Synthesis of Functionalized Chiral Carbocyclic Cleft Molecules Complementary to Tröger's Base Derivatives

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The synthesis of optically pure functionalized cleft molecules derived from dibenzobicyclo[*b*,*f*][3.3.1]-nona-5a,6a-diene-6,12-dione is reported. These clefts are reminiscent of Tröger's base but contain clefts with different dimensions and additional carbonyl (or alcohol) groups that may be utilized in molecular recognition studies. The 2,8-dimethyl and 2,8-dibromo derivatives were synthesized via an intramolecular Friedel−Crafts acylation and were resolved by chiral HPLC. The 2,8-dinitro derivative was prepared by regiospecific nitration of dibenzobicyclo[*b*,*f*][3.3.1]nona-5a,6a-diene-6,12-dione. The dibromo and dinitro derivatives allow direct access to a range of functionalized molecular clefts. Palladium-catalyzed coupling of the dibromo derivative afforded the disubstituted phenyl, anisole, and acetylene derivatives, while reduction of the dinitro derivative and acetylation provided amino-dione and amide-hydroxyl derivatives. X-ray crystal structures of the dimethyl **12**, dibromo **13**, di(*p*-methoxyphenyl) **16**, dinitro **18**, and dimethyl dinitro **22** derivatives show cleft angles between the planes between the aromatic rings of 84−104°. The synthetic route, structural features, and potential for molecular recognition studies of this class of clefts are compared with those of the more widely studied Tröger's base cleft molecules.

Introduction

Molecules featuring convergent functional groups in cleftlike shapes have emerged as useful receptors for small molecules.[1,2] The combination of a well-defined semirigid cavity to which tunable functional groups can be appended in predictable geometries has allowed the design of a number of host systems for molecular recognition studies and for the controlled assembly of complex molecular architectures. These concepts have been well illustrated in, for example, clefts derived from Kemp's acid for the recognition of nucleic bases,[3] the design of molecular tweezers,[4,5] and a number of acyclic hosts.[2,6]

The rigid cleftlike shape of Tröger's base **1** combined with the chirality conferred by the diazocine bridge, has resulted in incorporation of this framework into a number of macrocyclic host systems, and as a scaffold to which convergent functional groups can be appended to generate nonmacrocyclic synthetic receptors.[7−18] The resultant receptors have been used to allow recognition and binding of guest molecules including biotin, adenine and aminopyrimidines[19,20] via convergent directional hydrogen-bonding interactions and to develop water-soluble macrocyclic hosts.[9,11] In most host−guest studies involving Tröger's base, the chirality of the cleft has not been exploited for the discrimination between chiral substrates but has been used to position functional groups in a predictable geometry, and hence, most studies have used racemic cleft molecules.[8−10,17] However, optically pure porphyrin-based receptors incorporating Trögers base have been shown to selectively bind chiral amines and amino acids,[21] and enantioselective recognition of DNA by acridine-substitiuted Tröger's base systems has been demonstrated.[22]

A chiral cavity, similar to that found in Tröger's base **1**, is also present in a number of related systems including dibenzobicyclo[*b*,*f*][3.3.1]nona-5a,6a-diene-6,12-dione **2**, dibenzobicyclo[*b*,*f*][3.3.1]nona-5a,6a-diene **3**,[23] Kagan's ether **4**[24,25] and the tricyclic dibenzo[*b*,*f*][1,5]-diazocine ring system **5**.[26] These skeletons differ from Trögers base in the atoms involved in formation of the

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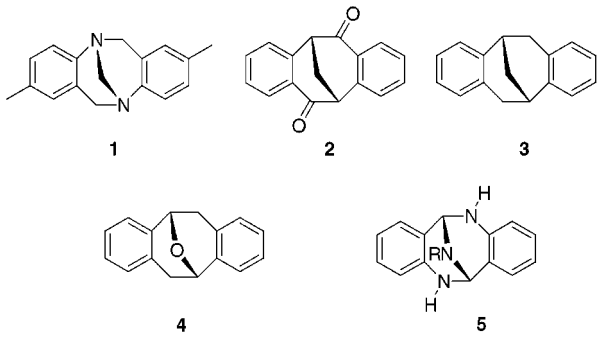
bridgehead structure, which confer different bite angles on the clefts. However, in contrast to Trögers base, they have been not been widely incorporated into the design of supramolecular systems. Dione **2** has been used to generate a chiral crown ether based receptor,[27−29] while **4** has been elaborated to give a number of rigid cleft systems and molecular tweezers.[30−33] More recently, functionalization of Kagan's ether[34] has afforded entry into metallomacrocycles.[35]



