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Rapid Communication

Cyclotriveratrylenes: Synthesis of a new C_3-symmetric chiral amino alcohols†

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Synthesis of a new class of chiral amino alcohols based on cyclotriveratrylene is described.

β-Amino alcohols have been shown to be particularly suitable versatile chiral auxillaries[1] for affecting the enantioselective addition of organometallic reagents to aldehydes, especially dialkyl zinc have received special attention due to development of chiral catalysts that enable the improvement of chemoselectivity and enantioselectivity of the addition[2]. In search of preparation of such new chiral catalyst we wish to report herein a novel type of β-amino alcohol based on optically active glycidyl cyclotriveratrylenes which can be exploited as a potential chiral auxillary in asymmetric synthesis.

Cyclotriveratrylenes are excellent rigid bowl shaped frame works which have drawn current interest in the field of host-guest chemistry[3]. Especially, the accessibility of possessing several C_3-symmetric functionalized congeners are particularly attractive for the design of ligands capable of transition metal coordination leading to complexes in which the metal could be accommodated in the cyclotriveratrylene cavity or placed in close proximity of this cavity[4]. Such systems are of great interest for the development of supramolecular catalysts. One of the most interesting aspect of C_3-cyclotriveratrylene is the chiroptical properties[5] which has been the object of many studies in the area of stereochemistry.

In this communication, we wish to report the synthesis of a novel C_3-symmetric cyclotriveratrylene bearing optically active glycidyl groups at the periphery of the aromatic rims with subsequent transformation to β-amino alcohols with potential applications as chiral auxillaries.

Our synthetic strategy is based on the C_3-racemic cyclotriphenolene[6] **1** as a key intermediate which on treatment with 3,3 equivalents of (*S*)-(+)glycidyl tosylate[7] in DMF at 50 °C in the presence of NaH gave a mixture which after usual workup and purification by chromatography furnished a mixture of diastereomeric trisglycidyl cyclotriveratrylene **2** in a overall yield of 53% (**Scheme I**). Several attempts were made to separate these diasteromers physically either by chromatography or crystallization. But all of them proved to be unsuccessful.

On close scrutiny of ^{1}H NMR spectrum revealed clearly a pair of signal pertaining to two distinct diastereomers (MSSS, PSSS) in almost 1:1 ratio. Thus, refluxing the diastereomeric trisglycidyl cyclotriveratrylene **2** in methanol with pyrolidine and morpholine afforded the unseparable diastereomeric β-amino alcohols **3** and **4** in >80% yield (**Scheme I**). At this juncture we could not provide an evidence for the diastereomers **3** and **4** in ^{1}H NMR spectra due to insignificant differences in chemical shifts of the diastereomers. However, the regioselective attack of the secondary amine at the terminal position of the epoxide to give **3** and **4** was firmly confirmed from the ^{1}H NMR analysis by the presence of a CHOH resonance at 4.13-4.25 ppm, indicating that the epoxide opening with the amine proceeded with very high regioselectivity without the loss of diastereomeric purity[8,9].

Compounds **3** and **4** belonged to the general class of dialkylamino alcohols. Preliminary results

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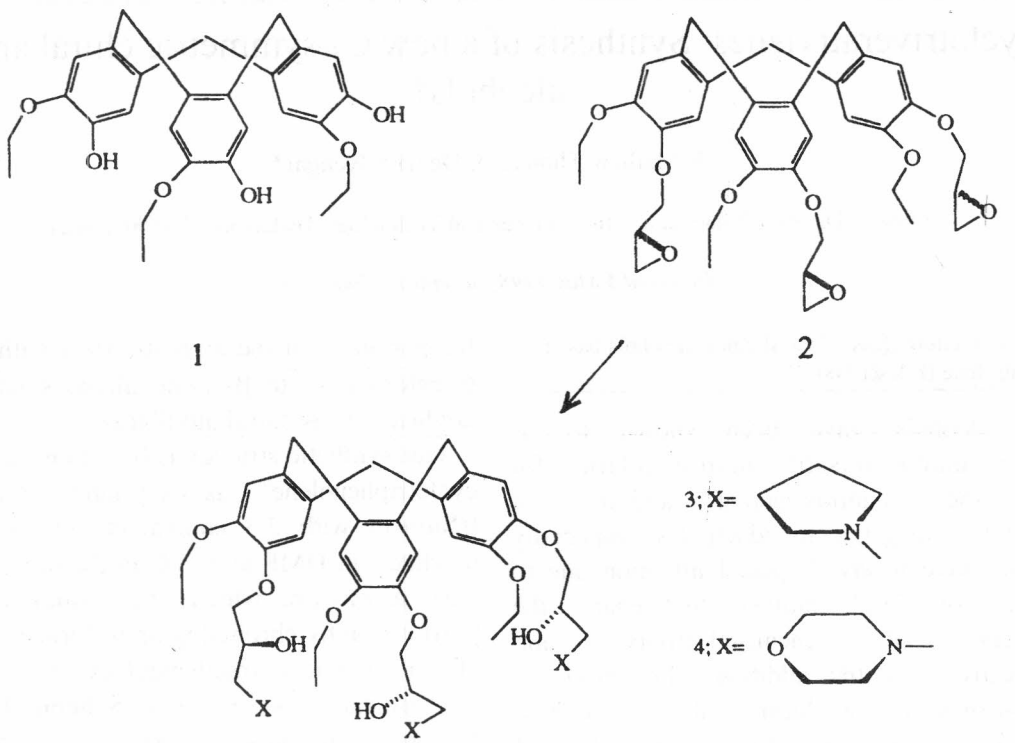

have shown that **3** and **4** possess complexing property toward Zn^{2+} cation.

