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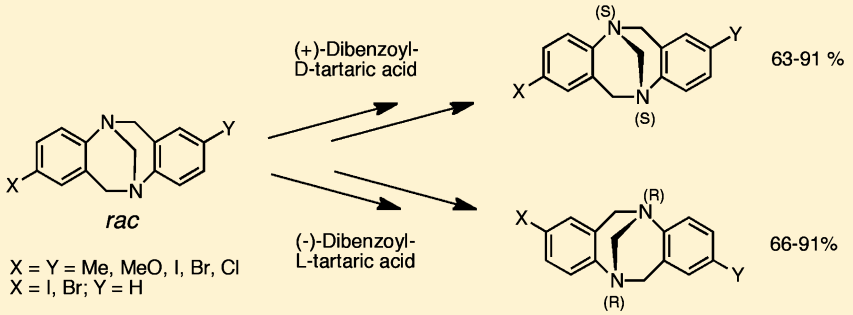
Application of Crystallization-Induced Asymmetric Transformation to a General, Scalable Method for the Resolution of 2,8-Disubstituted Tröger's Base Derivatives

Donald L. Jameson,* Thomas Field, Monica R. Schmidt, Alyson K. DeStefano, Christopher J. Stiteler, Vincent J. Venditto, Brooke Krovic, Christopher M. Hoffman, Matthew T. Ondisco, and Matthew E. Belowich†

Department of Chemistry, Gettysburg College, Gettysburg, Pennsylvania 17325, United States

Supporting Information



ABSTRACT: A general method for the gram scale resolution of 2-substituted and 2,8-disubstituted Tröger's base (TB) derivatives in 63−91% yield has been achieved through the application of crystallization-induced asymmetric transformation (CIAT). Enantiomeric ratios of the resolved TB derivatives range from 99.1:0.9 to >99.5:0.5. Among the Tröger's base compounds resolved are four synthetically valuable bromo and iodo derivatives.

Tröger's base (TB, **1**) (Figure 1), a chiral, tetracyclic diamine possessing a rigid, V-shaped structure, has received considerable attention as a scaffold for the construction of supramolecular assemblies.[1−5] The renaissance in TB chemistry originated with the work of Wilcox, who used the molecule for the design of chiral molecular clefts.[6] Recent research involves applications as diverse as TB fragments that have been incorporated into new materials for gas separation.[7]

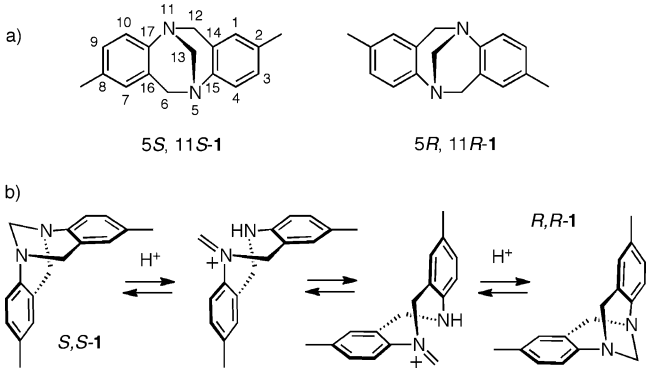


Figure 1. (a) The two enantiomers of TB **1** showing atomic numbering scheme. (b) The architecture of the enantiomers of TB **1**, showing the mechanism of acid-catalyzed racemization.

Of particular interest are TB derivatives with substituents in the 2- and 8-positions, which are projected at roughly a 90° angle, making these ideal "corner" structural components.

Wärnmark's method for preparing halogenated derivatives[8] was a leap forward in enabling cross-coupling strategies for the modification of the TB core. However, the absence of an efficient way to resolve these synthetically useful iodo and bromo derivatives hampers the preparation of homochiral molecules or assemblies possessing multiple TB fragments. While individual TB derivatives have been resolved by either diastereomeric salt formation or chiral HPLC, no general method for the scalable chemical resolution of this class of molecules has been reported.

The resolution of TB **1** and its derivatives and the assignment of absolute configuration have had a somewhat convoluted history. In 1944, Prelog and Wieland reported the partial resolution of 6 g of racemic Tröger's base **1** on 270 g of D-lactose giving only 5.5% yield of each pure enantiomer.[9] The paper also described unsuccessful attempts to resolve **1** as diastereomeric salts of both (1*R*)-(−)-10-camphorsulfonate and (1*R*)-(*endo*,*anti*)-(+)-3-bromo-camphor-8-sulfonate. This coupled with their finding that chiral **1** racemizes in acid

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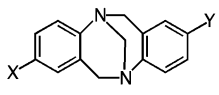
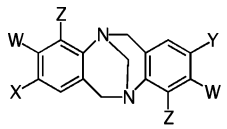
(Figure 1) led to the widely held belief that resolution via diastereomeric salt formation was not feasible.

In 1991, Wilen et al. refuted that hypothesis when they described the resolution of **1** via the (−)-[1,1′-binaphthalene]-2,2′-diyl phosphate salt.[10] The absolute configuration of the resolved **1** was confirmed as the (5*S*,11*S*)-(+) isomer by X-ray crystallography (settling earlier competing assignments).[11,12] The yield of the salt (from ethanol) was 93%, considerably higher than the theoretical 50% yield, which lead to the conclusion that a crystallization-induced asymmetric transformation (CIAT) had taken place. Tröger's bases **1**[13] and **2**[14] (as *O*,*O*′-dibenzoyl-L-tartaric acid complexes) and a naphthyl derivative[15] (as an *O*,*O*′-ditoluoyl-L-tartaric acid complex) have been resolved. The tartaric acid based resolutions have all used acetone as the solvent, and in no case was CIAT observed.

Despite these successes, synthetically more useful halogenated TB have resisted chemical resolution. Chiral HPLC has been used to resolve a dibromo-TB derivative (in 10 mg batches)[16] and diiodo-TB **4** (in 40 mg[17] and 200 mg[18] batches). Finally, several dihalogenated TB derivatives have been resolved using recycling chiral HPLC to increase peak resolution.[19]

The lack of a general and scalable method for the resolution of Tröger's base derivatives (particularly halogenated derivatives) prompted us to explore solutions to this problem. Our approach was to utilize the proven ability of *O*,*O*′-dibenzoyltartaric acid (DBTA) to form complexes with Tröger's base and screen solvents that would lead to selective precipitation of diastereomeric salts/complexes. Tröger's base derivatives **1**−**10**[20−23] (Figure 2) possess a variety of substituents and include symmetrically dihalogenated TB and unsymmetric monohalogenated TB.





1: Me_2TB X=Y=CH_3
2: MeO_2TB X=Y=OCH_3
3: Br_2TB X=Y=Br
4: I_2TB X=Y=I
5: Cl_2TB X=Y=Cl
6: HITB X=H; Y=I
7: HBrTB X=H; Y=Br
8: H_2TB X=Y=H

9: I_2Me_2TB W=H; X=Y=I; Z=CH_3
10: 3,9-Cl_2TB W=Cl; X=Y=Z=H

Figure 2. Tröger's base derivatives investigated in this study.

