Supporting Information

Resolution, Enantiomerization Kinetics, and Chiroptical Properties of 7,7'-Dihydroxy-8,8'-biquinolyl

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1. General Experimental Conditions

Preparative chromatographic separations were performed on silica gel 60 (35-75 μ m) and reactions followed by TLC analysis using silica gel 60 plates (2-25 μ m) with fluorescent indicator (254 nm) and visualized with UV or phosphomolybdic acid. All commercially available reagents were used as received unless otherwise noted.

Melting points were recorded on a melting point stage and are uncorrected. Infra-red spectra were recorded in Fourier transform mode using a thin film supported between NaCl plates for liquid samples and an ATR probe for solids. ¹H and ¹³C NMR spectra were recorded in Fourier transform mode at the field strength specified and from the indicated deuterated solvents in standard 5 mm diameter tubes. Chemical shift in ppm is quoted relative to residual solvent signals calibrated as follows: CDCl₃ δ_H (CHCl₃) = 7.26 ppm, δ_C = 77.2 ppm; (CD₃)₂SO δ_H (CD₃SOCHD₂) = 2.50 ppm, δ_C = 39.5 ppm; CD₃OD δ_H (CHD₂OD) = 3.31 ppm, δ_C = 49.0 ppm. Multiplicities in the ¹H NMR spectra are described as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Numbers in parentheses following carbon atom chemical shifts refer to the number of attached hydrogen atoms as revealed by the DEPT spectral editing technique. Low (MS) and high resolution (HRMS) mass spectra were obtained using electrospray (ES) ionization techniques. Ion mass/charge (*m/z*) ratios are reported as values in atomic mass units. CD spectra were acquired on a Jasco J-720 spectropolarimeter and step scans were collected at 1 nm/step with an integration time of 1 or 2 sec over the range 180-500 nm.

2. NMR Spectra for Bismenthylcarbonates

3. Enantiomerization Kinetic Experiments

3A. Protocol for enantiomerization kinetic experiments

Kinetic experiments: A magnetically stirred solution of enantioenriched 7,7'-dihydroxy-8,8'-biquinolyl (**6**, 4.5 mg, 16 μ mol) in H₂O (2.25 mL) residing in a 10 mL pear-shaped two-neck RB-flask equipped with thermometer and condenser was immersed in an isothermal bath. Once the internal temperature of the solution had equilibrated to a steady value, an aliquot (0.25 mL) was removed and converted to bismenthylcarbonates **9** (see below) for indirect determination of %ee: this value constituted %ee₀ (%ee at time $t = 0$ sec). The solution was then allowed to incubate in the isothermal bath over time and 0.25 mL aliquots removed at regular intervals and analyzed as before to obtain %ee as a function of time.

Aliquot processing and analysis: Immediately following removal, the sampled aliquot (0.25 mL) was injected into a vigorously stirred biphasic mixture of (-)-menthyl chloroformate [(-)-**8**, 2.2 μ L, $d = 1.03$, 2.3 mg, 10.4 μ mol] in tetrabutylammonium bromide solution (TBAB, 0.5 mL, 1.75 M in CH₂Cl₂) and aq. NaOH (0.25 mL, 1.5 M) at rt. After 60 min, H₂O (2 mL) and CH₂Cl₂ (2 mL) were added and the layers well shaken and separated. The aqueous phase was extracted (2x2 mL, CH₂Cl₂) and the combined organic extracts were dried (Na₂SO₄) and concentrated *in vacuo* to afford a mixture of diastereomeric bismenthylcarbonates, *lk*-**9** and *ul*-**9**. The mixture was analyzed by ¹H NMR (300 MHz, CDCl₃, 55 °C) to determine %de (**9**) [= %ee (**6**)] by examination of the integration trace for the well differentiated signals due to protons at C2/2': δ_H (*lk*-**9**) = 8.76 (1H, dd, $J = 4.2, 1.8$ Hz, C2/2'-*H*), δ_H (*ul*-**9**) = 8.80 (1H, dd, $J = 4.1, 1.6$ Hz, C2/2'-*H*). Figure S1 shows a representative %de (**9**) determination using this NMR method.

The appropriate rate law for first order enantiomerization of **6** is readily seen to be:

$$\ln (\%ee_0 / \%ee_t) = 2kt$$

(see Section 3B, over). Thus, plots of $\ln (\%ee_0 / \%ee_t)$ against t (slope $2k$) were constructed to extract enantiomerization rate constants, k (see Section 3C).

Figure S1. ¹H NMR analysis of an isomeric mixture of bismenthylcarbonates *lk*-**9** / *ul*-**9**.