In conclusion the β-amino alcohols **3** and **4** have unique structural features because of their rigid frame-work which can be used as a potential chiral auxilliary[10] for enantioselective ethylation of benzaldehydes. Work towards the application of the chiral auxillary is in progress and will be reported elsewhere.

Experimental Section

General. Melting points were determined using a Kjeldahl flask containing liquid paraffin and are uncorrected. ^{1}H NMR spectra were recorded at 400 MHz in $CDCl_3$ using TMS as internal reference (chemical shifts in δ, ppm). Mass spectra were recorded on LSIMS [FAB] using MNBA as a matrix.

2, 7, 12-Triethoxy-3,8,13-tris(2, 3-epoxypropoxy) cyclotriveratrylene (MSSS, PSSS). To a stirred solution of **1** (0.5g 1.1 mmoles) in DMF (9 mL) was added sodium hydride [0.14g of a 60% (w/w) dispersion in mineral oil, 5.8 mmoles] under nitrogen atmosphere, and the mixture heated at 80°C for 30 min., and then cooled to room temperature. To this tosylate (0.83g 3.6 mmoles) in DMF (4 mL) was added dropwise through a syringe. The reaction mixture was stirred at 50 °C for 3 hr. The solvent was stripped *in vacuo* and the dark brown residue partitioned between dichloromethane (40 mL) and water (23 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and the solvent evaporated. The residue was purified by flash chromatography on silica gel [eluting with benzene-ethyl acetate, 8:2 (v/v)] furnished **2** as a white crystalline solid (0.36g 53%), mp 112 °C; $[\alpha]_D^{25}$ + 7.5° (*c* 1, $CHCl_3$); ^{1}H NMR: 1.40 (t, 9H, $-CH_3$), 2.65 (m, 3H, 3-Gly H), 2.91 (m, 3H, 3-Gly H), 3.25 (m, 3H, 3-Gly H), 3.52 (d, *J*=14.2 Hz, 3H, $ArCH_2Ar$), 3.91 (m, 6H, $ArOCH_2Gly$), 4.01 (q, 6H, $ArOCH_2CH_3$), 4.72 (d,

14.2 Hz, 3H, $ArCH_2Ar$), 6.80 (2s, 6H, ArH); and 1.40 (t, 9H,-CH_3), 2.73 (m, 3H, 3-Gly H), 2.94 (m, 3H, 3-Gly H), 3.33 (m, 3H, 3-Gly H), 3.52 (d, *J*=14.2 Hz, 3H, $ArCH_2Ar$), 4.01(q, 6H, $ArOCH_2CH_3$), 4.21 (m, 6H, $ArOCH_2Gly$), 4.72(d, 14.2 Hz, 3H, $ArCH_2Ar$), 6.95 (2s, 6H, ArH); MS (FAB): m/z 618 [M^+ + H]. Anal. Calcd for $C_{36}H_{42}O_9$; C, 69.90; H, 6.79. Found: C, 69.41 H, 7.01%.

General procedure for the preparation of 3 and 4. In methanol (1 mL) were added **2** (0.08 mmole) and amine (0.25 mmole) and the mixture was refluxed under nitrogen atmosphere for 18 hr. Excess of solvent was evaporated under *vacuo*. The residue was purified over neutral Al_2O_3 column [eluting with ethyl acetate-methanol, 7:3 (v/v)] to afford the title compounds.

2, 7, 12-Triethoxy-3, 8, 13-tris(3-pyrolodinyl-2-hydroxy propoxy) cyclotriveratrylene (MSSS, PSSS) 3: Yield 61 mg (91%); $[\alpha]_D^{25}$ + 2.3° (*c* 1, EtOH); ^{1}H NMR: 1.41 (t, 9H,-CH_3), 1.59 (m, 12H, CH_2CH_2), 2.81 (m, 12H, *N*-CH_2), 3.53 (d, *J*=14.0Hz, 3H, $ArCH_2Ar$), 3.62 (m, 6H, *N*-CH_2), 4.21 (q, 12H, $ArOCH_2$), 4.35(m, 3H, C*H*OH), 4.72 (d, *J*=14.0Hz, 3H, $ArCH_2Ar$), 6.85 (2s, 6H, ArH); MS(FAB): m/z 832 [M^+ + H]. Anal. Calcd for $C_{48}H_{69}N_3O_9$: C, 69.31; H, 8.30; N; 5.05. Found: C, 69.10; H, 8.46; N 4.01%.

2, 7, 12-Triethoxy-3, 8, 13-tris(3-morpholinyl-2-hydroxypropoxy)cyclotriveratylene (MSSS, PSSS) 4: Yield 67 mg (94%); $[\alpha]_D^{25}$ + 3.4° (*c* 1,6.9, EtOH); ^{1}H NMR: 1.42 (t, 9H,-CH_3), 2.60 (m, 18H, N-CH_2), 3.01 (s, br, 3H,3OH), 3.43(d, *J*=14.0Hz, 3H, $ArCH_2Ar$), 3.71 (br, m, 12H, OCH_2), 4.01 (q, 6H, $ArOCH_2$), 4.13(m, 3H, C*H*OH), 4.72(d, *J*=14.0Hz, 3H, $ArCH_2Ar$), 6.83 (2s, 6H, ArH); MS(FAB): m/z 880 [M^+ + H], Anal. Calcd for $C_{48}H_{69}N_3O_{12}$: C, 65.52; H, 7.84; N, 4.77. Found: C, 65.27; H, 8.01; N, 4.35%.

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