Solvent polarity was seen as a potential factor that could improve the chances of successful resolution of TB with DBTA; lower solvent polarity would be expected to decrease the stability of charged intermediates leading to racemization (Figure 1). Our search revealed 1,2-dichloroethane (DCE) to be suitable for the resolution of TB **1**−**7**. Treatment of a 1:1 mixture of the TB derivative and DBTA in boiling DCE resulted in crystals that were deposited over periods ranging from minutes to hours, depending on the derivative. The resulting solids were resuspended in DCE and filtered to give complexes, which were revealed by ^{1}H NMR and elemental analysis to be 1:1 TB-DBTA dyads.

During the course of our investigation, two apparently anomalous observations were noted. Dyads of TB **2** consistently gave >50% yields (based on total TB) and concentration of dyad filtrates of TB **4** at elevated temperatures deposited second and even third crops of crystals giving total yields of 70−80%. This was not entirely surprising given the capacity for TB to racemize under acidic conditions (Figure 1) and Wilen's observation of CIAT in the resolution of **1**. These observations prompted us to explore the possibility of using CIAT to improve the efficiency of our resolution by heating TB-DBTA mixtures while varying time and temperature. Solubility of the individual dyads varied with temperature: **2**, **3**, **5**, **6**, and **7** precipitated rapidly at the boiling point of DCE, while dyads of **1** and **4** remained in solution at reflux and precipitated only slowly from cooled solutions. It was determined that heating TB-DBTA mixtures of **1** and **4** at 45−50 °C and **2**, **3**, **5**, **6**, and **7** at 55−60 °C for 120 h resulted in the isolation of dyads in yields ranging from 63 to 91% (based on total TB). Tröger's base **8**, bearing no substituents, deposited a 1:1 TB-DBTA dyad (as determined by ^{1}H NMR), but recovered TB exhibited low enantiomeric ratios (<80:20). Tröger's base derivatives **9** and **10**, bearing substituents in positions other than 2- and 8-, did not deposit crystalline dyads under the conditions of this procedure. This is particularly disappointing for compound **9**, whose value lies in its decreased tendency for acid-catalyzed racemization. We postulate that the varying yields for the TB dyads reflect a fine balance between solubility of the dyads, temperature of the CIAT, and time. It was our goal to devise a straightforward, general resolution method with as few variables as possible. It is possible that extension of reaction times and/or closer examination of temperature control for individual TB could result in marginally higher yields of dyads of TB **1**−**7**.

Enantiopure TB derivatives were recovered from the dyads in >95% yield by extraction from methylene chloride and aqueous sodium carbonate. The enantiopurity of the resolved TB derivatives was determined by HPLC. The efficiency of the resolution is shown in Figure 3, which depicts the chiral HPLC traces of (±)-**3**, (+)-*S*,*S*-**3**, and (−)-*R*,*R*-**3**. Enantiomeric ratios (er) of ≥99:1 were observed for resolved TB **1**−**7**, with er >99.5:0.5 for most derivatives. HPLC analysis revealed that the TB-DBTA dyads of TB bearing electron-withdrawing substituents possess a high degree of stereointegrity upon storage: enantiopure TB **4** recovered from dyad stored ∼60 days at rt, showed no measurable decrease in er. On the other hand, TB **1** from a dyad stored 45 days showed a slight decrease in er from 99:1 to 95:5. As a result, it is generally advantageous to recover the TB shortly after isolation of the dyads. In general, the high er observed for recovered TB indicates that racemization in the presence of DBTA, under these conditions, does not interfere with resolution.

Specific rotations of both enantiomers of **1**,[10,13] **2**,[14] **3**,[18] and **4**[17,18] were in agreement with literature values and allowed for the assignment of absolute configuration. In these cases, (−)-L-DBTA consistently formed dyads with (*R*,*R*)-(−)-TB, while (+)-D-DBTA formed dyads with (*S*,*S*)-(+)-TB. In addition, (*S*,*S*)-(+)-TB derivatives consistently eluted before (*R*,*R*)-(−)-TB derivatives under the conditions of chiral HPLC. On the basis of analogous behavior of TB **5**, **6**, and **7**, these (−)-TB stereoisomers were tentatively assigned *R*,*R* absolute configuration and the (+)-TB stereoisomers were tentatively assigned *S*,*S* absolute configuration. The results of the resolution of TB derivatives **1**−**8** are summarized in Table 1.

Caution should be exercised in assigning absolute configurations of Tröger's base derivatives. The relationship between the chiroptical properties and absolute configuration is sensitive to the structure of the chromophore.[16] Lützen et al.[19] determined the absolute configuration of a series of three 2,8-

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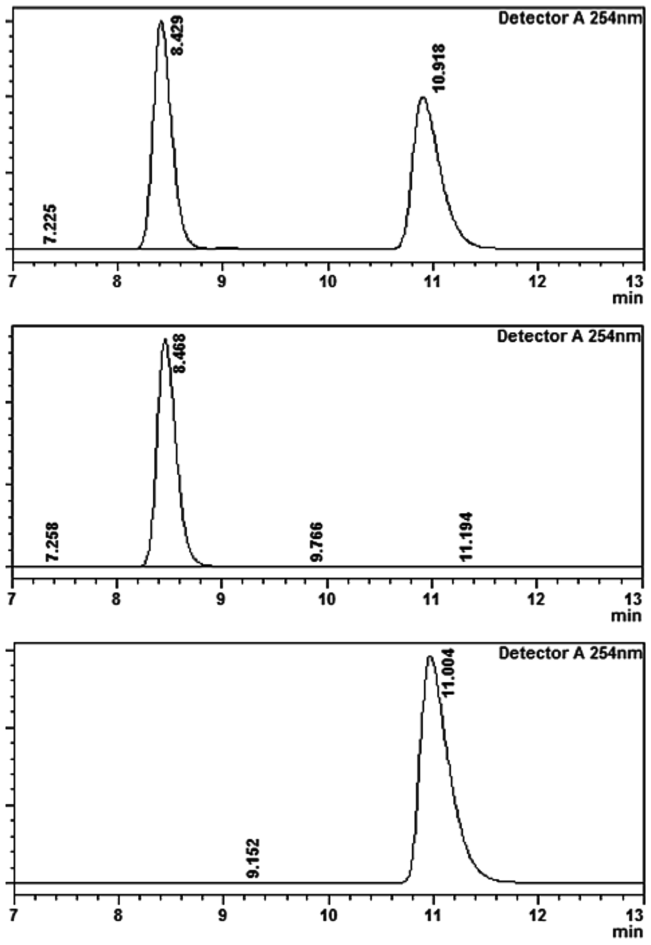

Figure 3. HPLC traces of racemic **3** (top), (+)-*S*,*S*-**3** (middle) and (−)-*R*,*R*-**3** (bottom). The er for both (+)-*S*,*S*-**3** and (−)-*R*,*R*-**3** is >99.5:0.5. HPLC conditions: Chiralpak 1A column, flow 0.8 mL/min, 100% ethanol.

dihalogenated TB molecules bearing additional substituents, and in each case the (−)-*R*,*R*-TB and (+)-*S*,*S*-TB relationship persisted (in agreement with the established absolute configuration of TB **1**−**4** and our tentative assignment for TB **5**−**7**). Tröger's base derivatives where the relationship between the absolute configuration and the specific rotation is reversed possess halogens in positions other than 2- and 8-.[16,19] Several other 2,8-disubstituted TB (nonhalogenated) maintain the (−)-*R*,*R*-TB and (+)-*S*,*S*-TB relationship.[16,18] Finally, in Lützen's series of halogenated TB,[19] the chiral HPLC order was consistent with the absolute configuration/specific rotation relationship; for the three examples of (−)-*R*,*R*-TB and (+)-*S*,*S*-TB, the (−)-*R*,*R*-TB stereoisomer eluted first. In the example where the halogens were not 2,8-disubstituted and possessed a (+)-*R*,*R*-TB relationship, the *R*,*R* isomer still eluted first.