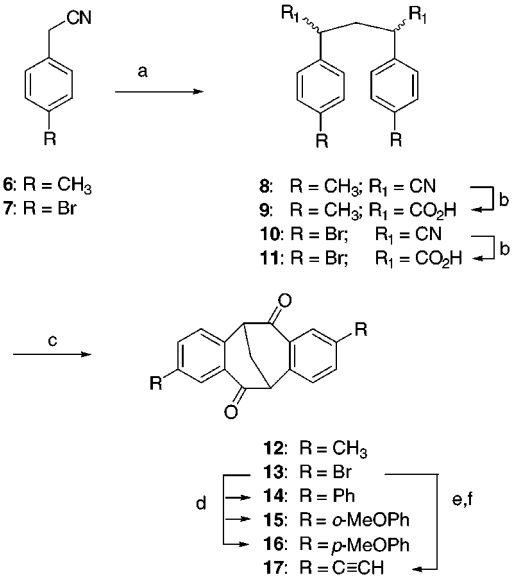
In this paper, we describe the synthesis, resolution and X-ray crystallographic analysis of a range of derivatives of the chiral dione **2**. Preliminary data on two of these analogues has been communicated previously.[36] In contrast to the synthesis of Tröger's base systems, which are restricted to electron-donating groups on the primary aromatic amine which is condensed with formaldehyde,[11,37,38] both electron-withdrawing and electron-donating groups can be directly incorporated into the structure of **2**. These derivatives, which may be readily resolved and elaborated to incorporate a range of different functionality, provide access to a range of new chiral molecular clefts that contain complementary, yet unique features, compared with Tröger's base-containing clefts.

Results and Discussion

Synthesis. The synthesis of the parent cleft **2** has been reported by Tatemitsu et al. (Scheme 1, R = H).[39] The key step in the synthesis is a double acid mediated Friedel−Crafts acylation that generates the bicyclo ring system. The only derivatives of **2** that have been reported have involved reduction of the carbonyl groups to the diol or a Wittig reaction to the bisalkene.[27] Both strongly basic conditions and acidic conditions are required in steps (b) and (c) (Scheme 1) which limits the type of substitution tolerated on the ring, and directive effects will influence the ring closure in step (c).

Our initial studies focused on establishing the functional groups that could be tolerated in the ring closure steps, to provide derivatives that could be easily be used as precursors in the synthesis of more complex chiral clefts, and also to assess whether different substituents influence the dimensions of the cleft. In particular, incorporation of a halogen was desirable as these derivatives provide an excellent handle for further modification through metal-catalyzed cross-coupling reactions.[40,41] Furthermore, symmetrically substituted halogen derivatives of Tröger's base cannot be prepared, although the preparation of unsymmetrical derivatives containing a single halogen is possible.[38]

Scheme 1



[a] (a) CH_2I_2, NaOH, 145°C; (b) EtOH, KOH, H_2O, 80°C; (c) H_2SO_4, 80°C; (d) $RB(OH)_2$, $PdCl_2(PPh_3)_2$, Na_2CO_3, DME:H_2O (5:1), 80°C; (e) TMS-acetylene, $PdCl_2(PPh_3)_2$, CuI, TEA ; (f) KOH, MeOH

Racemic dimethyl and dibromo derivatives, **12** and **13**, respectively, were prepared in three steps from benzylcyanides **6** and **7** respectively, via the same route described by Tatemitsu et al (Scheme 1).[39] The intermediate mixture of dinitrile stereoisomers, **8** and **10**, respectively, were not separated and characterized but converted directly to the corresponding mixtures of diacids **9** and **11**, respectively. Treatment of these diacids afforded racemic dimethyl dione **12** and dibromo dione **13** respectively. While chromatography was required to purify the dimethyl derivative **12**, the dibromo dione **13** crystallized directly from the final acid catalyzed cyclization step, and no chromatography was required to isolate gram amounts of pure material.

