80.61; H, 5.57. $C_{64}H_{54}O_8$. Calculated (%): C, 80.82; H, 5.72. ^{1}H NMR ($CDCl_3$), δ: 7.57—7.15 (m, 44 H, H arom.); 5.33 (d, 2 H, CH, *J* = 4.8 Hz); 5.12 (s, 2 H, CH); 5.16 (d, 2 H, CH, *J* = 2.04 Hz); 3.21 (s, 2 H, OH); 2.14 (s, 2 H, OH). UV (CH_2Cl_2), λ_{max}/nm (logε): 242.3 (3.87), 255 (4.17), 259.4 (4.29). MALDI-TOF MS (chloroform), *m/z*: 973 $[M + Na]^+$, 989 $[M + K]^+$.

2,2´-(1,3-Phenylene)bis[(4*R*,5*R*)-4,5-di(hydroxydiphenylmethyl)-1,3-dioxolane] (6b) was synthesized analogously. The yield was 0.41 g (74%), m.p. 139 °C (with decomp.), $[\alpha]_D^{25}$ +22° (*c* 1, $CHCl_3$). Found (%): C, 80.36; H, 5.69. $C_{64}H_{54}O_8$. Calculated (%): C, 80.82; H, 5.72. ^{1}H NMR ($CDCl_3$), δ: 7.53—7.18 (m, 44 H, H arom.); 5.31 (d, 2 H, CH, *J* = 5.2 Hz); 5.11 (s, 2 H, CH); 5.15 (d, 2 H, CH, *J* = 3.9 Hz); 3.74 (s, 2 H, OH); 2.98 (s, 2 H, OH). UV (CH_2Cl_2), λ_{max}/nm (logε): 242.6 (4.36), 253 (4.5), 259.2 (4.55). MALDI-TOF MS (chloroform), *m/z*: 973 $[M + Na]^+$, 989 $[M + K]^+$.

2,2´-(1,2-Phenylene)bis[(4*R*,5*R*)-4,5-di(hydroxydiphenylmethyl)-1,3-dioxolane] (6a) was synthesized analogously. The yield was 0.49 g (88%), m.p. 118 °C (with decomp.), $[\alpha]_D^{25}$ +100° (*c* 1, $CHCl_3$). Found (%): C, 80.67; H, 5.65. $C_{64}H_{54}O_8$. Calculated (%): C, 80.82; H, 5.72. ^{1}H NMR ($CDCl_3$), δ: 7.54—7.11 (m, 44 H, H arom.); 6.18 (s, 2 H, CH); 5.34 (d, 2 H, CH, *J* = 4.0 Hz); 5.28 (d, 2 H, CH, *J* = 4.0 Hz); 3.25 (s, 2 H, OH); 1.90 (s, 2 H, OH). UV (CH_2Cl_2), λ_{max}/nm (logε): 245.2 (4.35), 253.6 (4.46), 259.4 (4.51). MALDI-TOF MS (chloroform), *m/z*: 973 $[M + Na]^+$, 989 $[M + K]^+$.

Bis(4-formylphenyl)methane (7) was synthesized according to a procedure described earlier[24] in 48% yield, m.p. 87 °C (*cf.* lit. data[24]: m.p. 86 °C).

Bis{4-((4*R*,5*R*)-4,5-di(ethoxycarbonyl)-1,3-dioxolan-2-yl)phenyl}methane (8). A mixture of bis(4-formylphenyl)methane (0.5 g, 2.2 mmol), diethyl L-tartrate (0.92 g, 4.46 mmol), and TsOH (0.05 g, 0.29 mmol) in toluene (5 mL) was refluxed using a Dean—Stark trap for 20 h to remove the reaction water. Then the mixture was concentrated on a rotary evaporator. The product was isolated as oil by silica gel column chromatography using toluene as the eluent (R_f 0.3). The yield was 0.67 g (50%), $[\alpha]_D^{25}$ −4.6° (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$), δ: 7.56 (d, 4 H, H arom., *J* = 8.2 Hz); 7.26 (d, 4 H, H arom., *J* = 8.0 Hz); 6.18 (s, 2 H, CH); 4.98 (d, 2 H, CH, *J* = 4.1 Hz); 4.86 (d, 2 H, CH, *J* = 4.1 Hz); 4.39—4.31 (m, 8 H, CH_2); 4.06 (s, 2 H, CH_2); 1.43—1.33 (m, 12 H, Me).