In conclusion, we have described a general method for the resolution of five different 2,8-disubstituted and two different 2-substituted Tröger's base derivatives. Control of time and temperature results in yields of TB-DBTA dyads of >50% (based on total TB) and demonstrate the participation of a crystallization-induced asymmetric transformation (CIAT). The results contradict the widely held belief that a general procedure for the resolution of TB analogues via complexes with acids is not feasible. The method provides derivatives in multigram quantities, and access to the synthetically versatile bromo- and iodo-Tröger's bases should stimulate research on enantiopure derivatives in general and homochiral molecules/assemblies possessing multiple TB fragments in particular.

EXPERIMENTAL SECTION

General Information. NMR spectra were obtained on a 400 MHz spectrometer. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane (TMS) with reference to internal solvent for ^{1}H NMR and ^{13}C NMR spectra. Multiplicities are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). Optical rotations were obtained at a wavelength of 589 nm. The concentration "*c*" has units of g/100 mL. Enantiomeric purities were determined as enantiomeric ratios (er) using a Chiralpak 1A chiral column using HPLC detecting at 254 nm. The mobile phase was 100% ethanol at a flow rate of 0.800 mL/min. HPLC traces of resolved TB were compared to racemic samples. Column chromatography was performed using neutral alumina (activity III). (−)-*O*,*O*′-Dibenzoyl-L-tartaric acid monohydrate ((−)-L-DBTA•H_2O) and (+)-*O*,*O*′-dibenzoyl-D-tartaric acid ((+)-D-DBTA) were purchased from commercial sources and used as received. Preparations of Tröger's base derivatives (±)-**1** ((±)-Me_2TB),[20] (±)-**2** ((±)-MeO_2TB),[20] (±)-**3** ((±)-I_2TB),[20] (±)-**4** ((±)-Br_2TB),[20] (±)-**5** ((±)-Cl_2TB),[20] (±)-**6** ((±)-HITB),[21] (±)-**7** ((±)-HBrTB),[21] (±)-**8** ((±)-H_2TB),[20] (±)-**9** ((±)-I_2Me_2TB),[22] and (±)-**10** ((±)-3,9-Cl_2TB)[23] have been reported in the literature.

Representative Procedure for the Preparation of a Tröger's Base-DBTA Dyad. (−)-*R*,*R*-2,8-Dibromo-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine•(−)-*O*,*O*′-dibenzoyl-L-tartaric acid dyad, [(−)-Br_2TB•(−)-L-DBTA]. A 300 mL round-bottom flask charged with 11.60 g (30.83 mmol) of (−)-*O*,*O*′-dibenzoyl-L-tartaric acid monohydrate and 130 mL of dichloroethane (DCE) was heated to boiling, and the water of hydration and residual water (either from the solvent or as water of hydration) was carefully removed azeotropically. (±)-Br_2TB (11.40 g; 25.00 mmol) was added, and the solution heated to boiling. Crystals of the complex deposited almost immediately. The suspension was stirred at 55−60 °C for 120 h. The mixture was cooled and allowed to stand for 16 h, whereupon the solid was collected by filtration and washed with 3 × 15 mL of DCE to give 20.08 g of fine white crystals. The solid was resuspended in 70 mL of DCE, stirred for 30 min, filtered and washed with 3 × 15 mL of DCE to give 19.76 g (89%) of product as a white solid. The solid was dried under a vacuum at rt for 24 h: mp 173−174 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.19 (d, J = 17.2 Hz, 2H), 4.21 (s, 2H), 4.60 (d, J = 17.2 Hz, 2H), 5.92 (s, 2H), 7.07 (d, J = 8.4 Hz, 2H), 7.17 (d, J = 2.0 Hz, 2H), 7.30 (dd, J = 8.8, 2.4 Hz, 2H), 7.58−7.63 (m, 4H), 7.71−7.76 (m, 2H), 8.03−8.06 (m, 4H), 13.95 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 57.6, 65.7, 71.4, 115.3, 126.9, 128.4, 129.0, 129.39, 129.43, 129.9, 130.5, 134.1, 147.1, 164.64, 167.1. Anal. Calcd for $C_{33}H_{26}Br_2N_2O_8$: C, 53.68; H, 3.55; N, 3.79. Found: C, 53.59; H, 3.27; N, 3.76.

Note: The complexes of MeO_2TB, Br_2TB, Cl_2TB, HITB, and HBrTB deposited precipitates almost immediately, while the solution was still boiling. The complexes of Me_2TB and I_2TB often gave solid only after prolonged heating. Seed crystals and/or sonication often aided in the deposition of crystals. In these cases, once substantial crystallization occurs, the prolonged heating of the suspension can commence.

(+)-*S*,*S*-2,8-Dibromo-6,12-dihydro-5,11-methanodibenzo-[*b*,*f*][1,5]diazocine•(+)-*O*,*O*′-dibenzoyl-D-tartaric acid dyad, [(+)-Br_2TB•(+)-D-DBTA]. (±)-Br_2TB (7.60 g; 20.0 mmol) and (+)-*O*,*O*′-dibenzoyl-D-tartaric acid (7.34 g; 20.5 mmol) heated to 55−60 °C for 120 h yielded 13.0 g (88%) of the complex as a white solid: mp 172−173 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.19 (d, J = 17.2 Hz, 2H), 4.21 (s, 2H), 4.60 (d, J = 17.2 Hz, 2H), 5.91 (s, 2H), 7.07 (d, J = 8.8 Hz, 2H), 7.17 (d, J = 2.4 Hz, 2H), 7.30 (dd, J = 8.8, 2.4 Hz, 2H), 7.58−7.63 (m, 4H), 7.71−7.76 (m, 2H), 8.03−8.06 (m, 4H), 13.95 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ57.6, 65.7, 71.4, 115.3, 126.9, 128.4, 129.0, 129.39, 129.43, 129.9, 130.5,

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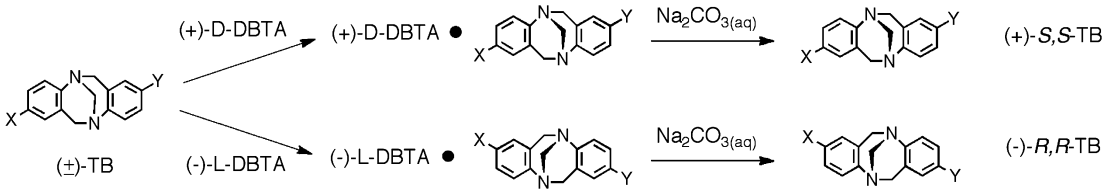
Table 1. Results for the resolution of TB 1−8[a]