3B. Derivation of first order rate law for enantiomerization

let, k = enantiomerization rate constant

$[S]$ = mole fraction of $(-)-(aS)\text{-}\mathbf{6}$
 $[R]$ = mole fraction of $(+)-(aR)\text{-}\mathbf{6}$

then, $[S] + [R] = 1$

and, $\frac{d[S]}{dt} = -k[S] + k[R] = -2k[S] + k$

$$\Rightarrow \int_{S_0}^{S_t} \frac{1}{-2k[S] + k} d[S] = \int_0^t 1 dt$$

$$\Rightarrow \left[\begin{array}{c} \frac{1}{-2k} \ln (-2k[S] + k) \end{array} \right]_{S_0}^{S_t} = \left[\begin{array}{c} t \\ 0 \end{array} \right]^t_0$$

$$\Rightarrow \ln(-2k[S_0] + k) - \ln(-2k[S_t] + k) = 2kt$$

$$\Rightarrow \ln \left(\frac{1 - 2[S_0]}{1 - 2[S_t]} \right) = 2kt \quad \Rightarrow \quad \ln \left(\frac{\%ee_0}{\%ee_t} \right) = 2kt$$

3C. Raw kinetic data and extraction of rate constants for enantiomerization of **6**

The following data were obtained according to the protocol given above and unless otherwise stated were collected from unbuffered aqueous solutions of 7 mM concentration in **6** (see Section 3A). Linear regression analysis was forced through the origin for slope determination.

t (sec)	%ee	$\ln (\%ee_0 / \%ee_t)$
0	47.3	0.00000
82440	46.7	0.01277
173520	44.6	0.05878
345540	40.2	0.16264
518580	38.8	0.19809

slope = 4.0020×10^{-7} ; $R^2 = 0.983$

$k(316\text{ K}) = 2.001 \times 10^{-7} \text{ s}^{-1}$

time (sec)	$\ln(ee_0/ee_t)$
0	0.00000
82440	0.01277
173520	0.05878
345540	0.16264
518580	0.19809

A repeat enantiomerization kinetic experiment was conducted at 329 K (56 °C) but with a two-fold diluted sample of **6** (3.5 mM rather than the usual 7 mM). The rate constant for enantiomerization obtained from this experiment was not significantly different (within limits of determination method) from that previously obtained thus confirming that enantiomerization of **6** is a first order process as assumed (see below).

The above enantiomerization experiment at 339 K (66 °C) was repeated in aq. NaOH (1.5 M, pH 13) at the same concentration of **6** (7 mM) (see below). The rate constant for enantiomerization of **6** in alkaline solution was found to be significantly smaller than that in neutral solution.

4. AM1 Enantiomerization Modeling Study

4A. Overview of computational method

All calculations were performed using Spartan '02 version 5.1 (Wavefunction Inc., Irvine, CA). Geometries for ground and transition state structures were located and optimized by application of the AM1 semi-empirical method with molecular symmetry enabled as the only constraint. Solvent effects were neglected throughout.

Enantiomerization transition state structure searches began from either an *s-cis* or *s-trans* eclipsed planar conformation of **6** (Figure S2). In this manner, symmetric transition states, *syn*-C₂-TS (AM1) and *anti*-C₂-TS (AM1), were located and identified by their single negative eigenvalues (imaginary vibrational frequencies of -37 cm^{-1} and -57 cm^{-1} , respectively).

Figure S2. Initial conformations of **6** for enantiomerization transition state searches: *s-cis* (left) for *syn*-C₂-TS, and *s-trans* (right) for *anti*-C₂-TS.

4B. Data for computed ground state of **6**, GS (AM1) (see Figure 5)

$E = 22.57\text{ kcal mol}^{-1}$; molecular charge = 0; spin multiplicity = 1; electrons = 106; point-grp = C₂

Table T1. Cartesian co-ordinates (Å) for GS (AM1)

atom	X	Y	Z	atom	X	Y	Z
01 H	-1.6959135	4.6982739	-2.1412107	18 C	0.3428724	0.6467350	0.6302368
02 C	-1.2365509	3.8980770	-1.5476309	19 O	-2.1693882	0.1484924	2.0321541
03 H	0.5105739	5.0170024	-0.9422313	20 C	-1.5576037	-0.8220073	1.2819023
04 C	-0.0396137	4.0651109	-0.8975421	21 C	-1.7438249	-3.1125012	0.5396216
05 N	-1.4257171	1.6054986	-0.7520991	22 C	0.2114120	-1.7525265	-0.1046830
06 C	0.5090905	2.9863938	-0.1488066	23 C	-2.2617085	-2.0625741	1.2460754
07 C	-1.8952917	2.6344170	-1.4353258	24 C	-0.5090905	-2.9863938	-0.1488066
08 C	-0.2114120	1.7525265	-0.1046830	25 N	1.4257171	-1.6054986	-0.7520991
09 C	1.7438249	3.1125012	0.5396216	26 H	-3.2166427	-2.1348738	1.7868731
10 H	-2.8662013	2.4768903	-1.9415412	27 H	-0.5105739	-5.0170024	-0.9422313
11 C	-0.3428724	-0.6467350	0.6302368	28 H	-2.2794897	-4.0734639	0.4905183
12 H	-1.6948812	0.9847746	1.9036890	29 C	1.8952917	-2.6344170	-1.4353258
13 C	2.2617085	2.0625741	1.2460754	30 H	1.6948812	-0.9847746	1.9036890
14 H	2.2794897	4.0734639	0.4905183	31 H	2.8662013	-2.4768903	-1.9415412
15 H	3.2166427	2.1348738	1.7868731	32 C	1.2365509	-3.8980770	-1.5476309
16 C	1.5576037	0.8220073	1.2819023	33 H	1.6959135	-4.6982739	-2.1412107
17 O	2.1693882	-0.1484924	2.0321541	34 C	0.0396137	-4.0651109	-0.8975421