To illustrate the potential of the dibromo dione **13** as a building block for the construction of new supramolecular hosts, a number of aryl derivatives were prepared. Thus, palladium-mediated coupling of racemic **13** under Suzuki conditions[40,42] with phenyl, *o*- or *p*-methoxyphenylboronic acid generated the corresponding bis-aryl diones **14**, **15**, and **16**, respectively, in >90% yield. Similarly, treatment of dibromo dione **13** with trimethylsilylacetylene in the presence of $PdCl_2(PPh_3)_2$, copper iodide,

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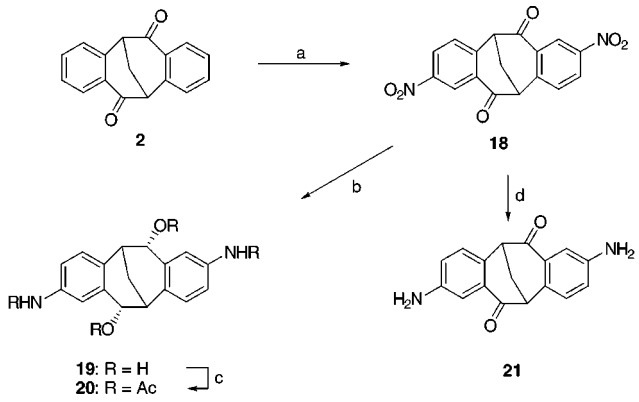
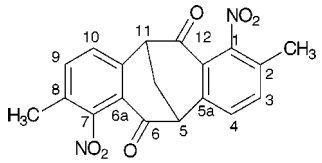
Scheme 2



[a] (a) KNO_3, H_2SO_4, 0°C-25°C; (b) H_2, Pd-C(5%), MeOH; (c) AcCl, pyridine, 25°C; (d) Fe, AcOH, EtOH.

and triethylamine, followed by deprotection, afforded the bisacetylene derivative **17**.

Preparation of the dinitro dione **18** was also highly desirable as a key building block that allows introduction of hydrogen bond donor and acceptor groups into the resultant clefts via amide and amino functional groups. However, the route shown in Scheme 1 (R = NO_2) was not followed as the strongly deactivating nitro groups would not allow the final ring closure step to occur. Instead, direct nitration of the parent dione **2** was carried out which resulted in regioselective nitration at the 2- and 8-positions to yield **18** in 75% yield. The 2,8-disubstitution pattern was established by NOE experiments from the benzylic protons to the ortho-coupled aromatic doublet and was independently confirmed by X-ray crystallography (see below). Similar nitration of the dimethyl dione **12** afforded exclusively the dimethyl dinitro dione **22** in 61% yield.



22

The dinitro dione **18** exhibited limited solubility in most organic solvents except DMF and hence was converted to the more soluble diacetamide derivative for characterization. Catalytic hydrogenation of **18** in the presence of palladium on charcoal catalyst resulted in reduction of both the nitro groups and the stereoselective reduction of the dione to the very polar amino diol **19** which was characterized as the acetamide derivative **20** (Scheme 2). The ^{1}H NMR spectrum of **20** showed a doublet (J = 5.2 Hz) at δ 6.09 ppm confirming the stereochemistry at the new chiral centers in which the acetate groups in **20** (and hydroxyls in **19**) are psuedo-axial and oriented toward to interior of the cleft; similar stereoselective reduction of the dione **2** has been reported previously.[39] Selective reduction of nitro groups at the 2- and 8-positions of dione **18** to give the bisaminodione **21** was achieved using iron-acetic acid.

Resolution of Diones. Resolution of the parent dione **2** has been previously carried out[39] via reduction to the racemic diol and subsequent conversion and resolution of the resultant menthoxyacetates. While similar preparation of crystalline diastereomeric derivatives of the diones **12** and **13** could be carried out, we chose to investigate chiral HPLC to generate optically pure material directly. Racemic diones **12** and **13** were resolved successfully by HPLC on a chiral column. The absolute configuration of each of the enantiomers was determined by circular dichroism (CD) spectroscopy on comparison with the previously assigned CD data for the parent compound **1**.[39] The CD spectra of each of the enantiomers (−)-**12** and (+)-**12** (Figure 1) show features similar to those of the dibromo dione enantiomers (−)-**13** and (+)-**13**.[36] While the dinitroderivative was not resolved, it can be readily obtained in optically pure form by using either (−)-**2** or (+)-**2**; these diones may be readily prepared by dehydrative cyclization of optically pure isomers of 1,3-diphenylglutaric.[27]

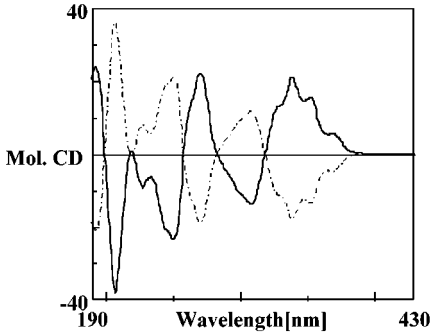


Figure 1. Circular dichroism spectra (CH_3CN), corrected to enantiomeric purity, of (−)-**12** (solid line) and (+)-**12** (0.8 mM).