entry	Tröger's base	X	Y	DBTA[b]	TB-DBTA yield g (%)	isolated resolved TB (yield)	$[\alpha]_D^{25}$ (c)[c]	lit. $[\alpha]_D$	er[d] (major:minor)
1[e]	(±)-**1**	Me	Me	(−)-L-DBTA	32.0 (66)	(−)-*R,R*-**1**(96%)	−276 (0.112)	−301[h]	99.1:0.9
2[e]	(±)-**1**	Me	Me	(+)-D-DBTA	22.3 (63)	(+)-*S,S*-**1**(98%)	+282 (0.112)	+279[h]	>99.5:0.5
3	(±)-**2**	MeO	MeO	(−)-L-DBTA	16.9 (88)	(−)-*R,R*-**2**(97%)	−240 (0.110)	−242[i]	>99.5:0.5
4	(±)-**2**	MeO	MeO	(+)-D-DBTA	13.2 (83)	(+)-*S,S*-**2**(98%)	+236 (0.110)	+236[i]	99.1:0.9
5[f]	(±)-**3**	Br	Br	(−)-L-DBTA	19.8 (89)	(−)-*R,R*-**3**(97%)	−383 (0.117)	−394[j]	>99.5:0.5
6[f]	(±)-**3**	Br	Br	(+)-D-DBTA	13.0 (88)	(+)-*S,S*-**3**(98%)	+379 (0.114)	+393[j]	>99.5:0.5
7[g]	(±)-**4**	I	I	(−)-L-DBTA	15.9 (76)	(−)-*R,R*-**4**(98%)	−441 (0.114)	−454[j]	>99.5:0.5
8[g]	(±)-**4**	I	I	(+)-D-DBTA	13.2 (79)	(+)-*S,S*-**4**(98%)	+443 (0.116)	+445[j]	>99.5:0.5
9	(±)-**5**	Cl	Cl	(−)-L-DBTA	14.8 (91)	(−)-*R,R*-**5**(97%)	−396 (0.110)		>99.5:0.5
10	(±)-**5**	Cl	Cl	(+)-D-DBTA	8.90 (91)	(+)-*S,S*-**5**(97%)	+393 (0.114)		>99.5:0.5
11	(±)-**6**	I	H	(−)-L-DBTA	6.36 (90)	(−)-*R,R*-**6**(98%)	−323 (0.110)		>99.5:0.5
12	(±)-**6**	I	H	(+)-D-DBTA	6.21 (88)	(+)-*S,S*-**6**(96%)	+326 (0.114)		>99.5:0.5
13	(±)-**7**	Br	H	(−)-L-DBTA	4.53 (69)	(−)-*R,R*-**7**(98%)	−302 (0.110)		>99.5:0.5
14	(±)-**7**	Br	H	(+)-D-DBTA	5.20 (79)	(+)-*S,S*-**7**(98%)	+302 (0.109)		>99.5:0.5
15	(±)-**8**	H	H	(−)-L-DBTA	[k]				
16	(±)-**8**	H	H	(+)-D-DBTA	[k]				

[a]Conditions: [TB] = [DBTA] ∼ 0.20−0.25 M in DCE at 55−60 °C for 120 h. [b]DBTA: *O,O′*-dibenzoyltartaric acid. [c]*c* = g/100 mL; performed in $CHCl_3$. [d]er = enantiomeric ratio. HPLC conditions: Chiralpak 1A column, flow 0.8 mL/min, 100% ethanol. [e][TB] = [DBTA] ∼ 0.50 M; *T* = 45−50 °C. [f][TB] = [DBTA] ∼ 0.30 M. [g]*T* = 45−50 °C. [h]ref 10. [i]ref 14. [j]ref 18. [k]Deposited 1:1 dyad, but recovered TB had er <80:20.

134.1, 147.1, 164.64, 167.1. Anal. Calcd for $C_{33}H_{26}Br_2N_2O_8$: C, 53.68; H, 3.55; N, 3.79. Found: C, 53.60; H, 3.20; Br; N, 3.76.

(−)-*R,R*-2,8-Dimethyl-6,12-dihydro-5,11-methanodibenzo-[*b,f*][1,5]diazocine•(−)-*O,O′*-dibenzoyl-L-tartaric acid dyad, [(−)-Me$_2$TB•(−)-L-DBTA]. (±)-Me$_2$TB (20.00 g; 80.00 mmol) and (−)-*O,O′*-dibenzoyl-L-tartaric acid monohydrate (30.52 g; 81.12 mmol) heated to 45−50 °C for 120 h yielded 32.04 g (66%) of the complex as a white solid: mp 162−164 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.15 (s, 6H), 4.00 (d, *J* = 16.8 Hz, 2H), 4.19 (s, 2H), 4.54 (d, *J* = 16.8 Hz, 2H), 5.91 (s, 2H), 6.71 (s, 2H), 6.92 (dd, *J* = 8.0, 1.6 Hz, 2H), 6.98 (d, 8.4 Hz, 2H), 7.58−7.63 (m, 4H), 7.72−7.76 (m, 2H), 8.03−8.06 (m, 4H), 13.97 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 20.3, 58.2, 66.4, 71.5, 124.4, 127.0, 127.6, 127.7, 128.5, 129.0, 129.4, 132.2, 134.1, 145.5, 164.7, 167.2. Anal. Calcd for $C_{35}H_{32}N_2O_8$: C, 69.07; H, 5.30; N, 4.60. Found 68.82; H, 5.34; N, 4.56.

(+)-*S,S*-2,8-Dimethyl-6,12-dihydro-5,11-methanodibenzo-[*b,f*][1,5]diazocine•(+)-*O,O′*-dibenzoyl-D-tartaric acid dyad, [(+)-Me$_2$TB•(+)-D-DBTA]. (±)-Me$_2$TB (15.00 g; 60.00 mmol) and (+)-*O,O′*-dibenzoyl-D-tartaric acid (21.86 g; 61.00 mmol) heated to 45−50 °C for 120 h yielded 22.26 g (63%) of the complex as a white solid: mp 161−162 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.15 (s, 6H), 4.00 (d, *J* = 16.8 Hz, 2H), 4.19 (s, 2H), 4.54 (d, *J* = 16.8 Hz, 2H), 5.91 (s, 2H), 6.71 (s, 2H), 6.92 (dd, *J* = 8.0, 1.6 Hz, 2H), 6.98 (d, 8.0 Hz, 2H), 7.58−7.63 (m, 4H), 7.71−7.76 (m, 2H), 8.03−8.06 (m, 4H), 13.97 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 20.3, 58.2, 66.4, 71.5, 124.4, 127.0, 127.6 (2 carbons), 128.5, 129.0, 129.4, 132.3, 134.1, 145.4, 164.7, 167.2. Anal. Calcd for $C_{35}H_{32}N_2O_8$: C, 69.07; H, 5.30; N, 4.60. Found 68.97; H, 5.32; N, 4.59.

(−)-*R,R*-2,8-Dimethoxy-6,12-dihydro-5,11-methanodibenzo-[*b,f*][1,5]diazocine•(−)-*O,O′*-dibenzoyl-L-tartaric acid dyad, [(−)-MeO$_2$TB•(−)-L-DBTA]. (±)-MeO$_2$TB (8.47 g; 30.0 mmol) and (−)-*O,O′*-dibenzoyl-L-tartaric acid monohydrate (11.44 g; 30.40 mmol) heated to 55−60 °C for 120 h yielded 16.88 g (88%) of the complex as a white solid: mp 174−175 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) d 3.64 (s, 6H), 4.00 (d, *J* = 16.8 Hz, 2H), 4.17 (s, 2H), 4.54 (d, *J* = 16.8 Hz, 2H), 5.90 (s, 2H), 6.51 (d, *J* = 3.2 Hz, 2H), 6.72 (dd, *J* = 8.8, 3.2 Hz, 2H), 7.02 (d, *J* = 8.8 Hz, 2H), 7.59−7.64 (m, 4H), 7.72−7.77 (m, 2H), 8.02−8.05 (m, 4H), 13.94 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) d 55.0, 58.3, 66.6, 71.5, 110.6, 113.7, 125.6, 128.5, 128.8, 129.0, 129.4, 134.1, 140.8, 155.3,164.7, 167.2. Anal. Calcd for $C_{35}H_{32}N_2O_{10}$: C, 65.62; H, 5.03; N, 4.37. Found: C, 65.55; H, 5.00; N, 4.38.

