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Tetra-*tert*-butyltrioxabicyclo[3.3.1]nonadienedicarboxylic Acid: Optical Resolution, Absolute Configuration and Application in Chiral Discrimination

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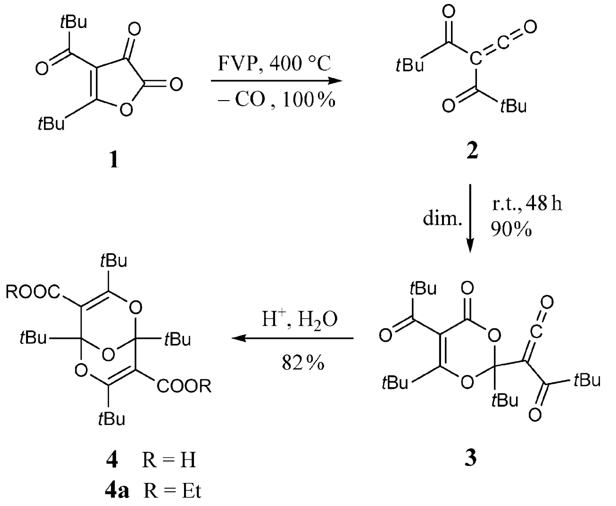
The enantiopure bridged bis-dioxine **4**, a dissymmetric dicarboxylic acid exhibiting axial chirality, can easily be synthesized and serve as host for separating and/or transporting chiral guest molecules. Racemic **4** gives with (*R*)- and (*S*)-1-phenylethylamine the corresponding pure diastereomeric salts **7** and **8**. The absolut configuration of the diacid **4** in the diastereomeric salt **7** containing (*R*)-1-phenylethylamine was confirmed to be *R* by X-ray crystal structure analysis, which also confirmed its concave nature. Release of the acid-sensitive pure enantiomers (*R*)-**4** as well as (*S*)-**4** was achieved conveniently by use of dry flash-chromatography on silica. The CD spectrum shows a positive Cotton effect of the (*S*)-enantiomer at 206 nm. The enantiomeric purity was proved by ^{1}H NMR discrimination of the diastereomeric salts with (*R*,*R*)-1,2-bis(4-methoxyphenyl)ethane-1,2-diamine as the base. The dicarboxylic acid (*R*)-**4** can be used as chiral auxiliary as demonstrated by the difficult resolution of racemic *N*,*N′*-di-*tert*-butyl-1,2-bis(4-methoxyphenyl)ethane-1,2-diamine **9**.

Introduction

Preparative flash vacuum pyrolysis of the furan-2,3-dione **1** affords the dipivaloyl ketene **2** in quantitative yield, which at room temperature dimerizes smoothly to the remarkably stable α-oxoketene **3**.[1] The acid-catalyzed hydrolysis easily converts **3** by a one-pot procedure into the diacid **4** thus representing the rare heterocyclic trioxa[3.3.1]nonadiene ("bridged bis-dioxine") skeleton.[2] Molecules of this type are concave and dissymmetric and in general exhibit axial chirality,[3] which was also established for the diacid **4** (Scheme 1) itself from ^{1}H NMR spectroscopic measurements applying Eu(hfc)$_3$ as a chiral shift reagent. The 50:50 splitting of the signal of the *tert*-butyl protons at δ = 1.25 ppm (shifted and split to 1.39 and 1.43 ppm) indicates the presence of a mixture.

Furthermore, the diacid **4** serves as a novel spacer unit and has already successfully been incorporated into a great variety of macrocyclic ring systems of the crown ether and polymethylene type (for instance **5**),[4] the bridged bis-dioxine skeleton itself could also be attached to aromatic amines and amino-substituted benzocrown ethers (for instance **6**) (Scheme 2).[5] Both species have also been successfully applied as host molecules in supramolecular interactions with metal ions[4] as well as organic guests.[5]



Scheme 1.

The aim of this work was to prepare the enantiopure diacid **4** [(*R*)- and/or (*S*)-form] from mainly two points of view: (a) to serve as an alternative to tartaric acid (and derivatives) as the so far best known reagents for chiral discrimination of bases in NMR spectroscopy as well as in preparative scale,[6] and (b) to potentially synthesize macrocyclic systems bearing (*R*)- [or (*S*)-] bis-dioxine spacers for separating and/or transporting chiral guest molecules as single enantiomers.

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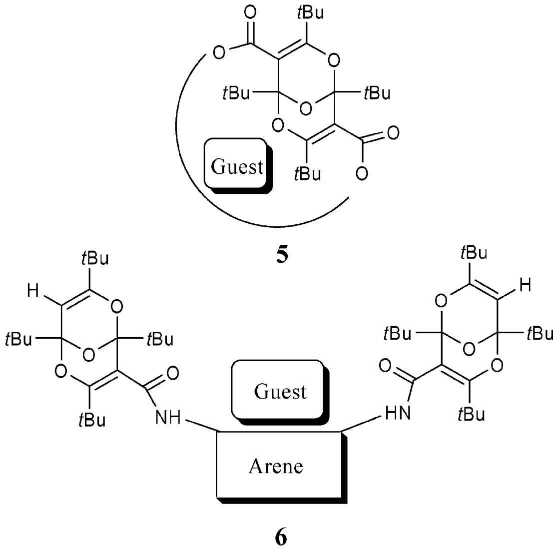


Scheme 2.