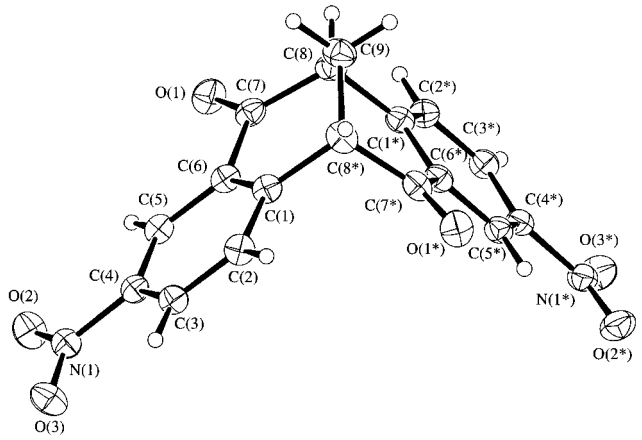
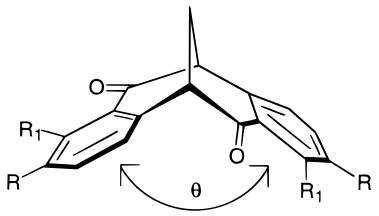


Figure 2. ORTEP plot of dinitro dione **18**.

X-ray Crystallography. Crystals suitable for diffraction of the dimethyl **12**, dibromo **13**, diphenyl **14**, di(*p*-anisole) **16**, dinitro **18**, and dimethyl dinitro **22** derivatives were obtained, and X-ray structures of these five derivatives were determined. Figure 2, which shows the ORTEP view of the dinitro dione **18**, illustrates the rigid cleft shape of the molecule and the position of the two carbonyl groups that are orientated toward the interior of the cleft.

Table 1 shows the variation in the interplanar angle between the two aromatic rings, or cleft angle, as the R substituents on the aryl rings are varied. For comparison, the analogous interplanar angles in related cleft molecules including Tröger's base **1** and Kagan's ether **4** are also included. In the case of Tröger's base **1**, X-ray crystallography has shown that there is a moderate degree of flexibility in the dimensions of the cleft that may be fine-tuned or exploited in the design of biomimetic

Table 1. Interplanar Angle θ between Planes Defined by Benzene Rings in Cleft Molecules



(*S*, *S*)-enantiomer

derivatives of **2**	R	R_1	θ,[a] deg
12	CH_3	H	104.3, 101.7 [b]
13	Br	H	91.4
14	Ph	H	100.4
16	*p*-MeOPh	H	99.7
18	NO_2	H	83.9
22	CH_3	NO_2	102.7
related clefts	type of bridge		
1	diazocine		92.9, 97.4[11] [b]
4	ether		93[43]
5	substituted amine		77.9,76.6[26] [b]

[a] All data were obtained on crystalline racemates. [b] Two types of molecules in unit cell.

systems through substitution of the aryl rings, and clefts with interplanar angles between 88 and 104° were observed.[11] Some variation in the bite angle of clefts incorporating Kagan's ether has also been noted.[30,32] In the case of the chiral diones derived from **2**, the R substituents were also observed to influence the dimensions of the cavity, which vary from 84° with the electron-withdrawing nitro groups, to 104° with the electron-donating methyl groups. In the case of dione **22**, which contains both methyl and nitro substituents, the cleft angle is very close to that of the dimethyl dione **12**, suggesting that the electronic effect of the 2,8-dimethyl substituents, rather than the 1,7-dinitro groups, is more significant in influencing the cleft angle. These variable cleft angles need to be taken into account, and potentially may also be utilized, in the design of new hosts incorporating molecular clefts based on dione **2**.

Conclusions

The dibromo **13** and dinitro **18** diones are new chiral building blocks that may be used in the design of functionalized molecular clefts and related supramolecular structures. Compared with the synthesis of the analogous Tröger's base derivatives, the synthesis of the dione clefts has several advantages. First, synthesis of Trögers base **1** is restricted to electron-donating groups para to the precursor amine used to form the diazocine bridge, and the direct synthesis of the corresponding dinitro and dibromo derivatives is not possible. Hence, formation of the diazocine bridge is often the last step in the synthetic scheme. Second, an important feature of the diones that is not present in any of the related cleft molecules **1** or **3**−**5** is the presence of the two carbonyl groups within the chiral cavity. Stereoselective reduction of these groups to hydroxyls[36,39] provides a mechanism whereby the recognition features of the cleft may be further tailored to target recognition of chiral substrates. Very recently, a bistriflate derivative of Kagan's ether **4** has been synthesized[34] and metal-catalyzed coupling to a bispyridyl derivative communicated.[35] This Kagan's ether bistriflate derivative shows similar potential to the dibromo dione **13** as both compounds allow a wide-range of functionality to be introduced into the clefts. Elaboration of diones **13** and **18** into new chiral clefts is currently under investigation in these laboratories.