(+)-*S,S*-2,8-Dimethoxy-6,12-dihydro-5,11-methanodibenzo-[*b,f*][1,5]diazocine•(+)-*O,O′*-dibenzoyl-D-tartaric acid dyad, [(+)-MeO$_2$TB•(+)-D-DBTA]. (±)-MeO$_2$TB (7.06 g; 25.0 mmol) and (+)-*O,O′*-dibenzoyl-D-tartaric acid (9.14 g; 25.5 mmol) heated to 55−60 °C for 120 h yielded 13.22 g (83%) of the complex as a white solid: mp 172−173 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) d 3.64 (s, 6H), 4.00 (d, *J* = 16.8 Hz, 2H), 4.18 (s, 2H), 4.55 (d, *J* = 16.8 Hz, 2H), 5.90 (s, 2H), 6.51 (d, *J* = 2.8 Hz, 2H), 6.72 (dd, *J* = 8.8, 3.2 Hz, 2H), 7.02 (d, *J* = 8.8 Hz, 2H), 7.59−7.63 (m, 4H), 7.71−7.77 (m, 2H), 8.02−8.05 (m, 4H), 13.92 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) d 55.0, 58.3, 66.6, 71.5, 110.6, 113.7, 125.6, 128.5, 128.8, 129.0, 129.4, 134.1, 140.8, 155.3, 164.7, 167.2. Anal. Calcd for $C_{35}H_{32}N_2O_{10}$: C, 65.62; H, 5.03; N, 4.37. Found: C, 65.40; H, 4.83; N, 4.31.

(−)-*R,R*-2,8-Diiodo-6,12-dihydro-5,11-methanodibenzo[*b,f*]-[1,5]diazocine•(−)-*O,O′*-dibenzoyl-L-tartaric acid dyad, [(−)-I$_2$TB•(−)-L-DBTA]. (±)-I$_2$TB (11.85 g; 25.00 mmol) and (−)-*O,O′*-dibenzoyl-L-tartaric acid monohydrate (9.80 g; 26.0 mmol) heated to 45−50 °C for 120 h yielded 15.88 g (76%) of the complex as a white solid: mp 170−171 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.09 (d, *J* = 17.2 Hz, 2H), 4.19 (s, 2H), 4.56 (d, *J* = 16.8 Hz, 2H), 5.89 (s, 2H), 6.92 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 2.0 Hz, 2H), 7.45 (dd, *J* = 8.4, 2.0 Hz, 2H), 7.59−7.64 (m, 4H), 7.72−7.77 (m, 2H), 8.02−8.05 (m, 4H), 13.93 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 57.4, 65.6, 71.4, 87.4, 127.1, 128.4, 129.0, 129.4, 130.9, 134.1, 135.3, 135.6, 147.7, 164.6, 167.1. Anal. Calcd for $C_{33}H_{26}I_2N_2O_8$: C, 47.62; H, 3.15; N, 3.37. Found: C, 47.60; H, 2.77; N, 3.32.

(+)-*S,S*-2,8-Diiodo-6,12-dihydro-5,11-methanodibenzo[*b,f*]-[1,5]diazocine•(+)-*O,O′*-dibenzoyl-D-tartaric acid dyad, [(+)-I$_2$TB•(+)-D-DBTA]. (±)-I$_2$TB (9.48 g; 20.0 mmol) and (+)-*O,O′*-dibenzoyl-D-tartaric acid (7.34 g; 20.5 mmol) heated to 45−50 °C for 120 h yielded 13.16 g (79%) of the complex as a white

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solid: mp 166−167 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.09 (d, J = 17.2 Hz, 2H), 4.19 (s, 2H), 4.56 (d, J = 17.2 Hz, 2H), 5.90 (s, 2H), 6.92 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 1.6 Hz, 2H), 7.45 (dd, J = 8.4, 2.0 Hz, 2H), 7.59−7.63 (m, 4H), 7.71−7.76 (m, 2H), 8.02−8.05 (m, 4H), 13.94 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 57.5, 65.6, 71.4, 87.4, 127.1, 128.4, 129.0, 129.4, 130.9, 134.1, 135.3, 135.6, 147.7, 164.6, 167.2. Anal. Calcd for $C_{33}H_{26}I_2N_2O_8$:C, 47.62; H, 3.15; N, 3.37. Found: C, 47.51; H, 2.78; N, 3.35.

(−)-*R*,*R*-2,8-Dichloro-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine•(−)-*O*,*O*′-dibenzoyl-L-tartaric acid dyad, [(−)-Cl$_2$TB•(−)-L-DBTA]. (±)-Cl$_2$TB (7.28 g; 25.0 mmol) and (−)-*O*,*O*′-dibenzoyl-L-tartaric acid monohydrate (9.52 g; 25.3 mmol) heated to 55−60 °C for 120 h yielded 14.76 g (91%) of the complex as a white solid: mp 173−174 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) d 4.12 (d, J = 16.8 Hz, 2H), 4.21 (s, 2H), 4.59 (d, J = 16.8 Hz, 2H), 5.91 (s, 2H), 7.05 (d, J = 2.4 Hz, 2H), 7.13 (d, J = 8.8 Hz, 2H), 7.18 (dd, J = 8.8, 2.4 Hz, 2H), 7.58−7.63 (m, 4H), 7.71−7.76 (m, 2H), 8.02−8.05 (m, 4H), 13.95 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 57.8, 65.8, 71.5, 126.5, 126.6, 127.0, 127.2, 128.5, 129.0, 129.4, 130.0, 134.1, 146.7, 164.6, 167.2. Anal. Calcd for $C_{33}H_{26}Cl_2N_2O_8$: C, 61.03; H, 4.04; N, 4.31. Found: C, 60.91; H, 3.80; N, 4.29.

(+)-*S*,*S*-2,8-Dichloro-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine•(+)-*O*,*O*′-dibenzoyl-D-tartaric acid dyad, [(+)-Cl$_2$TB•(+)-D-DBTA]. (±)-Cl$_2$TB (4.37 g; 15.0 mmol) and (+)-*O*,*O*′-dibenzoyl-D-tartaric acid (5.45 g; 15.2 mmol) heated to 55−60 °C for 120 h yielded 8.90 g (91%) of the complex as a white solid: mp 173−174 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) d 4.12 (d, J = 17.2 Hz, 2H), 4.21 (s, 2H), 4.59 (d, J = 16.8 Hz, 2H), 5.92 (s, 2H), 7.04 (d, J = 2.4 Hz, 2H), 7.13 (d, J = 8.8 Hz, 2H), 7.18 (dd, J = 8.4, 2.4 Hz, 2H), 7.58−7.63 (m, 4H), 7.71−7.76 (m, 2H), 8.03−8.06 (m, 4H), 13.95 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 57.8, 65.8, 71.5, 126.5, 126.5, 127.0, 127.2, 128.5, 129.0, 129.4, 130.0, 134.1, 146.6, 164.6, 167.2. Anal. Calcd for $C_{33}H_{26}Cl_2N_2O_8$: C, 61.03; H, 4.04; N, 4.31. Found: C, 61.06; H, 3.82; N, 4.28.