Results and Discussion

The racemic dicarboxylic acid **4** was prepared in approximately 72% overall yield following the synthetic protocol outlined in Scheme 1.[1,2] Final confirmation of the concave nature of the trioxabicyclo[3.3.1]nonadiene scaffold in **4** was achieved by an X-ray crystal structure analysis of the corresponding diethyl ester **4a**.

X-ray Crystal Structure: In the crystal structure of compound **4a**[2b] a crystallographic twofold axis passes through the bridging O atom O9 (see Figure 1 and Figure 2). The least-squares plane of the ethoxycarbonyl group is inclined at an angle of 70.35(9)° to the plane defined by the atoms C3, C4, C40 and C1′. The latter includes the plane with the plane defined by the atoms C3, C4, C30 and O2 at an angle of 6.74(10)°. This prominent distortion of the double bond between the atoms C3 and C4 is attributed to the sterically demanding substituents.

Synthesis of Diastereomeric Salts: In order to get separation of the two enantiomers of **4**, fractional crystallization of the diastereomeric salts was chosen.[7] Actually, from NMR titration experiments a clear 50:50 splitting of the signal at $\delta = 1.11$ ppm in the ^{1}H NMR spectrum can be observed when applying (*R*)-(+)-1-phenylethylamine as a chiral auxiliary in a fourfold excess. This indicates that the *tert*-butyl groups located at the sp^3-carbon of the bridged bis-dioxine ring of **4** are affected by the chiral interaction, because the signal at $\delta = 1.27$ ppm assigned to the *tert*-butyl groups at the sp^2-carbon atoms[1] remains completely unchanged. In order to transfer this analytical finding to preparative scale, (*R*)-(+)- as well as (*S*)-(–)-1-phenylethylamine were added to a solution of racemic **4** (1 mmol) in dichloromethane (5 mL) in a 1:4 molar ratio.

After 3–5 h precipitates were formed which after recrystallization from acetonitrile were identified as amazingly pure diastereomeric salts (*R*)-**4**·(*R*)-(+)-1-phenylethylamine **7** or (*S*)-**4**·(*S*)-(–)-1-phenylethylamine **8** (Scheme 3).

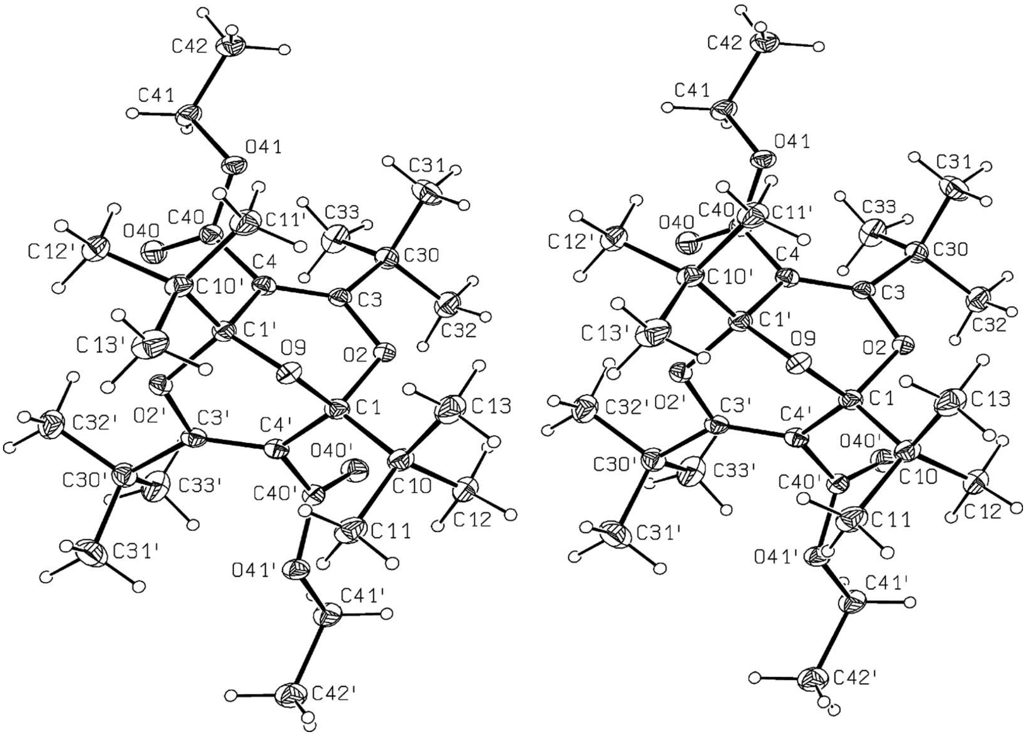


Figure 1. Stereoscopic ORTEP[13] plot of **4a** showing the atomic numbering scheme. The probability ellipsoids are drawn at the 50% probability level.