4C. Data for *syn* enantiomerization transition state, *syn*-C₂-TS (AM1) (see Figure 5)E = 56.66 kcal mol⁻¹; molecular charge = 0; spin multiplicity = 1; electrons = 106; point-grp = C₂**Table T2.** Cartesian co-ordinates (Å) for *syn*-C₂-TS (AM1) eigenvalue = -37

atom	X	Y	Z	atom	X	Y	Z
01 H	4.1104403	-0.2807221	3.4365634	18 C	0.7224842	0.1259829	-0.6838495
02 C	3.4720314	-0.1464528	2.5553436	19 O	-0.5728560	-0.9802763	-2.9232385
03 H	4.9647312	-0.6522133	1.0762569	20 C	-1.3367870	-0.4432989	-1.9085076
04 C	3.9228502	-0.3622651	1.2777632	21 C	-3.5461114	0.1466620	-1.1439995
05 N	1.2601596	0.4165997	1.7148871	22 C	-1.6503720	-0.0933932	0.4352250
06 C	3.0379865	-0.1753498	0.1791115	23 C	-2.7244031	-0.2495721	-2.1600799
07 C	2.1250339	0.3001401	2.7072375	24 C	-3.0379865	0.1753498	0.1791115
08 C	1.6503720	0.0933932	0.4352250	25 N	-1.2601596	-0.4165997	1.7148871
09 C	3.5461114	-0.1466620	-1.1439995	26 H	-3.1050567	-0.3968102	-3.1811255
10 H	1.7520990	0.5931874	3.7060761	27 H	-4.9647312	0.6522133	1.0762569
11 C	-0.7224842	-0.1259829	-0.6838495	28 H	-4.6037350	0.3915148	-1.3215241
12 C	-3.9228502	0.3622651	1.2777632	29 C	-2.1250339	-0.3001401	2.7072375
13 C	2.7244031	0.2495721	-2.1600799	30 H	-4.1104403	0.2807221	3.4365634
14 H	4.6037350	-0.3915148	-1.3215241	31 H	-1.7520990	-0.5931874	3.7060761
15 H	3.1050567	0.3968102	-3.1811255	32 C	-3.4720314	0.1464528	2.5553436
16 C	1.3367870	0.4432989	-1.9085076	33 H	-0.9799422	-0.7316718	-3.7661398
17 O	0.5728560	0.9802763	-2.9232385	34 H	0.9799422	0.7316718	-3.7661398

4D. Data for *anti* enantiomerization transition state, *anti*-C₂-TS (AM1) (see Figure 5)E = 62.83 kcal mol⁻¹; molecular charge = 0; spin multiplicity = 1; electrons = 106; point-grp = C₂**Table T3.** Cartesian co-ordinates (Å) for *anti*-C₂-TS (AM1) eigenvalue = -57

atom	X	Y	Z	atom	X	Y	Z
01 H	1.1469516	-5.6564320	0.0009561	18 C	1.8645157	0.4226770	-0.2216227
02 C	0.7566201	-4.6342709	-0.0727117	19 C	2.0467027	2.4821131	1.0542534
03 H	-0.8807839	-4.8917156	1.3178786	20 C	0.0519997	1.9555010	-0.3055546
04 C	-0.3365978	-4.2091242	0.6475814	21 C	2.6044139	1.3190366	0.6252185
05 N	0.9928802	-2.4292035	-1.0576261	22 C	0.7976435	2.8768373	0.5013070
06 C	-0.7976435	-2.8768373	0.5013070	23 N	-0.9928802	2.4292035	-1.0576261
07 C	1.3686475	-3.6959081	-0.9473644	24 H	3.6240527	1.0144521	0.9064100
08 C	-0.0519997	-1.9555010	-0.3055546	25 H	0.8807839	4.8917156	1.3178786
09 C	-2.0467027	-2.4821131	1.0542534	26 H	2.5617793	3.1489034	1.7605321
10 C	0.4750056	0.5555753	-0.4076853	27 C	-1.3686475	3.6959081	-0.9473644
11 C	-2.6044139	-1.3190366	0.6252185	28 H	-2.2079927	4.0063798	-1.5972798
12 H	-2.5617793	-3.1489034	1.7605321	29 C	-0.7566201	4.6342709	-0.0727117
13 H	-3.6240527	-1.0144521	0.9064100	30 H	-1.1469516	5.6564320	0.0009561
14 C	-1.8645157	-0.4226770	-0.2216227	31 C	0.3365978	4.2091242	0.6475814
15 O	-2.7083481	0.4806442	-0.7868267	32 H	2.2079927	-4.0063798	-1.5972798
16 C	-0.4750056	-0.5555753	-0.4076853	33 H	-2.2184556	1.0438306	-1.4174658
17 O	2.7083481	-0.4806442	-0.7868267	34 H	2.2184556	-1.0438306	-1.4174658