Experimental Section

General Experimental Procedures. Melting points are uncorrected. ^{1}H NMR spectra were recorded at 200 or 400 MHz and are referenced to residual solvent protons. Circular dichroism (CD) measurements were recorded using a 0.1 cm cell and the following parameters; range 300−600 nm, accumulation 10 scans, temperature 20 °C, step 0.5 nm, speed 50 nm min^{-1}, response 2 s, and bandwidth 1.0 nm.

2,8-Dimethyldibenzobicyclo[*b,f*][3.3.1]nona-5a,6a-diene-6,12-dione 12. *p*-Methylphenylacetonitrile **6** (8.0 g, 0.061 mol) and powdered sodium hydroxide (2.4 g, 0.061 mol) were dissolved in diiodomethane (8.3 g, 0.031 mol), and the resultant mixture was heated at 165 °C for 45 min. The reaction mixture was cooled, and water and dichloromethane were added in portions. The two-phase system was shaken vigorously, the organic phase was separated, washed with brine, dried over anhydrous sodium sulfate, and the solvent was removed to give a mixture of crude (±)- and *meso*-phenylpentanedinitrile **8** (8.1 g), which was hydrolyzed by heating at 80 °C for 18 h in a mixture of ethanol and potassium hydroxide solution (40%). Ethanol was removed under vacuum and the residue was diluted with water and washed with dichloromethane. The aqueous phase was acidified to pH < 1 by the addition of hydrochloric acid (3 M) and extracted with ethyl acetate. The combined organic extracts were dried over anhydrous sodium sulfate, and the solvent removed to give a mixture of crude (±)- and *meso*-phenylpentanedioic acids **9** (6.2 g). The crude acids were heated at 100 °C for 45 min in sulfuric acid (18 M), poured onto ice, and extracted with ether. The organic layers were combined, washed with potassium hydroxide solution (3%), dried over anhydrous sodium sulfate, filtered and evaporated to dryness to give crude **12**. Purification by chromatography over silica afforded pure **12** (0.99 g, 16%) as a white solid: mp 183−186 °C; IR (film) 1660 cm^{-1}; ^{1}H NMR (200 MHz; $CDCl_3$) δ 7.75−7.77 (2 H, m), 7.32−7.35 (4 H, m), 3.96 (2 H, t, J = 3.0 Hz), 2.96 (2 H, t, J = 3.0 Hz), 2.31 (6 H, s, CH_3); UV λ_{max} ($CHCl_3$) 315 (ϵ 1458), 341 (sh) (2255), 308 (4548), 300 (sh) (4328), 273 (15429), 262 (sh) (20137), 253 (30664), 245 (sh) (29184); CIMS *m*/*z* 276 (MH^+, 100), 248 (60), 206 (42). Anal. Calcd: C, 82.58; H, 5.84. Found: C, 82.61; H, 5.83. Crystals suitable for X-ray diffraction were obtained by recrystallization from CH_2Cl_2. The enantiomers were resolved on a Pirkle type 1A chiral column (3 mL/min, 1.5% 2-propanol/light petroleum). A sample of **12** (20 mg) was dissolved in dichloromethane (approximately 0.5 mL) and this solution was injected in 20 μL portions. (+)-**12**, the (5*R*,11*R*)-isomer, eluted first (6.2 mg, 99.4% pure), retention time 20 min, $[\alpha]^{22}_D = +480$ (*c* 0.62, CH_3CN); followed by (−)-**12**, the (5*S*,11*S*)-isomer, (4.1 mg, 97.3% pure), retention time 22 min. Fractions were passed through a silica column Whatman Partisil 10 (10% ethyl acetate/light petroleum) to remove an impurity that formed during the chromatography.