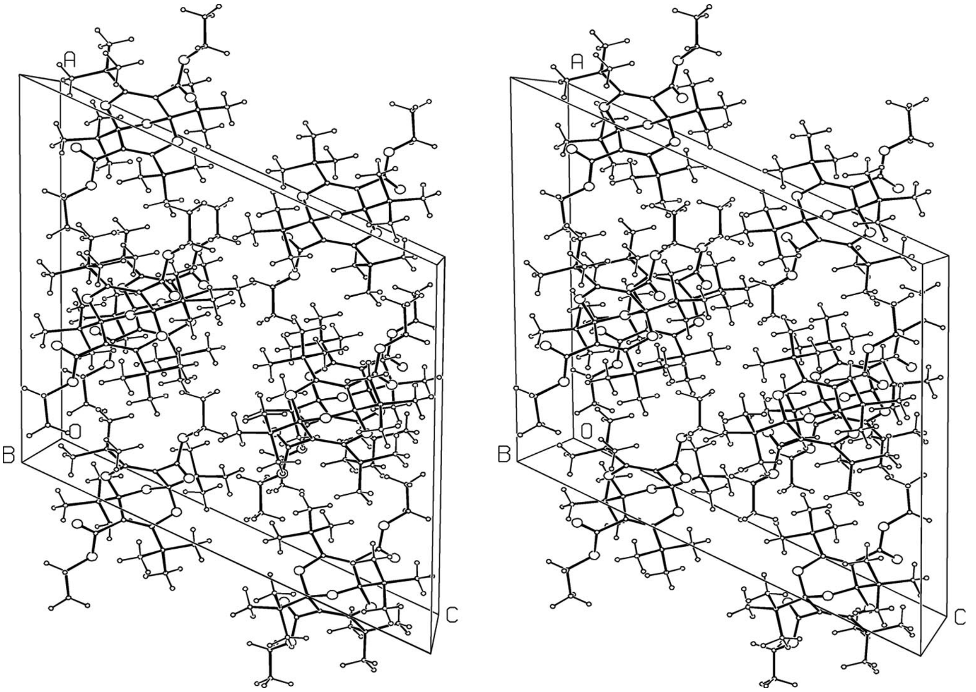
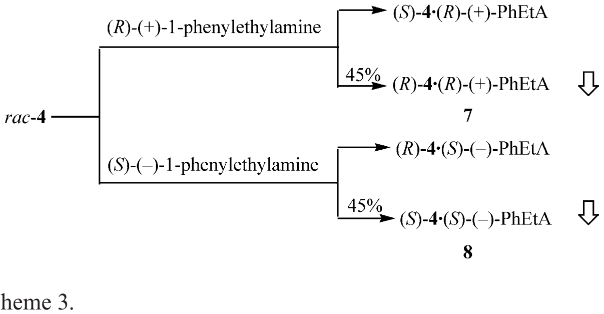


Figure 2. Stereoscopic ORTEP[13] plot of the packing of **4a**. The atoms are drawn with arbitrary radii.

From NMR monitoring in chloroform (see below) no evidence for the presence of the second diastereomer was found. The diastereomeric ratio of the acid in both cases could be estimated at >98%. From the mother liquors of both reaction mixtures the enrichment of the respective alternative diastereomeric salts [(*R*),(*S*)- and (*S*),(*R*)-compounds] could be observed by NMR monitoring, however, a preparative separation and isolation in pure state could not be achieved. Nevertheless, of course purification is possible after isolation of the scalemic mixture of the free acid and use of the antipode 1-phenylethylamine. Isolation of the acid-sensitive free acid from the diastereomeric salts is described below.



Scheme 3.

Crystal Structure of 7: Fortunately, the elucidation and confirmation of the absolute configuration of diacid **4** in the diastereomeric salt **7** could be successfully obtained from an X-ray crystal structure analysis.

X-ray Crystal Structure: From the crystal structure analysis of the diastereomeric compound **7** the absolute configuration of the diacid **4** could be determined as the (*R*)-enantiomer because the absolute configuration of the base (*R*)-(+)-1-phenylethylamine was known. During the crystallization of the salt one solvent molecule ethanol and one water molecule per formula unit were included thus resulting in bis[(*R*)-(+)-1-phenylethylammonium] (*R*,*R*)-1,3,5,7-tetra-*tert*-butyl-2,6,9-trioxabicyclo[3.3.1]nona-3,7-diene-4,8-dicarboxylate/ethanol/water (**7**). The atomic numbering scheme and the conformation of the asymmetric unit of **7** is shown in Figure 3. The water molecule bridges over the two carboxylate groups of the same di-anion which are oriented almost normal to the six-membered rings of the bicyclic sub-unit due to the adjacent *tert*-butyl groups. The packing (see Figure 4) is predominantly determined by the hydrogen-bonding system. The geometric parameters of the nine different hydrogen bonds formed by the 6 H atoms of the ammonium groups of the two cations, the 2 H atoms of the water molecule and the OH group of the ethanol molecule are compiled in Table 1.

Release of the Enantiomers of 4 From the Salts 7 and 8: A frequently used methodology to release enantiomeric acids from their diastereomeric salts is simple acidification. However, because the diacid **4** is sensitive to acidic hydrolysis, which converts the bridged bis-dioxine skeleton into a tetraoxaadamantane system[8] (see Scheme 4) the amount of acid necessary to free the diacid must be adapted very carefully.

