3-[(Methanesulfonyl)oxy]-2-cyclohexenone (19).[8] Mesylate **19** was prepared (2.92 g, 85%) from 1,3-cyclohexanedione (2.02 g, 18.0 mmol) and mesyl chloride (2.81 g, 24.6 mmol, 1.36 equiv) by following a literature procedure:[8] TLC (EtOAc) R_f 0.60; IR (neat) 3040, 1680, 1660, 1360 cm^{-1}; ^1H NMR (90 MHz) δ 2.17 (apparent pent, J = 6.1 Hz, 2 H), 2.21 (t, J = 6.3 Hz, 2 H), 2.68 (t, J = 5.9 Hz, 2 H), 3.33 (s, 3 H), 6.09 (br s, 1 H).

The IR and NMR of **19** were identical with those reported.[8] The mesylate was immediately used for cross-coupling without further purification.

3-((*E*)-Hex-1-en-1-yl)-2-cyclohexenone (20, Table I, Entry 8). Treatment of **19** (0.22 g, 1.20 mmol) and stannane **10** (0.46 g, 1.20 mmol, 1.0 equiv) as described above afforded a yellow oil, which was purified by radial chromatography (SiO_2, 2.5% EtOAc/hexane) followed by distillation to give **20** as a colorless oil (0.10 g, 50%): bp (bulb-to-bulb) 75–90 °C (0.8 mmHg); TLC (5% EtOAc/hexane) R_f 0.11; IR (neat) 3040, 2970, 1660, 1630, 1585, 980, 900 cm^{-1}; ^1H NMR (360 MHz) δ 0.86 (t, J = 7.2 Hz, 3 H), 1.24–1.42 (m, 4 H), 1.94–2.02 (m, 2 H), 2.13–2.18 (m, 2 H), 2.35 (t, J = 6.0 Hz, 2 H), 2.42 (t, J = 6.0 Hz, 2 H), 5.82 (br s), 6.14 (br s); ^{13}C NMR (91 MHz) δ 13.8 (q, J = 124.6 Hz), 22.2 (t, J = 130.9 Hz), 22.3 (t, J = 129.2 Hz), 25.0 (t, J = 125.7 Hz), 30.9 (t, J = 127.0 Hz), 32.8 (t, J = 124.0 Hz), 37.6 (t, J = 128.0 Hz), 126.2 (d, J = 160.4 Hz), 131.3 (d, J = 162.2 Hz), 139.0 (d, J = 153.5 Hz), 157.5 (s), 200.2 (s); LRMS m/z (rel intensity) 178 (33); HRMS calcd for $C_{12}H_{18}O$ 178.1358, found 178.1368. Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.43, H, 9.91.

Trace peaks in the ^{13}C NMR at δ 157.5, 138.7, 128.7, and 127.3 indicated the presence of the Z isomer. No attempt was made to separate the mixture of isomers. The E dienone:Z dienone ratio of 91:9 was determined by GC.

Methyl 2-[(Methanesulfonyl)oxy]cyclopentenecarboxylate (21). Mesylate **21** was prepared by using a modified literature method.[8] Treatment of methyl 2-oxocyclopentanecarboxylate (0.62 mL, 4.99 mmol) with mesyl chloride (1.00 mL, 12.9 mmol, 2.59 equiv) as described above afforded **21** (0.78 g, 71%): bp (bulb-to-bulb) 120–125 °C (0.55 mmHg); TLC (25% EtOAc/hexanes) R_f 0.21; IR (neat) 1720, 1360, 1150 cm^{-1}; ^1H NMR (300 MHz) δ 1.95–2.00 (m, 2 H), 2.62–2.67 (m, 2 H), 2.77–2.83 (m, 2 H) 3.25 (s, 3 H), 3.75 (s, 3 H); ^{13}C NMR (91 MHz) δ 20.9, 22.0, 25.1, 28.7, 30.2, 39.1, 128.6, 149.6, 199.1. The mesylate was immediately used for cross-coupling without further purification.