2,8-Dibromodibenzobicyclo[*b,f*][3.3.1]nona-5a,6a-diene-6,12-dione 13. Dione **13** was prepared from *p*-bromobenzylcyanide **7** (5.0 g, 25.5 mmol) using the same method outlined above to prepare **12**. The crude product was recrystallized from dichloromethane to yield pure **13** (0.73 g, 17%) as a colorless crystalline solid: mp 259−262 °C; IR (Nujol) 1695 cm^{-1}; ^{1}H NMR (200 MHz; $CDCl_3$) δ 8.08 (2 H, d, J = 2.3 Hz), 7.64 (2 H, dd, J = 11.1, 2.3 Hz), 7.30 (2 H, d, J = 11.1 Hz), 2.97 (2 H, t, J = 3.0 Hz), (3.99, 2 H, t, J = 3.0 Hz); UV λ_{max} ($CHCl_3$) 355 (1194), 441 (1549), 327 (sh) (1704), 311 (3827), 302 (sh) (3481), 280 (5846), 248 (13905), 243 (14313), 230 (16150); CIMS *m*/*z* 406 (MH^+, 100). Anal. Calcd for $C_{17}H_{10}O_2Br_2$: C, 50.28; H, 2.48. Found: C, 50.31; H, 2.57. Crystals suitable for X-ray diffraction were obtained by recrystallization from CH_2Cl_2. The enantiomers were resolved on a Pirkle type 1A chiral column (3 mL/min, 1.5% 2-propanol/light petroleum). A sample of **13** (40 mg)

was dissolved in dichloromethane (approximately 1.0 mL) and this solution was injected in 30 μL portions. Dione (+)-**13**, the (5*R*,11*R*) isomer, eluted first (8.3 mg, 99.8% pure), retention time 22 min, $[\alpha]^{22}_D = +430$ (*c* 0.13, CH_3CN); followed by (−)-**13**, the (5*S*,11*S*) isomer, (8.7 mg, 93.5% pure), retention time 23.5 min.

General Method for Suzuki Couplings. Dione **13** (101 mg, 0.25 mmol), the aryl boronic acid (0.54 mmol), Na_2CO_3 (78 mg, 0.74 mmol), and $PdCl_2(PPh_3)_2$ (7 mg, 0.001 mmol) in DME (5 mL) and H_2O (1 mL) were refluxed at 80 °C for 16 h under an atmosphere of nitrogen. The reaction was cooled and the reaction partitioned between CH_2Cl_2 and water. The aqueous layer was extracted with CH_2Cl_2, the combined organic layers were dried over anhydrous sodium sulfate, and the solvent was removed to give the crude product, which was purified by chromatography on silica gel eluting with CH_2Cl_2. In this way, the following compounds were obtained.

(±)-2,8-Diphenyldibenzobicyclo[*b,f*][3.3.1]nona-5a,6a-diene-6,12-dione 14. Chromatography (R_f 0.22, CH_2Cl_2) yielded the title compound as a white crystalline solid (95 mg, 96%): mp 259−261 °C; IR (Nujol) 1690 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.22 (2H, d, J = 2.0 Hz), 7.75 (2H, dd, J = 2.0, 8.0 Hz), 7.58−7.53 (6H, m), 7.46−7.34 (6H, m), 4.10 (2H, m), 3.06 (2H, m); UV λ_{max} ($CHCl_3$) 371 (ϵ 1156), 358 (2814), 327 (3198), 342 (3677), 255 (58952); CIMS *m*/*z* 400 (MH^+, 100). Anal. Calcd for $C_{29}H_{20}O_2$: C, 86.98; H, 5.03. Found: C, 86.96; H, 4.95.

(±)-2,8-Bis(*o*-methoxyphenyl)dibenzobicyclo[*b,f*][3.3.1]nona-5a,6a-diene-6,12-dione 15. Chromatography (R_f 0.55, CH_2Cl_2) yielded the title compound as a white solid (110 mg, 97%): mp 103−105 °C; IR (Nujol) 1690 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.13 (2H, d, J = 2.0 Hz), 7.71 (2H, dd, J = 2.0, 8.0 Hz), 7.50 (2H, d, J = 8.0 Hz), 7.24−7.36 (2H, m), 6.93−7.04 (4H, m), 4.06 (2H, m), 3.79 (6H, s), 3.02 (2H, m); UV λ_{max} ($CHCl_3$) 372 (sh) (ϵ 1168), 353 (2995), 341 (3473), 295 (sh) (12844), 254 (44855); CIMS *m*/*z* 460 (MH^+, 100), 354 (83). Anal. Calcd for $C_{31}H_{24}O_4$: C, 80.85; H, 5.25. Found: C, 80.65; H, 5.43.