In order to avoid any excess of hydrochloric acid it was generated in situ from addition of a defined quantity of acetyl chloride to a calculated volume of ethanol. This methodology worked in principle, but the yields were rather poor [(*R*)-**4**: 20%; (*S*)-**4**: only 5% for an unknown reason]. Therefore, since a distinct separation of acid and base was observed on TLC-plates, attempts were made to obtain the free diacids out of the diastereomers **7** and **8** by chromatographic methods. In fact, with the aid of DFC (dry flash chromatography, silica gel 60H (Merck), eluant: methanol/

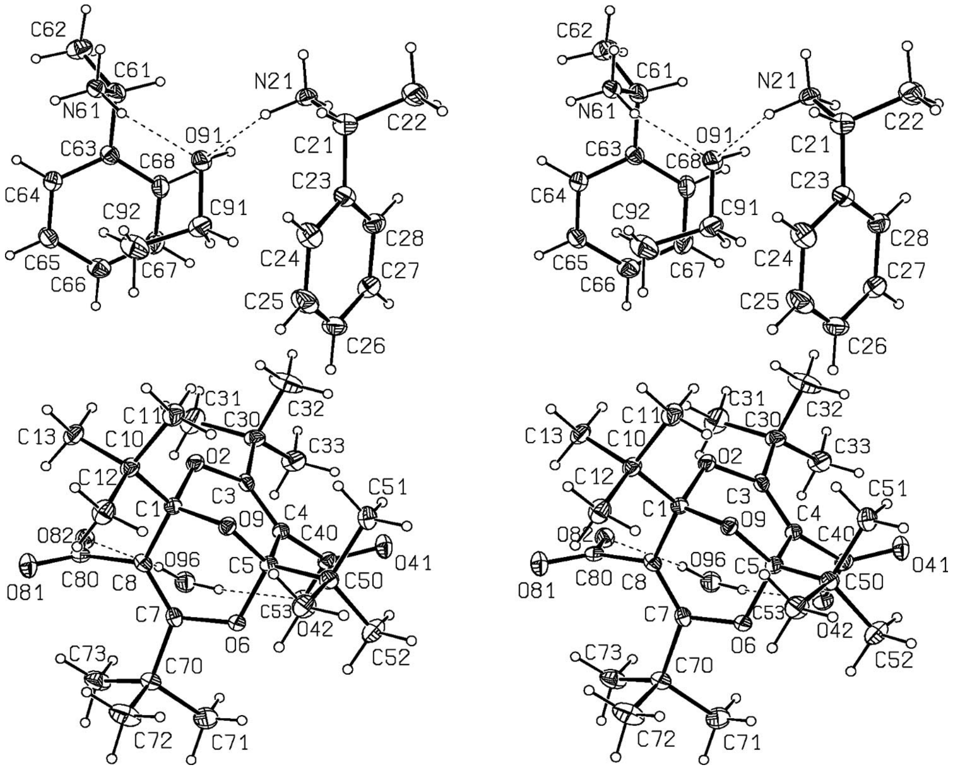


Figure 3. Stereoscopic ORTEP[13] plot of **7** showing the atomic numbering scheme. The probability ellipsoids are drawn at the 50% probability level, hydrogen bonds are drawn with dotted lines.

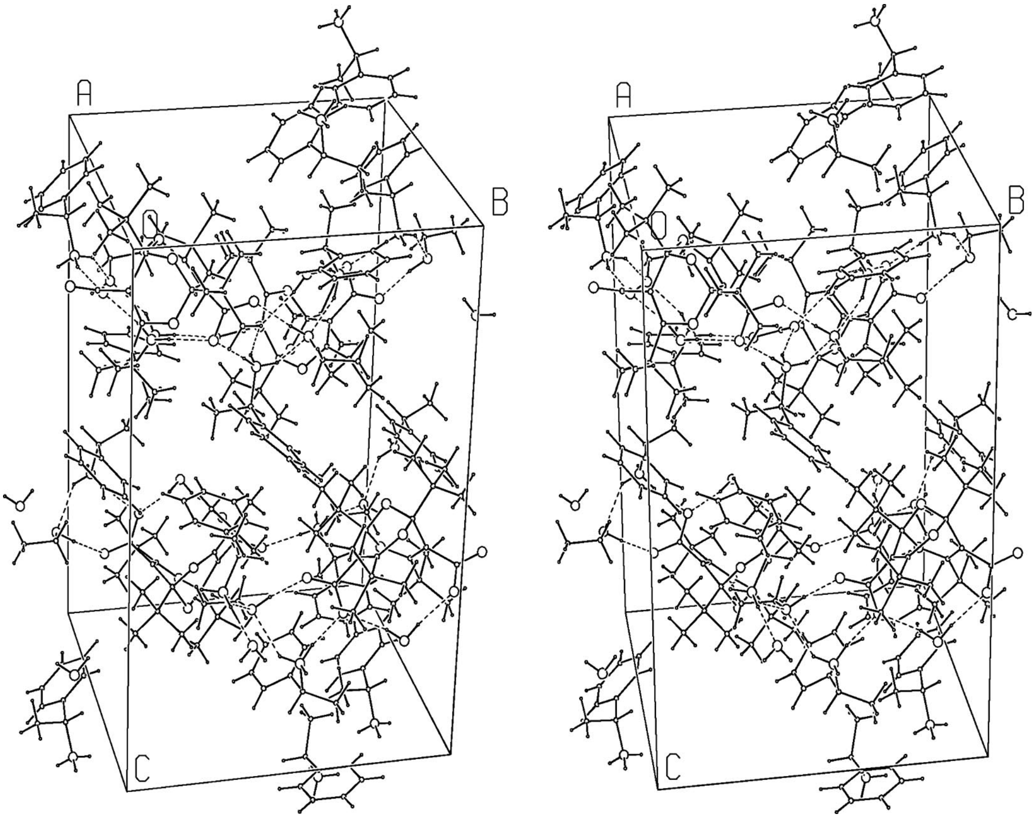
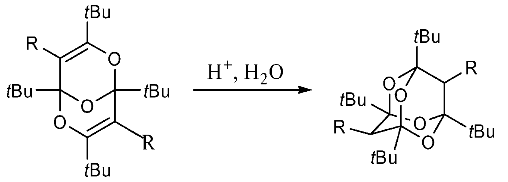