(−)-*R*,*R*-2-Iodo-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine•(−)-*O*,*O*′-dibenzoyl-L-tartaric acid dyad, [(−)-HITB•(−)-L-DBTA]. (±)-HITB (3.48 g; 10.0 mmol) and (−)-*O*,*O*′-dibenzoyl-L-tartaric acid monohydrate (3.84 g; 10.2 mmol) heated to 55−60 °C for 120 h yielded 6.36 g (90%) of the complex as a white solid: mp 172−173 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ4.09 (d, J = 17.2 Hz, 1H), 4.14 (d, J = 17.2, 1H), 4.16−4.23 (m, 2H), 4.59 (d, J = 16.8 Hz, 1H), 4.62 (d, J = 16.8 Hz, 1H), 5.90 (s, 2H), 6.94−6.96 (m, 2H), 7.07−7.10 (m, 2H), 7.12−7.18 (m, 2H), 7.29 (dd, J = 8.8, 2.4 Hz, 1H), 7.59−7.64 (m, 4H), 7.72−7.77 (m, 2H), 8.02−8.05 (m 4H), 13.95 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 57.5, 58.1, 65.8, 71.4, 87.2, 123.5, 124.7, 126.9, 127.0, 127.1, 127.8, 128.4, 129.0, 129.4, 131.1, 134.1, 135.3, 135.5, 147.8, 148.0. Anal. Calcd for $C_{33}H_{27}IN_2O_8$: C, 56.10; H, 3.85; N, 3.97. Found: C, 56.05; H, 3.36; N, 3.97.

(+)-*S*,*S*-2-Iodo-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine•(+)-*O*,*O*′-dibenzoyl-D-tartaric acid dyad, [(+)-HITB•(+)-D-DBTA]. (±)-HITB (3.48 g; 10.0 mmol) and (+)-*O*,*O*′-dibenzoyl-D-tartaric acid (3.65 g; 10.2 mmol) heated to 55−60 °C for 120 h yielded 6.21 g (88%) of the complex as a white solid: mp 172−173 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ4.09 (d, J = 16.4 Hz, 1H), 4.12 (d, J = 16.4, 1H), 4.14−4.23 (m, 2H), 4.57 (d, J = 16.8 Hz, 1H), 4.61 (d, J = 16.8 Hz, 1H), 5.90 (s, 2H), 6.92−6.96 (m, 2H), 7.07−7.10 (m, 2H), 7.12−7.18 (m, 2H), 7.29 (dd, J = 8.8, 2.4 Hz, 1H), 7.59−7.63 (m, 4H), 7.72−7.77 (m, 2H), 8.02−8.05 (m, 4H), 13.95 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 57.5, 58.1, 65.8, 71.4, 87.2, 123.5, 124.7, 126.9, 127.0, 127.1, 127.8, 128.5, 129.0, 129.4, 131.1, 134.1, 135.3, 135.5, 147.8, 148.0. Anal. Calcd for $C_{33}H_{27}IN_2O_8$: C, 56.10; H, 3.85; N, 3.97. Found: C, 55.99; H, 3.43; N, 3.95.

(−)-*R*,*R*-2-Bromo-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine•(−)-*O*,*O*′-dibenzoyl-L-tartaric acid dyad, [(−)-HBrTB•(−)-L-DBTA]. (±)-HBrTB (3.01 g; 10.0 mmol) and (−)-*O*,*O*′-dibenzoyl-L-tartaric acid monohydrate (3.84 g; 10.2 mmol) heated to 55−60 °C for 120 h yielded 4.53 g (69%) of the complex as a white solid: mp 163−164 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ4.09 (d, J = 17.2 Hz, 1H), 4.14 (d, J = 17.2 Hz, 1H), 4.16−4.25 (m, 2H), 4.59 (d, J = 16.8 Hz, 1H), 4.62 (d, J = 16.8 Hz, 1H), 5.90 (s, 2H), 6.94−6.96 (m, 2H), 7.07−7.10 (m, 2H), 7.12−7.18 (m, 2H), 7.29 (dd, J = 8.8, 2.4 Hz), 7.59−7.63 (m, 4H), 7.72−7.77 (m, 2H), 8.02−8.05 (m, 4H), 13.95 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 57.8, 58.1, 65.9, 71.5, 115.1, 123.5, 124.8, 126.9, 127.1, 127.8, 128.5, 129.0, 129.4, 129.7, 130.8, 134.1, 147.5, 147.7, 164.7, 167.2. Anal. Calcd for $C_{33}H_{27}BrN_2O_8$: C, 60.10; H, 4.13; N, 4.25. Found: C, 60.05; H, 3.97; N, 4.21.

(+)-*S*,*S*-2-Bromo-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine•(+)-*O*,*O*′-dibenzoyl-D-tartaric acid dyad, [(+)-HBrTB•(+)-D-DBTA]. (±)-HBrTB (3.01 g; 10.0 mmol) and (+)-*O*,*O*′-dibenzoyl-D-tartaric acid (3.65 g; 10.2 mmol) heated to 55−60 °C for 120 h yielded 5.20 g (79%) of the complex as a white solid: mp 163−164 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ4.09 (d, J = 17.2 Hz, 1H), 4.14 (d, J = 17.6 Hz, 1H), 4.17−4.25 (m, 2H), 4.60 (d, J = 17.2 Hz, 1H), 4.62 (d, J = 16.8 Hz, 1H), 5.91 (s, 2H), 6.94−6.96 (m, 2H), 7.07−7.10 (m, 2H), 7.12−7.18 (m, 2H), 7.29 (dd, J = 8.4, 2.4 Hz), 7.58−7.63 (m, 4H), 7.71−7.76 (m, 2H), 8.03 (d, J = 1.2 Hz, 4H), 13.95 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 57.8, 58.1, 65.9, 71.4, 115.1, 123.5, 124.8, 126.9, 127.1, 127.8, 128.5, 129.0, 129.4, 129.7, 130.8, 134.1, 147.5, 147.7, 164.6, 167.1. Anal. Calcd for $C_{33}H_{27}BrN_2O_8$: C, 60.10; H, 4.13; N, 4.25. Found: C, 60.15; H, 3.85; N, 4.18.

Representative Procedure for the Recovery of Resolved TB from TB•DBTA Complex. (−)-*R*,*R*-2,8-Dibromo-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine, [(−)-*R*,*R*-3; (−)-*R*,*R*-Br$_2$TB]. (−)-Br$_2$TB•(−)-L-DBTA (5.00 g; 6.77 mmol) was suspended in 50 mL of CH_2Cl_2 and extracted with 50 mL of 5% aqueous Na_2CO_3. The organic layer was separated, and the aqueous layer extracted with 2 × 10 mL of CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and passed through a 2 × 8 cm column of activity III neutral alumina. Evaporation of the eluate gave a white solid, which was dried under a vacuum at rt for 24 h (2.49 g; 97%): mp 173−174 °C; ^{1}H NMR (400 MHz, $CDCl_3$) d 4.80 (d, J = 16.8 Hz, 2H), 4.23 (s, 2H), 4.62 (d, J = 16.8 Hz, 2H), 6.90, (d, J = 8.4 Hz, 2H), 7.03 (d, J = 2.4 Hz, 2H), 7.26 (dd, J = 8.4, 2.4, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ58.3, 66.4, 116.8, 126.7, 129.68, 129.72, 130.6, 146.8; $[\alpha]_D^{25}$ = −383 (*c*, 0.117, $CHCl_3$). The er was measured by HPLC Chiralpak 1A column, flow 0.8 mL/min, 100% ethanol, 254 nm, t_R = 8.5 min (minor = 0.2%), t_R = 11.0 min (major = 99.8%) for an er >99.5:0.5.