(±)-2,8-Bis(*p*-methoxyphenyl)dibenzobicyclo[*b,f*][3.3.1]nona-5a,6a-diene-6,12-dione 16. Chromatography (R_f 0.59, CH_2Cl_2) yielded the title compound as a white solid (105 mg, 93%): mp 248−250 °C; IR (Nujol) 1690 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.15 (2H, d, J = 2.2 Hz), 7.71 (2H, dd, J = 2.2, 8.2 Hz), 7.51 (2H, d, J = 8.2 Hz), 7.47 (4H, m), 6.93 (4H, m), 4.06 (2H, m), 3.82 (6H, s), 3.03 (2H, m); UV λ_{max} ($CHCl_3$) 370 (sh) (ϵ 3000), 343 (4928), 358 (5246), 292 (sh) (24197), 264 (52677); CIMS *m*/*z* 460 (MH^+, 42), 354 (18). Anal. Calcd for $C_{31}H_{24}O_4$: C, 80.85; H, 5.25. Found: C, 80.95; H, 5.17. Crystals suitable for X-ray diffraction were obtained by recrystallization from CH_2Cl_2.

(±)-2,8-Bisacetylenedibenzobicyclo[*b,f*][3.3.1]nona-5a,-6a-diene-6,12-dione 17. Dione **13** (300 mg, 0.739 mmol), trimethylsilylacetylene (726 mg, 7.39 mmol), $PdCl_2(PPh_3)_2$ (52 mg, 0.074 mmol), and CuI (7 mg, 0.04 mmol) were heated to 60 °C in dry triethylamine (25 mL) under N_2 for 3 days. The reaction was cooled, the solvent removed, and the residue dissolved in methanol (10 mL) and stirred with KOH (10%, 10 mL) for 3 h. The reaction was extracted with CH_2Cl_2, the organic layers were combined and dried, and the solvent was removed to give the crude product. Purification by chromatography (R_f 0.45, CH_2Cl_2) afforded the title compound **17** as a white solid (165 mg, 75%): mp 210−214 °C dec; IR (Nujol) 1675 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 8.07 (2H, d, J = 1.6 Hz). 7.61 (2H, dd, J = 1.7, 8.0 Hz), 7.42 (2H, d, J = 8.0 Hz), 4.02 (2H, m), 3.10 (2H, s), 2.98 (2H, m); UV λ_{max} ($CHCl_3$) 358-(ϵ 256), 341(1219), 310(4334), 270(sh) (11089), 244(66984); CIMS *m*/*z* 296 (MH^+, 100), 269 (50). Anal. Calcd for $C_{21}H_{12}O_2$: C, 85.12; H, 4.08. Found: C, 84.89; H, 4.07.

(±)-2,8-Dinitrodibenzobicyclo[*b,f*][3.3.1]nona-5a,6a-diene-6,12-dione 18. Dione **2**[39] (500 mg, 2.014 mmol) was dissolved in H_2SO_4 (15 mL) and stirred at 0 °C while KNO_3 (1.02 g, 10.1 mmol) was added in portions over 30 min. The solution was stirred at room temperature for 16 h. The mixture was poured onto ice and the white precipitate collected by filtration and washed successively with cold water and diethyl ether. Recrystallization from DMF affforded the title compound **18** as a yellow crystalline solid (503 mg, 75%): mp >300 °C; IR (Nujol) 1695, 1601, 1510, 1442, 1250, 1205 cm^{-1}; ^1H NMR (200 MHz, d_6-DMSO/$CDCl_3$) δ 8.53 (2H, d, J = 2.5 Hz), 8.36 (2H, dd, J = 2.5, 8.4 Hz), 7.76 (2H, d, J = 8.4 Hz), 4.30 (2H, m), 3.05 (2H, m); UV λ_{max} ($CHCl_3$) 375 (ϵ 790), 358 (1395), 329 (1844), 344 (2072), 265 (sh) (25766), 248 (37048); CIMS *m*/*z* 338 (MH^+, 100), 292 (23). Anal. Calcd for $C_{17}H_{10}N_2O_6$,: C, 60.36; H, 2.98; N, 8.28. Found: C, 60.21; H, 2.71; N, 8.30. Crystals suitable for X-ray diffraction were obtained by recrystallization from DMF.