Methyl 2-Ethenyl-1-cyclopentenecarboxylate. Treatment of **22** (0.67 g, 3.04 mmol) and stannane **4** (1.18 g, 3.72 mmol, 1.2 equiv) as described above afforded a yellow oil, which was purified by radial chromatography (SiO_2, 2.5% EtOAc/hexanes) followed by distillation to give the methyl ester as a colorless oil (0.10 g, 50%): bp (bulb-to-bulb) 63–68 °C (0.70 mmHg); TLC (25% EtOAc/hexanes) R_f 0.76; IR (neat) 3030, 1710, 1630, 1585, 900 cm^{-1}; ^1H NMR (300 MHz) δ 1.85 (tt, J = 8.9, 8.9 Hz, 2 H), 2.65 (t, J = 8.9 Hz, 2 H), 2.71 (t, J = 8.9 Hz, 2 H), 3.73 (s, 3 H), 5.40 (d, J = 17.6 Hz, 1 H), 5.41 (d, J = 10.8 Hz, 1 H), 7.51 (dd, J = 17.6, 10.8 Hz, 1 H); ^{13}C NMR (75 MHz) δ 21.2 (t, J = 130.6 Hz), 33.6 (t, J = 129.4 Hz), 34.3 (t, J = 129.3 Hz), 51.2 (q, J = 146.6 Hz), 120.5 (t, J = 157.8 Hz), 129.6 (s), 131.7 (d, J = 162.2 Hz), 152.1 (s), 166.2 (s); LRMS m/z (rel intensity) 152 (24).

2-Ethenyl-1-cyclopentenecarboxylic Acid (22, Table I, Entry 9). In a separate experiment, the mixture resulting from reaction of mesylate **21** (0.58 g, 2.65 mmol) with **4** (1.02 g, 3.20 mmol, 1.2 equiv) as described was treated with LiOH (15 mL, 10% in 50% MeOH/H_2O) for 12 h and then washed with hexanes (3 × 25 mL). The aqueous layer was acidified (pH 2), saturated with NaCl, and extracted with Et_2O (3 × 20 mL). The combined organics were washed with water (2 × 20 mL) and saturated NaCl solution (2 × 20 mL), dried (Na_2SO_4), and concentrated to give **22** as a yellow-white solid (0.30 g, 82%): mp 98–101 °C; TLC (50% EtOAc/1% HOAc/hexanes) R_f 0.48; IR ($CDCl_3$) 3000 (br), 1670, 1620, 1560, 950 cm^{-1}; ^1H NMR (300 MHz) δ 1.89 (tt, J = 7.6 Hz, 2 H), 2.71 (d, J = 7.6 Hz, 2 H), 2.75 (d, J = 7.6 Hz, 2 H), 5.43 (d, J = 8.9 Hz, 1 H), 5.47 (d, J = 15.8 Hz, 1 H), 7.26 (s, 1 OH), 7.56 (dd, J = 8.9, 15.8 Hz, 1 H); ^{13}C NMR (75 MHz) δ 21.1 (t, J = 128.0 Hz), 34.0 (t, J = 123.5 Hz), 34.1 (t, J = 132.0 Hz), 121.3 (t, J = 157.3 Hz), 129.2 (s), 131.8 (d, J = 159.2 Hz), 154.7 (s), 171.2 (s); LRMS m/z (rel intensity) 138 (50); HRMS calcd for $C_8H_{10}O_2$ 138.0681, found 138.0676. Anal. Calcd for $C_8H_{10}O_2$: C, 69.55; H, 7.30. Found: C, 69.79; H, 6.92.

Acknowledgment. We gratefully acknowledge support for this project by the donors of the Petroleum Research Fund, as administered by the American Chemical Society, and by the Office of the Vice President for Research at the University of Iowa. Palladium was generously loaned through the Johnson Matthey Precious Metal Loan Program. (*Z*)-Prop-1-en-1-yltributylstannane was a gift of the Bristol-Myers Company, for which the authors thank Dr. Vittorio Farina and Dr. Greg Roth. Mass spectra were obtained in the University of Iowa High Resolution Mass Spectrometry Facility. NMR spectra were obtained in the University of Iowa High Field NMR Facility. J.K.K. gratefully acknowledges support through the University of Iowa Summer Undergraduate Research Fellowship Program, funded in part by the National Science Foundation (REU CHE-8942577).

Supplementary Material Available: ^1H and ^{13}C NMR spectra for compounds **1**, **11**, **13**, **15**, **18**, **20**, and **22** (14 pages). Ordering information is given on any current masthead page.