All resolved TB derivatives were recovered from their DBTA complexes in the same way in yields >95%.

(+)-*S*,*S*-2,8-Dibromo-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine, [(+)-*S*,*S*-3; (+)-*S*,*S*-Br$_2$TB]. From 5.00 g (6.77 mmol) of (+)-Br$_2$TB•(+)-D-DBTA, 2.52 g (98%) (+)-*S*,*S*-Br$_2$TB as a white solid: mp 172−173 °C (dec); ^{1}H NMR (400 MHz, $CDCl_3$) d 4.80 (d, J = 16.8 Hz, 2H), 4.24 (s, 2H), 4.63 (d, J = 16.8 Hz, 2H), 6.90, (d, J = 8.4 Hz, 2H), 7.04 (d, J = 2.4 Hz, 2H), 7.26 (dd, J = 8.4, 2.4, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ58.3, 66.4, 116.8, 126.7, 129.68, 129.72, 130.6, 146.8; $[\alpha]_D^{25}$ = +379 (*c*, 0.114, $CHCl_3$); HPLC t_R = 8.5 min (major = 99.9%), t_R = 11.2 min (minor = 0.1%) for an er >99.5:0.5.

(−)-*R*,*R*-2,8-Dimethyl-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine, [(−)-*R*,*R*-1; (−)-*R*,*R*-Me$_2$TB]. From 5.00 g (8.22 mmol) of (−)-Me$_2$TB•(−)-L-DBTA, 1.98 g (96%) (−)-*R*,*R*-Me$_2$TB as a white solid: mp 128−129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.20 (s, 6H), 4.10 (d, J = 16.8 Hz, 2H), 4.29, s, 2H), 4.63 (d, J = 16.8 Hz, 2H), 6.69, s, 2H), 6.96 (dd, J = 8.0 Hz, 2H), 7.03 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 58.7, 67.1, 124.8, 127.3, 127.6, 128.2, 133.4, 145.5; $[\alpha]_D^{25}$ = −276 (*c*, 0.112, $CHCl_3$); HPLC t_R = 6.2 min (minor = 0.9%), t_R = 9.1 min (major = 99.1%) for an er = 99.1:0.9.

(+)-*S*,*S*-2,8-Dimethyl-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine, [(+)-*S*,*S*-1; (+)-*S*,*S*-Me$_2$TB]. From 5.00 g (8.22 mmol) of (+)-Me$_2$TB•(+)-D-DBTA, 2.02 g (98%) (+)-*S*,*S*-Me$_2$TB as a white solid: mp 129−130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.20 (s, 6H), 4.10 (d, J = 16.8 Hz, 2H), 4.29, s, 2H), 4.63 (d, J = 16.8 Hz, 2H), 6.69, s, 2H), 6.96 (dd, J = 8.0 Hz, 2H), 7.03 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 58.7, 67.1, 124.8, 127.3, 127.6, 128.2, 133.4, 145.5; $[\alpha]_D^{25}$ = +282 (*c*, 0.112, $CHCl_3$); HPLC t_R = 6.3 min

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(major = 100%), t_R = 9.0 min (minor = 0%; none detected) for an er >99.5:0.5.

(−)-*R*,*R*-2,8-Dimethoxy-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine, [(−)-*R*,*R*-2; (−)-*R*,*R*-MeO$_2$TB]. From 5.00 g (7.80 mmol) of (−)-MeO$_2$TB•(−)-L-DBTA, 2.14 g (97%) (−)-*R*,*R*-MeO$_2$TB as a white solid: mp 141−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.70 (s, 6H), 4.08 (d, J = 16.8 Hz, 2H), 4.29 (s, 2H), 4.64 (d, J = 16.8 Hz, 2H), 6.42 (d, J = 2.8 Hz, 2H), 6.73 (dd, J = 8.8, 2.8, 2H), 7.06 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 58.9, 67.3, 110.9, 114.0, 126.0, 128.6, 140.9, 156.1; $[\alpha]_D^{25}$ = −240 (*c*, 0.110, $CHCl_3$); HPLC t_R = 9.8 min (major = 99.8%) for an er >99.5:0.5.

(+)-*S*,*S*-2,8-Dimethoxy-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine, [(+)-*S*,*S*-2; (+)-*S*,*S*-MeO$_2$TB]. From 5.00 g (7.80 mmol) of (+)-MeO$_2$TB•(+)-D-DBTA, 2.16 g (98%) (+)-*S*,*S*-MeO$_2$TB as a white solid: mp 140−141 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.69 (s, 6H), 4.07 (d, J = 16.8 Hz, 2H), 4.29 (s, 2H), 4.64 (d, J = 16.8 Hz, 2H), 6.42 (d, J = 2.8 Hz, 2H), 6.73 (dd, J = 8.8, 2.8, 2H), 7.05 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 58.9, 67.3, 110.9, 114.0, 126.0, 128.6, 140.9, 156.1; $[\alpha]_D^{25}$ = +236 (*c*, 0.110, $CHCl_3$); HPLC t_R = 7.9 min (major = 99.1%), t_R = 9.7 min (minor = 0.9%) for an er = 99.1:0.9.

(−)-*R*,*R*-2,8-Diiodo-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine, (−)-*R*,*R*-4; (−)-*R*,*R*-I$_2$TB]. From 6.00 g (7.21 mmol) of (−)-I$_2$TB•(−)-L-DBTA, 3.36 g (98%) (−)-*R*,*R*-I$_2$TB as a white solid: mp 203−204 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.08 (d, J = 16.8 Hz, 2H), 4.23 (s, 2H), 4.61 (d, J = 16.8 Hz, 2H), 6.86 (d, J = 8.4 Hz, 2H), 7.22−7.24 (m, 2H), 7.45 (dd, J = 8.4, 2.0, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 58.1, 66.5, 87.6, 127.0, 130.2, 135.7, 136.5, 147.6; $[\alpha]_D^{25}$ = −441 (*c*, 0.114, $CHCl_3$); HPLC t_R = 9.9 min (minor = 0.1%), t_R = 11.3 min (major = 99.9%) for an er >99.5:0.5.

(+)-*S*,*S*-2,8-Diiodo-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine, [(+)-*S*,*S*-4; (+)-*S*,*S*-I$_2$TB]. From 6.00 g (7.21 mmol) of (+)-I$_2$TB•(+)-D-DBTA, 3.35 g (98%) (+)-*S*,*S*-I$_2$TB as a white solid: mp 204−205 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.07 (d, J = 16.8 Hz, 2H), 4.23 (s, 2H), 4.61 (d, J = 16.8 Hz, 2H), 6.86 (d, J = 8.4 Hz, 2H), 7.22−7.24 (m, 2H), 7.45 (dd, J = 8.4, 2.0, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 58.1, 66.5, 87.6, 127.0, 130.2, 135.7, 136.5, 147.6; $[\alpha]_D^{25}$ = +443 (*c*, 0.116, $CHCl_3$); HPLC t_R = 9.7 min (major = 99.9%), t_R = 11.2 min (minor = 0.1%) for an er >99.5:0.5.