(±)-2,8-Dimethyl-1,7-dinitrodibenzobicyclo[*b,f*][3.3.1]nona-5a,6a-diene-6,12-dione 22. Dione **12** (200 mg, 0.724 mmol) was dissolved in H_2SO_4 (10 mL) and stirred at 0 °C while KNO_3 (366 mg, 3.619 mmol) was added in portions over 30 min. The solution was stirred at room temperature for 16 h. The mixture was poured onto ice and the white precipitate collected and washed successively with cold water and diethyl ether. The resultant solid was recrystallized from DMF to yield the title compound **22** as white plates (162 mg, 61%): mp >300 °C; IR (Nujol) 1695, 1610, 1525, 1282, 1205 cm^{-1}; ^1H NMR (200 MHz, d_6-DMSO): δ 7.78 (2H, d, J = 8.0 Hz), 7.57 (2H, d, J = 8.0 Hz), 4.13 (2H, m), 3.03 (2H, m), 2.15 (6H, s); UV λ_{max} ($CHCl_3$) 377 (ϵ 269), 359 (927), 343 (1350), 329 (1491), 310 (3418), 254 (sh) (20513), 248 (22766); CIMS *m*/*z* 366 (MH^+, 40), 318 (65). Anal. Calcd for $C_{19}H_{14}N_2O_6$: C, 62.30; H, 3.85; N, 7.65. Found: C, 62.09; H, 3.73; N, 7.67.

(±)-2,8-Bisacetamidobisacetoxydibenzobicyclo[*b,f*]-[3.3.1]nona-5a,6a-diene 20. Dinitro dione **18** (100 mg, 0.29 mmol) was stirred in methanol (75 mL) under an atmosphere of H_2 in the presence of palladium-on-charcoal catalyst (10%, 5 mg) for 16 h. The solution was filtered through Celite and the methanol removed under reduced pressure to yield a colorless oil containing the crude amine **19**. The oil was dissolved in dry pyridine (5 mL) and cooled to 0 °C under a nitrogen atmosphere while acetyl chloride was added (90 μL, 1.15 mmol). The solution was stirred overnight at room temperature for 16 h and poured onto water (5.0 mL) and the aqueous layer extracted with CH_2Cl_2. The resultant organic layers were combined, washed with HCl (1 M, 70 mL), and dried over anhydrous sodium sulfate, and the solvent was removed to yield the title compound as a beige solid (100 mg, 77%): mp >300 °C; IR (Nujol) 3410, 1735, 1675, 1620 cm^{-1}; ^1H NMR (200 MHz, d_6-DMSO) δ 9.72 (2H, s), 7.45 (2H, dd, J = 2.2, 8.4 Hz), 7.28 (2H, d, J = 2.4 Hz), 6.91 (2H, d, J = 8.4 Hz), 6.09 (2H, d, J = 5.2 Hz), 3.31 (2H, m), 2.35 (2H, m), 2.15 (6H, s), 1.95 (6H, s); UV λ_{max} ($CHCl_3$) 290 (sh) (ϵ 2385), 282 (sh) (3426), 249 (32078); CIMS *m*/*z* 450 (MH^+, 100); HRMS calcd for $C_{25}H_{26}O_6N_2$ 450.1791, found 450.1799. Anal. Calcd for $C_{25}H_{26}N_2O_6 \cdot H_2O$: C, 64.09; H, 6.02; N, 5.98. Found: C, 64.21; H, 5.87; N, 5.84.

(±)-2,8-Diaminodibenzobicyclo[*b,f*][3.3.1]nona-5a,6a-diene-6,12-dione 21. Dinitro dione **18** (250 mg, 0.739 mmol), iron powder (295 mg, 5.2 mmol), acetic acid (0.60 mL, 10.346 mmol), and ethanol (20 mL) were refluxed under an nitrogen atmosphere for 6 h. The reaction was poured onto water and the aqueous layer extracted with CH_2Cl_2. The combined organic extracts were washed with $NaHCO_3$ and dried over anhydrous sodium sulfate, and the solvent was removed to give the title compound **21** as a yellow solid (192 mg, 93%): mp 288−291 °C; IR (Nujol) 3450, 3340, 1682, 1645, 1620 cm^{-1}; ^1H NMR (200 MHz, d_6-acetone), 7.13 (2H, d, J = 2.6 Hz), 7.08 (2H, d, J = 8.3 Hz), 6.84 (2H, dd, J = 2.6, 8.3 Hz), 3.71 (2H, m), 2.86 (2H, m), 2.77 (4H, s); UV λ_{max} ($CHCl_3$) 358 (ϵ 4614), 345 (4756), 244 (34796); CIMS *m*/*z* 278 (MH^+, 71); HRMS calcd for $C_{17}H_{14}N_2O_2$ ($M^{\bullet+}$) 278.1055, found 278.1058.

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Supporting Information Available: Details of the X-ray analyses of compounds **12**, **13**, **16**, **18**, and **22** are in available in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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