Figure 4. Stereoscopic ORTEP[13] plot of the packing of **7**. The atoms are drawn with arbitrary radii, hydrogen bonds are drawn with dotted lines.

Table 1. Hydrogen bonds for **7** (angles given in °, lengths in Å).

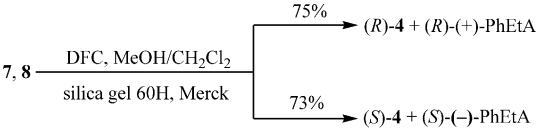
D–H···A	d(D–H)	d(H···A)	d(D···A)	<(DHA)
N(21)–H(211)···O(91)	0.91	2.06	2.893(2)	151.3
N(21)–H(212)···O(82)[a]	0.91	1.79	2.704(2)	178.4
N(21)–H(213)···O(42)[b]	0.91	1.79	2.671(2)	161.8
N(61)–H(611)···O(96)[b]	0.91	1.90	2.795(3)	165.9
N(61)–H(612)···O(91)	0.91	2.01	2.849(2)	152.1
N(61)–H(613)···O(41)[c]	0.91	1.93	2.839(2)	179.1
O(91)–H(91)···O(81)[a]	0.88(3)	1.82(3)	2.685(2)	166(3)
O(96)–H(961)···O(82)	0.86(2)	2.02(2)	2.875(2)	168(3)
O(96)–H(962)···O(42)	0.86(2)	1.98(2)	2.836(2)	172(3)

[a] Symmetry transformations used to generate equivalent atoms: $1 - x, y + 1/2, 3/2 - z$. [b] $x - 1, y, z$. [c] $1 - x, y - 1/2, 3/2 - z$.



Scheme 4.

dichloromethane, 1:9) the desired diacids (*R*)-**4** and (*S*)-**4** were isolated in acceptable chemical yields (75% and 73%, respectively) and NMR-measured enantiomeric purity without further recrystallization (Scheme 5). To the best of our knowledge this is the first reported example of utilizing DFC methodology during resolution of a mixture by formation of diastereomers.



Scheme 5.

CD-Spectra: Methanolic solutions of (*R*)-**4** and (*S*)-**4** were recorded with a Jasco J-715 spectropolarimeter (Figure 5). The spectra confirm the presence of the two enantiomers in about equal enantiomeric purity, the (*S*)-diacid **4** exhibiting a positive Cotton effect at 206 nm.

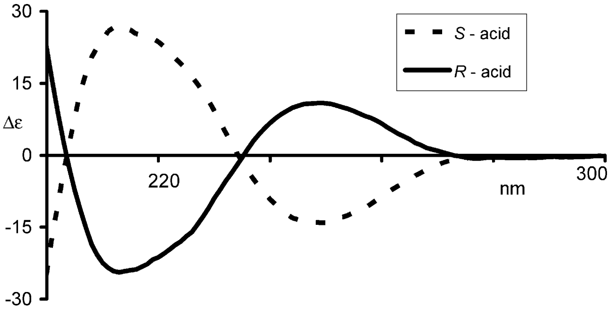
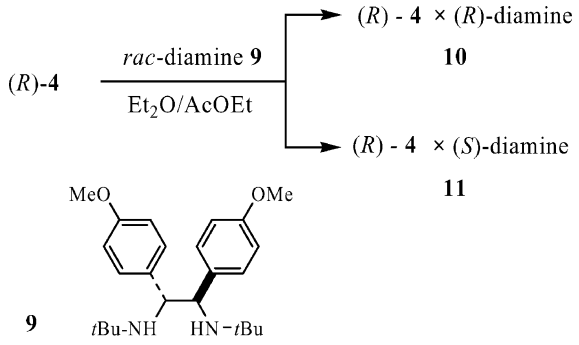


Figure 5. CD spectra of (*R*)-**4** and (*S*)-**4**.