Heteroaromatic Fused Derivatives of Tetracyclo[6.3.0.0^{4,11}.0^{5,9}]undecane

Jean-Luc Lim, Sara Chirayil, and Randolph P. Thummel*

Department of Chemistry, University of Houston, Houston, Texas 77204-5641

Received May 1, 1990

A series of rigid *syn*-orthocyclophanes is prepared by the Friedländer condensation of appropriate *o*-aminobenzaldehyde derivatives with tetracyclo[6.3.0.0^{4,11}.0^{5,9}]undecane-2,7-dione. The reaction may proceed in a stepwise fashion so that unsymmetrical layered compounds can be prepared. These species can be further elaborated by oxidation to quinolinequinones or *N*-oxides and quaternization to quinolinium salts. Molecular mechanics calculations agree closely with X-ray analysis in describing the structural properties of these cyclophanes. Analysis of the ^1H NMR and UV spectra as well as the reduction potentials of these molecules support a moderate electronic interaction between the decks. Initial investigations regarding their ability to serve as cleft-type hosts are described.

Introduction

Ever since the pioneering work of Cram and associates, the field of cyclophane chemistry has continued to capture the interest of the chemical community.[1] The principal attraction of these compounds lies in their ability to juxtapose two aromatic rings close to one another in parallel planes. This orientation is accomplished by the use of two or more bridges whose number, position, and length govern the properties of the system. Considerable attention has been devoted to [*m.n*]para- and [*m.n*]metacyclophanes while the corresponding orthocyclophanes have received

(1) Keehn, P. M.; Rosenfeld, S. M. *Cyclophanes*; Academic Press: New York, 1983; Vols. I and II.

0022-3263/91/1956-1492$02.50/0

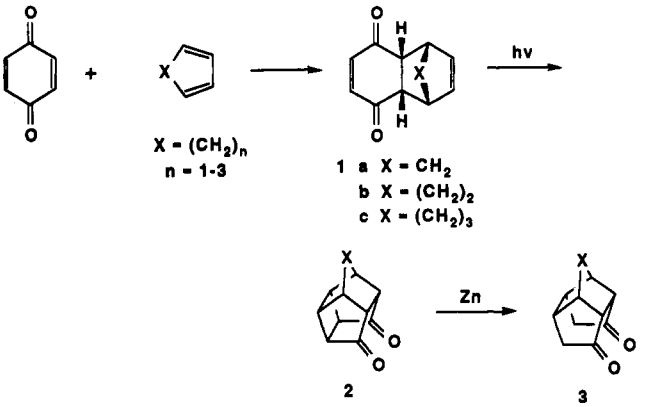
comparatively little attention. This latter class of cyclophane does not normally adopt a parallel arrangement of the aromatic rings due to its increased conformational mobility. In fact, the syn conformation of [2.2]orthocyclophane would necessitate unfavorable eclipsing interactions in the ethano bridges.

More recent work in the design of molecular receptors has indicated that orthocyclophanes might function as useful host molecules. In fact, the cleft between the two layered aromatic rings would be more accessible to guest molecules than analogous para- and metacyclophanes. Various spacer groups have been employed to promote a syn parallel arrangement of the aromatic rings and to control the distance between the decks.[2-8] In most every case studied, the cleft created by the spacer group has involved the stacking of benzene rings. Physical studies have centered around the electronic interaction between these rings as determined by absorption and photoelectron spectroscopy. Other related forms of molecular clefts have been designed using rigid spacer groups such as dibenz[*c*,*h*]acridine.[9]

We have recently developed a synthetic approach to a class of *syn*-orthocyclophanes which utilize tetracyclo[6.3.0.0^{4,11}.0^{5,9}]undecane (TCU) as a rigid spacer group.[10] Subsequent work by Marchand and Annapurna used the same methodology to prepare an analogous [2.2]orthocyclophane based on quinoline having a pentacyclo[6.5.0.0^{4,12}.0^{5,10}.0^{9,13}]tridecane spacer group which gives the system a more splayed geometry.[11] The advantage of constructing such systems containing heteroaromatic as opposed to benzenoid subunits is that the heteroatom may serve as a useful handle for both studying and controlling the chemistry of the molecule. This paper will provide the details of our earlier work as well as more recent studies on a variety of related systems.