(−)-*R*,*R*-2,8-Dichloro-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine, [(−)-*R*,*R*-5; (−)-*R*,*R*-Cl$_2$TB]. From 5.00 g (7.70 mmol) of (−)-Cl$_2$TB•(−)-L-DBTA, 2.18 g (97%) (−)-*R*,*R*-Cl$_2$TB as a white solid: mp 117−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.07 (d, J = 16.8 Hz, 2H), 4.23 (s, 2H), 4.62 (d, J = 16.8 Hz, 2H), 6.88 (J = 2.4 Hz, 2H), 7.04 (d, J = 8.8 Hz, 2H), 7.12 (dd, J = 8.8, 2.4, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 58.5, 66.7, 126.4, 126.8, 127.7, 129.1, 129.2, 146.3; $[\alpha]_D^{25}$ = −396 (*c*, 0.110, $CHCl_3$); HPLC t_R = 7.6 min (minor = 0.1%), t_R = 10.0 min (major = 99.9%) for an er >99.5:0.5.

(+)-*S*,*S*-2,8-Dichloro-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine, [(+)-*S*,*S*-5; (+)-*S*,*S*-Cl$_2$TB]. From 5.00 g (7.70 mmol) of (+)-Cl$_2$TB•(+)-D-DBTA, 2.17 g (97%) (+)-*S*,*S*-Cl$_2$TB as a white solid: mp 117−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.08 (d, J = 16.8 Hz, 2H), 4.23 (s, 2H), 4.62 (d, J = 16.8 Hz, 2H), 6.88 (J = 2.4 Hz, 2H), 7.04 (d, J = 8.8 Hz, 2H), 7.12 (dd, J = 8.8, 2.4, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 58.5, 66.7, 126.4, 126.8, 127.7, 129.1, 129.2, 146.3; $[\alpha]_D^{25}$ = +393 (*c*, 0.114, $CHCl_3$); HPLC t_R = 7.5 min (major = 99.9%), t_R = 10.1 min (minor = 0.1%) for an er >99.5:0.5.

(−)-*R*,*R*-2-Iodo-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]-diazocine, [(−)-*R*,*R*-6; (−)-*R*,*R*-HITB]. From 3.00 g (4.25 mmol) of (−)-HITB•(−)-L-DBTA, 1.45 g (98%) (−)-*R*,*R*-HITB as a white solid: mp 130−131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.11 (d, J = 16.8 Hz, 2H), 4.19−4.30 (m, 2H), 4.59 (d, J = 16.8 Hz, 1H), 4.65 (d, J = 16.8 Hz, 1H), 6.85−6.89 (m, 2H), 6.97 (td, J = 7.6, 1.6, 1H), 7.10 (dd, J = 8.0, 1.2 Hz, 1H), 7.13−7.19 (m, 2H), 7.41 (dd, J = 8.4, 2.0, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 58.2, 58.7, 66.7, 87.5, 124.2, 125.1, 127.0, 127.1, 127.56, 127.60, 130.6, 135.7, 136.3, 147.7, 148.0; $[\alpha]_D^{25}$ = −323 (*c*, 0.110, $CHCl_3$); HPLC t_R = 7.7 min (minor = 0.0%; none detected), t_R = 9.2 min (major = 100%) for an er >99.5:0.5.

(+)-*S*,*S*-2-Iodo-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]-diazocine, [(+)-*S*,*S*-6; (+)-*S*,*S*-HITB]. From 3.00 g (4.25 mmol) of (+)-HITB•(+)-D-DBTA, 1.45 g (98%) (+)-*S*,*S*-HITB as a white solid: mp 130−131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.11 (d, J = 16.8 Hz, 2H), 4.19−4.30 (m, 2H), 4.59 (d, J = 16.8 Hz, 1H), 4.66 (d, J = 16.8 Hz, 1H), 6.85−6.89 (m, 2H), 6.97 (td, J = 7.6, 1.2, 1H), 7.10 (dd, J = 8.0, 1.2 Hz, 1H), 7.13−7.20 (m, 2H), 7.41 (dd, J = 8.4, 2.0, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 58.2, 58.7, 66.7, 87.5, 124.2, 125.1, 127.0, 127.1, 127.56, 127.60, 130.6, 135.7, 136.3, 147.7, 148.0; $[\alpha]_D^{25}$ = +326 (*c*, 0.114, $CHCl_3$); HPLC t_R = 7.6 min (major = 100%), t_R = 9.3 min (minor = 0.0%; none detected) for an er >99.5:0.5.

(−)-*R*,*R*-2-Bromo-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine, [(−)-*R*,*R*-7; (−)-*R*,*R*-HBrTB]. From 3.00 g (4.55 mmol) of (−)-HBrTB•(−)-L-DBTA, 1.34 g (98%) (−)-*R*,*R*-HBrTB as a white solid: mp 162−163 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.11 (d, J = 16.8 Hz, 1H), 4.13 (d, J = 16.8 Hz, 1H), 4.22−4.32 (m, 2H), 4.63 (d, J = 17.6 Hz, 1H), 4.67 (d, J = 17.2 Hz, 1H), 6.89 (dd, J = 7.6, 0.4 Hz, 1H), 6.95−7.02 (m, 3H), 7.09−7.19 (m, 2H), 7.22−7.26 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 58.4, 58.7, 66.7, 116.5, 124.2, 125.1, 126.8, 127.0, 127.6, 129.7, 130.1, 130.4, 147.2, 147.7; $[\alpha]_D^{25}$ = −302 (*c*, 0.110, $CHCl_3$); HPLC t_R = 7.3 min (minor = 0.0%; none detected), t_R = 9.0 min (major = 100%) for an er >99.5:0.5.

(+)-*S*,*S*-2-Bromo-6,12-dihydro-5,11-methanodibenzo[*b*,*f*][1,5]diazocine,[(+)-*S*,*S*-7; (+)-*S*,*S*-HBrTB]. From 3.00 g (4.55 mmol) of (+)-HBrTB•(+)-D-DBTA, 1.32 g (96%) (+)-*S*,*S*-HBrTB as a white solid: mp 162−163 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.12 (d, J = 16.8 Hz, 1H), 4.14 (d, J = 16.8 Hz, 1H), 4.22−4.33 (m, 2H), 4.64 (d, J = 17.2 Hz, 1H), 4.68 (d, J = 16.8 Hz, 1H), 6.89 (dd, J = 7.6, 0.4 Hz, 1H), 6.96−7.03 (m, 3H), 7.09−7.19 (m, 2H), 7.23−7.26 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 58.4, 58.7, 66.7, 116.5, 124.2, 125.1, 126.8, 127.0, 127.5, 129.7, 130.1, 130.4, 147.2, 147.7; $[\alpha]_D^{25}$ = +302 (*c*, 0.109, $CHCl_3$); HPLC t_R = 7.2 min (major = 100%), t_R = 9.0 min (minor = 0.0%; none detected) for an er >99.5:0.5.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

NMR spectra of dyads and isolated TB, and chiral HPLC traces of racemic and resolved TB derivatives. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: djameson@gettysburg.edu.

Present Address

†The Dow Chemical Company, 727 Norristown Road, Spring House, Pennsylvania 19477, United States.

Notes

The authors declare no competing financial interest.

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