^{1}H NMR Spectroscopy: Attempts to determine the enantiomeric purity of the diacids (*R*)-**4** and (*S*)-**4** utilizing the methodology presented by Lesot et al.[9] by two-dimensional NMR techniques of a liquid-crystalline layer formed by the peptide poly-γ-benzyl-L-glutamate and the sample failed due to severe solubility problems. Therefore, we again employed (*R*)-(+)-1-phenylethylamine as chiral shift-reagent which allowed to determine the spectra in $CDCl_3$ solution (see above). In fact, while the *tert*-butyl groups at the sp^3-carbon of the racemic **4** in presence of an excess of the amine split into two signals (δ = 1.110 and 1.106 ppm) they appear as singlets when (*R*)-**4** (δ = 1.076 ppm) or (*S*)-**4** (δ = 1.094 ppm) are recorded. The difference in the chemical shifts is due to different amounts of the (*R*)-(+)-1-phenylethylamine added directly to the NMR tube. Because in both cases there is no trace of signals arising from the corresponding second enantiomer observable we conclude the *ee* for the enantiomeric acids to be >96%. Attempts to determine the enantiomeric excess of (*R*)- and (*S*)-acids by chiral HPLC applying the S,S-ULMO as chiral phase were not successful. This obviously was due (i) mainly to assoziation/dimerization reactions of the highly lipophilic acids during analysis, which is a well known problem of acids in general, (ii) the very weak chromophore, low ε-values and high concentrations needed for a proper detection.

Resolution of the (*R*,*R*)- and (*S*,*S*)-1,2-Diphenyl-1,2-ethanediamine 9: In order to check the ability of enantiopure (*R*) [or (*S*)]-**4** to serve as a suitable reagent in resolving bases, some preliminary experiments were performed. For example, the diacid (*R*)-**4** was treated with *rac*-*N*,*N′*-di-*tert*-butyl-1,2-bis(4-methoxyphenyl)ethane-1,2-diamine (**9**)[10] which should afford a mixture of diastereomeric salts **10** and **11** (Scheme 6). C_2-symmetrical diamines of this type have drawn considerable interest as ligands for catalysis in enantioselective synthesis.[11] With (*R*,*R*)-tartaric acid we had got after several attempts only a diastereomeric ratio of 80:20.



Scheme 6.

The interaction of the diamine **9** with the diacid **4** was determined by ^{1}H NMR spectroscopy in $CDCl_3$ solution. Depending on their molar ratio a splitting either of the CH-moieties (**9**/**4** = 1:1 or 2:1) or of the methoxy-group (**9**/**4** = 1:2) was observed. Furthermore, the CH signals shifted upfield from δ = 3.99 to 3.82 (1:2), 3.73 (1:1) and 3.67 ppm (2:1). In preparative scale equimolar amounts of (*R*)-**4** and *rac*-**9** were dissolved in equal amounts of ether/ethyl acetate as a proper solvent and stirred at room temperature for 12 h. During that time a colourless precipitate was formed which after suction and recrystallization from acetonitrile was found as a 1:1 diastereomeric salt (**10/11**, 37% yield), evidenced by elemental analysis and NMR spectroscopy.

Enantiomeric Purity and Proof of Usability: In order to examine the success of the resolution of the diasteromeric salts of **9** we used HPLC-measurements of the free base applying S,S-ULMO as a chiral phase.[12] From integration of the appropriate, baseline separated peaks a molar ratio of 94:6 of the two enantiomers of **9** could be calculated. This unambiguously indicates the possibility of a successful resolution of the diamine by use of enantiomerically pure diacid (*R*)-**4** as chiral auxiliary.

Conclusions

The racemic bridged bis-dioxinedicarboxylic acid **4** can readily be separated into its enantiomers (*R*)-**4** as well as (*S*)-**4** by formation of the corresponding diastereomeric salts **7** and **8**, respectively, after addition of (*R*)- and (*S*)-1-phenylethylamine as bases. The absolute configuration of (*R*)-**4** in the diastereomeric salt **7** was confirmed by an X-ray crystal structure analysis. Release of the pure enantiomers (*R*)-**4** and (*S*)-**4** in about 70% yields was successfully achieved by means of dry flash chromatography on silica. As an example, acid (*R*)-**4** could also be used as a chiral auxiliary in resolving racemic *N*,*N'*-di-*tert*-butyl-1,2-bis(4-methoxyphenyl)ethane-1,2-diamine.

Experimental Section

General: ^{1}H NMR Spectra: Bruker AMX 360 at 360 MHz, in the solvents indicated, chemical shifts (δ) in ppm relative to internal TMS. IR-Spectra: Mattson Galaxy 7000 FT-IR spectrometer HPLC measurements were performed with a Hewlett–Packard series HP 1050 instrument consisting of a pumping system, an autosampler and a multiwavelength detector. Separation parameters were obtained with the Hewlett–Packard Chemstation Software. 1,3,5-Tri-*tert*-butylbenzene was used as void volume marker. The ULMO-Column containing the (*S*,*S*)-enantiomer of 3,5-dinitrobenzoylated 1,2-diphenylethane-1,2-diamine as selector was obtained from REGIS Tech., Morton Groove, IL, USA, dimension 250 × 4.6 mm.[12] The racemic bis-dioxinedicarboxylic acid **4** and the corresponding twofold ester **4a** were prepared following already published four-step procedures.[1,2]

Separation of Racemic 4 into Enantiomers

A) Formation of the Diastereomeric Salts 7 and 8: *rac*-**4** (440 mg, 1 mmol) was suspended in dichloromethane (5 mL) at room temperature with stirring. After addition of enantiomerically pure (*R*) (+)-or (*S*) (–)-phenylethylamine (485 mg, 4 mmol) a clear solution was formed. Then five drops of EtOH as well as water were added from a syringe (2 mL volume) and after 3–5 h a precipitate was formed, which was separated by suction and recrystallized from acetonitrile. The precipitates were identified as diastereomeric salts **7** and **8**, respectively, with aid of NMR spectroscopy.