Bis[4-{[(4*R*,5*R*)-4,5-di(hydroxydiphenylmethyl)]-1,3-dioxolan-2-yl}phenyl]methane (9). Compound **9** was synthesized according to the procedure described above for **6a—c**, purified by silica gel chromatography using a 5 : 1 toluene—ethyl acetate mixture as the eluent (R_f 0.5), and recrystallized from a 1 : 2 toluene—heptane mixture. The yield was 1.2 g (70%), m.p. 160 °C, $[\alpha]_D^{25}$ +43.1° (*c* 1, $CHCl_3$). Found (%): C, 80.03; H, 5.91. $C_{71}H_{60}O_8$. Calculated (%): C, 81.90; H, 5.81. ^{1}H NMR ($CDCl_3$), δ: 7.70—7.10 (m, 48 H, H arom.); 5.38 (d, 2 H, CH, *J* = 5.0 Hz); 5.20 (d, 2 H, CH, *J* = 5.2 Hz); 5.17 (s, 2 H, CH); 3.96 (s, 2 H, CH_2); 3.42 (s, 2 H, OH); 2.21 (s, 2 H, OH). MALDI-TOF MS (chloroform), *m/z*: 1064 $[M + Na + H]^+$, 1080 $[M + K + H]^+$.

Mandelonitrile trimethylsilyl ether. A 10-mL two-neck flask was heated to 200 °C, evacuated, filled with argon, and cooled. Then a catalyst (9.2 μg, 9.6 μmol), dichloromethane (0.5 mL), benzaldehyde (0.05 mL, 0.47 mmol), and Me_3SiCN (0.1 mL, 0.74 mmol) were placed in the flask under argon. The reaction mixture was stirred under argon at ~20 °C for 30 min and passed through a thin layer of silica gel (*d* = 0.5 cm, *h* = 2 cm) to separate the mixture from the catalyst. The filtrate was concentrated on a rotary evaporator. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR spectroscopy (no signals of other products were observed). ^{1}H NMR ($CDCl_3$), δ: 7.49—7.39 (m, 5 H, H arom.); 5.36 (s, 1 H, CH); 0.24 (s, 9 H, Me) (*cf.* lit. data[14]: ^{1}H NMR (400 MHz, $CDCl_3$), δ: 7.49—7.39 (m, 5 H, H arom.); 5.50 (s, 1 H, CH); 0.24 (s, 9 H, Me)).

^{1}H NMR spectroscopic study of the addition of Me_3SiCN to benzaldehyde catalyzed by (*R*,*R*)-TADDOLs 6a—c. Kinetic studies of the reaction were carried out on a Bruker Avance 600 instrument. Bis-(*R*,*R*)-TADDOL (4.48, 8.96, 22.4, or 44.8 mg, 4.7, 9.4, 23, or 47 μmol, respectively), benzene-d_6 (0.5 mL), and benzaldehyde (0.05 mL, 0.47 mmol) were placed in a standard NMR tube.* The tube was placed in the NMR spectrometer magnet, and the initial spectrum was recorded. Then the NMR tube was taken out, Me_3SiCN (0.1 mL, 0.74 mmol) was added, the solution was vigorously stirred, the tube was again placed in the spectrometer, and the spectra of the reaction mixture were recorded at certain intervals.

1-Cyano-2-trimethylsilyloxycyclohexane. The Schlenk flask was evacuated and filled with argon. A catalyst (0.08 g, 0.084 mmol), dichloromethane (4 mL), cyclohexene oxide (0.1 mL, 0.98 mmol), and Me_3SiCN (0.27 mL, 2.02 mmol) were placed in the flask. The reaction mixture was stirred at ~20 °C for 60 h. Then the mixture was passed through a layer of silica gel (d = 0.5 cm, h = 2 cm) to separate the mixture from the catalyst, and the filtrate was concentrated on a rotary evaporator. To determine the yield of the product, the residue was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR spectroscopy (no signals of by-products were observed). ^{1}H NMR ($CDCl_3$), δ: 3.77—3.69 (m, 1 H, CH); 2.50—2.42 (m, 1 H, CH); 2.18—2.12 and 2.00—1.94 (both m, 1 H each, CH_2); 1.79—1.61 and 1.36—1.23 (both m, 3 H each, CH_2); 0.23 (s, 9 H, Me) (*cf.* lit. data[19]: ^{1}H NMR (400 MHz, $CDCl_3$), δ: 3.64—3.70 (m, 1 H); 2.38—2.44 (m, 1 H); 2.08—2.11 (m, 1 H); 1.90—2.07 (m, 1 H); 1.55—1.75 (m, 3 H); 1.25—1.33 (m, 3 H); 0.17 (s, 9 H)).

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* The amount of bis-(*R*,*R*)-TADDOL was chosen so that the total concentration of the catalyst in the reaction mixture was 1, 2, 5, and 10 mol.%, respectively.

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