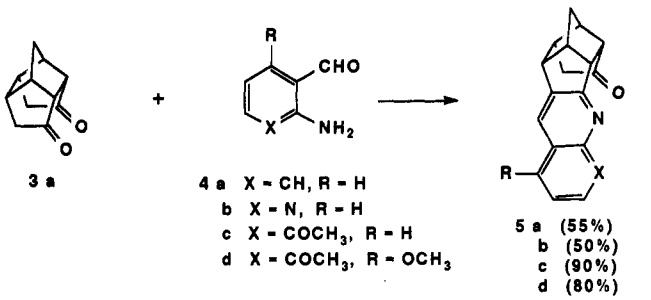
Results

Our key synthon for the construction of *syn*-orthocyclophanes by the Friedländer condensation of aromatic *o*-aminoaldehydes is TCU-2,7-dione (**3a**). This material may be readily prepared in three high yield steps from 1,3-cyclopentadiene and *p*-benzoquinone.[12] The chemistry of TCU and related cage-type compounds has recently been reviewed.[13] It was our original intention to also prepare the higher homologue **3b** and **3c** by utilizing the appropriate 1,3-cycloalkadiene in the same sequence of steps. In accord with the observations of other workers,[2c,14] we found that the zinc reduction to provide **3b** was impractical. Apparently twisting of the molecule due to the

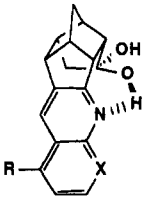


dimethylene bridge causes a transannular reaction between the carbonyl groups rather than the desired reductive cleavage. Presumably this situation would only be worse for the trimethylene analogue **3c**.

Under basic conditions, **3a** undergoes Friedländer condensation with 2-aminobenzaldehyde (**4a**) to provide 55% of the monoketone **5a**. This same result was obtained even when 2 or more equiv of **4a** were employed in the reaction. The failure to observe a double Friedländer reaction was a general phenomenon which was also observed for 2-aminonicotinaldehyde (**4b**) as well as the mono- and dimethoxyaminobenzaldehyde derivatives **4c** and **4d**.



The Friedländer reaction produces two molecules of water via steps which involve imine formation and aldol-type condensation.[15] We reasoned that the second carbonyl group of **5** could readily hydrate especially by attack of the water molecule released upon imine formation. The resultant species **6** would be stabilized by intramolecular hydrogen bonding and thereby inert toward a Friedländer condensation. Evidence for the involvement of **6** was provided by the reaction of **3a** with 2 equiv of **4a**



(2) (a) Prinzbach, H.; Sedelmeier, G.; Krüger, C.; Goddard, R.; Martin, H.-D.; Gleiter, R. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 271. (b) Sedelmeier, G.; Fessner, W.-D.; Grund, C.; Spurr, P. R.; Fritz, H.; Prinzbach, H. *Tetrahedron Lett.* **1986**, *27*, 1277. (c) Fessner, W.-D.; Sedelmeier, G.; Krothe, L.; Prinzbach, H.; Rihs, G.; Yang, Z.; Kovac, B.; Heilbronner, E. *Helv. Chim. Acta* **1987**, *70*, 1816. (d) Murty, B. A. R. C.; Spurr, P. R.; Pinkos, R.; Grund, C.; Fessner, W.-D.; Hunkler, D.; Fritz, H.; Roth, W. R.; Prinzbach, H. *Chimia* **1987**, *41*, 32 and references therein.

(3) Golden, J. H. *J. Chem. Soc.* **1961**, 3741.

(4) Cristol, S. J.; Lewis, D. C. *J. Am. Chem. Soc.* **1967**, *89*, 1476.

(5) Collin, P. J.; Roberts, D. B., Sugowdz, G.; Wells, D.; Sasse, W. H. F. *Tetrahedron Lett.* **1972**, 321.

(6) Toyoda, T.; Otsubo, I.; Otsubo, T.; Sakata, Y.; Misumi, S. *Tetrahedron Lett.* **1972**, 1731.

(7) Mataka, S.; Takahashi, K.; Mimura, T.; Hirofa, T.; Takuma, K.; Kobayashi, H.; Tashiro, M.; Imada, K.; Kuniyoshi, M. *J. Org. Chem.* **1987**, *52*, 2653.

(8) Harmata, M.; Murray, T. *J. Org. Chem.* **1989**, *54*, 3761.

(9) (a) Zimmerman, S. C.; VanZyl, C. M.; Hamilton, G. S. *J. Am. Chem. Soc.* **1989**, *111*, 1373. (b) Zimmerman, S. C.; Wu, W. *J. Am. Chem. Soc.* **1989**, *111*, 8054. (c) Zimmerman, S. C.; Mrksich, M.; Baloga, M. *J. Am. Chem. Soc.* **1989**, *111*, 8528.

(10) Thummel, R. P.; Lim, J.-L. *Tetrahedron Lett.* **1987**, *28*, 3319.

(11) Marchand, A. P.; Annapurna, P. *Tetrahedron Lett.* **1988**, *29*, 6681.