Bis[(*R*)-(+)-1-Phenylethylammonium] [(*R*)-1,3,5,7-Tetra-*tert*-butyl-2,6,9-trioxabicyclo[3.3.1]nona-3,7-diene-4,8-dicarboxylate]·EtOH·H$_2$O (7): M.p. 90–92 °C, yield 335 mg (90%) ^{1}H NMR (CDCl$_3$): δ = 1.09 (s, 18 H, *t*Bu), 1.25 (*t*, EtOH Me), 1.25 (s, 18 H, *t*Bu), 1.45 (d, 6 H, Me), 3.73 (q, 2 H, EtOH CH$_2$), 4.17 (q, 2 H, CH), 7.26–7.35 (m, 10 H, Ph) ppm. IR (Br): $\tilde{\nu}$ = 3426 (OH), 3065–2882 (CH), 1619, 1536, 1456, 1388, 1200, 1108 cm^{-1}.

Bis[(*S*)(–)-1-phenylethylammonium] [(*S*)-1,3,5,7-Tetra-*tert*-butyl-2,6,9-trioxabicyclo[3.3.1]nona-3,7-diene-4,8-dicarboxylate]·EtOH·H$_2$O (8): M.p. 92–94 °C, yield 320 mg (86%). ^{1}H NMR (CDCl$_3$): δ = 1.10 (s, 18 H, *t*Bu), 1.26 (t, 3 H, EtOH Me), 1.26 (s, 18 H, *t*Bu), 1.44 (d, 6 H, Me), 3.71 (q, 2 H, EtOH CH$_2$), 4.07 (q, 2 H, CH), 7.27–7.35 (m, 10 H, Ph) ppm. IR (KBr): $\tilde{\nu}$ = 3420 (OH), 3065 –2884 (CH), 1619, 1529, 1456, 1385, 1199, 1108 cm^{-1}.

B) Isolation of (*R*)-4 and (*S*)-4 from the Salts 7 or 8

(a) By Acidification. General Procedure: A solution of acetic acid chloride (71 µL, 1 mmol) in dry ethanol (10 mL) was prepared as acid reagent. A volume containing 1.1 equiv. of this solution was added to the salt **7** (or **8**) in the solid state and solution was observed. After 1–2 d at 20 °C the corresponding diacid [(*R*)-**4** or (*S*)-**4**] precipitatet and was recrystallized from acetonitrile. In case the precipitate was not formed after 2 d, the solvent was evaporated and the oily residue was dissolved in acetonitrile. The reaction product then crystallized after standing for 12 h at 20 °C. The average yield of (*R*)-**4** was about 20% [5% for (*S*)-**4**], as the result of several experiments.

(b) By Dry Flash Column Chromatography (DFCC):[14] General methodology of DFCC see ref.[14]. A sintered funnel (height 50 mm) was filled with silica gel 60H (30 g, Merck) and washed several times with the eluant (methanol/dichloromethane, 1:9) by suction. Then 750 mg (ca. 1 mmol) of the salt **7** (or **8**, respectively), dissolved in the minimum amount of the eluant, were distributed on the surface of the column with the aid of a syringe. Fractions of 10 mL each were collected and the presence of (*R*)-**4** or (*S*)-**4** was monitored with the aid of the racemic sample by TLC. Fractions containing the desired products were combined and the solvents evaporated to dryness. The products isolated were analytically pure.

(*R*)-4: Yield 330 mg (75%), m.p. 198 °C ^{1}H NMR (CDCl$_3$): δ = 1.26 (s, 18 H, *t*Bu), 1.10 (s, 18 H, *t*Bu) ppm. IR (KBr): $\tilde{\nu}$ = 3425 (OH), 3067 –2880 (CH), 1689, 1618, 1485, 1396, 1304 cm^{-1}.

(*S*)-4: Yield 320 mg (73%), m.p. 203 °C ^{1}H NMR (CDCl$_3$): δ = 1.25 (s, 18 H, *t*Bu), 1.10 (s, 18 H, *t*Bu) ppm. IR (KBr): $\tilde{\nu}$ = 3425 (OH), 3077 –2880 (CH), 1688, 1618, 1483, 1396, 1304 cm^{-1}.

Resolution of Racemic *N*,*N'*-Di-*tert*-butyl-1,2-bis(4-methoxyphenyl)ethane-1,2-diamine

(a) Formation of Diastereomeric Salts 10/11: (*R*)-**4** (190 mg, 0.43 mmol) together with equimolar amounts (165 mg, 0.43 mmol) of the racemic diamine was dissolved in a mixture of ether (3.5 mL) and ethyl acetate (3.5 mL) and stirred at room temp. in an open vessel to allow the ether to evaporate slowly overnight. The precipitate formed was isolated by suction and recrystallized from acetonitrile to give 130 mg (37%) of salts **10/11**, m.p. 115 °C. IR (KBr): $\tilde{\nu}$ = 3434, 3003 (–2876), 1613, 1515, 1391, 1254, 1200 cm^{-1}. ^{1}H NMR (CDCl$_3$): δ = 7.22 (b, 4 H, arom), 6.72 (d, 4 H, arom), 3.99 (s, 2 H, CH), 3.73 (s, 6 H, OMe), 1.26 (s, 36 H, *t*Bu), 1.10 (s, 18 H, *t*Bu) ppm. ^{13}C NMR (CDCl$_3$): δ = 172 (C=O), 162 (C3/C7 acid), 129, 113 (C arom), 104 (C4/C8 acid), 98.5 (C1/C5, acid), 63.3 (CH, base) 55 (OMe), 39.7 (C, *t*Bu, base), 37.6, 31.6 (C, *t*Bu, acid), 29.7 (Me, *t*Bu, base), 28.9, 25.0 (Me, *t*Bu, acid) ppm. MS: HP-LC/MSD (ARCI pos.mode): 2 peaks of high intensity: 385 ([M$^+$ + 1] base); 420 ([M$^+$ + 1] acid). $C_{24}H_{38}O_7{\cdot}C_{24}H_{34}N_2O_2$: calcd. C 70.24; H 8.84; N 3.41; found C 70.06; H 9.13; N 3.35.

(b) Isolation of the Enriched Base: The diastereomeric salt **10/11** (80 mg, 0.1 mmol) was separated and purified by a DFCC, exactly following the procedure described under B (see above). The crude product obtained was recrystallized from acetonitrile to give 11 mg (30%) of enriched diamine (racemate: m.p. 120 °C, methanol). ^1H NMR ($CDCl_3$): $\delta = 7.06$ (d, 4 H, arom), 6.71 (d, 4 H, arom), 3.75 (s, 6 H, OMe), 3.60 (s, 2 H, CH), 1.80 (s, 2 H, NH), 0.83 (s, 18 H, *t*Bu) ppm. Analytical direct enantiomer separation: HPLC-conditions: mobile phase: *n*-heptane and 2-propanol (90:10) v/v as eluant containing 0.1% v/v each trifluoroacetic acid and diisopropylamine, flow = 1 mL/min, detection at 215 nm. Enantiomeric purity of *N*,*N*′-di-*tert*-butyl-1,2-bis(4-methoxyphenyl)ethane-1,2-diamine: 88 *ee*, $k_1 = 2.83$, $\alpha = 1.34$, resolution = 1.90.

X-ray Diffraction Data of 4a: All measurements were performed using graphite-monochromatized Mo-K_α radiation at 95 K: $C_{28}H_{46}O_7$, M_r 494.65, monoclinic, space group *C*2/*c*, $a = 19.479(7)$ Å, $b = 8.272(2)$ Å, $c = 19.703(7)$ Å, $\beta = 117.98(2)°$, $V = 2803.7(16)$ Å^3, $Z = 4$, $d_{calcd.} = 1.172$ g cm^{-3}, $\mu = 0.082$ mm^{-1}. A total of 3134 reflections were collected ($\Theta_{max} = 25.0°$), from which 2463 were unique ($R_{int} = 0.0177$), with 2107 having $I > 2\sigma(I)$. The structure was solved by direct methods (SHELXS-97)[15] and refined by full-matrix least-squares techniques against F^2 (SHELXL-97).[16] The non-hydrogen atoms were refined with anisotropic displacement parameters. The H atoms were refined with common isotropic displacement parameters for the H atoms bonded to the same C atom and idealized geometry with tetrahedral angles. The H atoms of the methyl groups were enabled to rotate around the X–C bond and refined with C–H distances of 0.98 Å. The H atoms of the CH_2 groups were refined with C–H distances of 0.99 Å. For 174 parameters final *R* indices of $R = 0.0373$ and $wR_2 = 0.0875$ (GOF = 1.064) were obtained. The largest peak in a difference Fourier map was 0.192 eÅ^{-3}.

X-ray Diffraction Data of 7: All measurements were performed using graphite-monochromatized Mo-K_α radiation at 90 K: $(C_8H_{12}N^+)_2C_{24}H_{36}O_7^{-}\cdot C_2H_5OH\cdot H_2O$, $M_r = 744.98$, orthorhombic, space group $P2_12_12_1$, $a = 14.104(4)$ Å, $b = 14.304(4)$ Å, $c = 21.417(4)$ Å, $V = 4320.7(19)$ Å^3, $Z = 4$, $d_{calcd.} = 1.145$ g cm^{-3}, $\mu = 0.079$ mm^{-1}. A total of 5338 reflections were collected ($\Theta_{max} = 26.0°$), from which 4714 were unique ($R_{int} = 0.0254$), with 4284 having $I > 2\sigma(I)$. The structure was solved by direct methods (SHELXS-97)[15] and refined by full-matrix least-squares techniques against F^2 (SHELXL-97).[16] The non-hydrogen atoms were refined with anisotropic displacement parameters. The H-atoms were refined with common isotropic displacement parameters for the H-atoms bonded to the same C or N atom and idealized geometries. The absolute structure could be determined from the known one of the cations. For 528 parameters final *R* indices of $R = 0.0347$ and $wR_2 = 0.0801$ (GOF = 1.049) were obtained. The largest peak in a difference Fourier map was 0.153 eÅ^{-3}.

CCDC-675328 (for **4**) and -675327 (for **7**) contain the supplementary crystallographic data. These files contain crystal data and structure refinements, atomic coordinates and displacement parameters as well as the full list of bond lengths [Å] and angles [°] for compounds **4a** and **7**. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data request/cif.

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