(12) (a) Metha, G.; Srikrishna, A.; Veera Reddy, A.; Nair, M. S. *Tetrahedron* **1981**, *37*, 4543. (b) Cookson, R. C.; Crundwell, E.; Hudec, J. *Chem. Ind. (London)* **1958**, 1003. (c) Wenkert, E.; Yoder, J. E. *J. Org. Chem.* **1970**, *35*, 2986.

(13) Marchand, A. P. In *Advances in Theoretically Interesting Molecules*; Thummel, R. P., Ed.; JAI Press: Greenwich, CT, 1989; pp 357-399.

(14) (a) Sedelmeier, G.; Prinzbach, H.; Martin, H.-P. *Chimia* **1979**, *33*, 329. (b) Martins, F. J. C.; Fourie, L.; Venter, H. J.; Wessels, P. L. *Tetrahedron* **1990**, *46*, 623.

(15) Cheng, C.-C.; Yan, S.-J. *Org. React.* **1982**, *7*, 37.

Table I. Aromatic Proton Chemical Shift Data for Fused TCU Derivatives and Model Compounds[a]

compd	$H_{4'}$	$H_{4''}$	$H_{5'}$	$H_{5''}$	$H_{6'}$	$H_{6''}$	$H_{7'}$	$H_{7''}$	$H_{8'}$	$H_{8''}$
9a	7.62		7.67		7.42		7.58		7.97	
9b	7.61		8.03		7.36		8.93			
10a	7.43 (0.33)	7.43	7.39 (0.26)	7.39	7.19 (0.21)	7.19	7.34 (0.22)	7.34	7.75 (0.25)	7.75
10a (C_6D_6)	7.04 (0.28)		7.09 (0.38)		6.82 (0.40)		6.96 (0.43)		7.93 (0.25)	
10b	7.58 (0.22)	7.58	7.89 (0.15)	7.89	7.22 (0.11)	7.22	8.79 (0.17)	8.79		
10c	7.45 (0.31)	7.45 (0.35)	7.39 (0.26)	7.74 (0.30)	7.18 (0.22)	7.10 (0.23)	7.33 (0.23)	8.69 (0.27)	7.74 (0.26)	
10d	7.41	7.41	6.97	6.97	7.06	7.06	6.68	6.68		
10e	7.47	7.86	7.41		7.17	6.35	7.32	6.51	7.76	
10f	7.89 (0.43)	7.89			6.00 (0.69)	6.00	6.07 (0.79)	6.07		
11	8.03				6.98/7.08		6.98/7.08			
12	7.81/7.83		8.01		7.47	6.75	7.62	6.84	8.62	
13	7.73 (0.38)	7.73			6.78 (0.15)	6.78	6.87 (0.25)	6.87		
15a	7.76		7.65		7.40		7.56		8.00	
15a (C_6D_6)	7.32		7.47		7.22		7.39		8.18	
15b	7.80		8.04		7.33		8.96			
15c	8.32				6.69		6.86			
16	8.11				6.93		7.12			

[a] Chemical shifts given for $CDCl_3$ solutions (except where indicated) in ppm downfield from internal Me_4Si. The values in parentheses represent differences (in ppm) from model compounds **15**, **16**. For unsymmetrical layered compounds the single primed numbers refer to the quinoline ring.

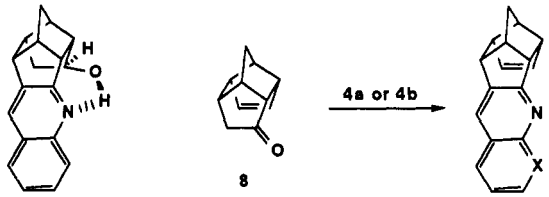
Table II. Pertinent Interatomic Distances of 2,3:6,7-Bisquinoline Fused Cage Compounds

atoms[a]	measured **10a**, Å	estimated[b] **10a**, Å	calculated,[c] Å $n = 1$ (**10a**)	$n = 2$	$n = 3$
C4–C3	1.59	1.54	1.55	1.55	1.56
C5–C2	2.78	2.40	2.81	2.69	2.62
N6–N1	3.65	3.05	3.70	3.45	3.34
C7–C27	4.72	3.94	4.74	4.36	4.21
C8–C26	5.71	4.68	5.75	5.23	5.01
C9–C25	6.79	5.52	6.80	6.15	5.88
C15–C19	1.59	1.54	1.55	1.55	1.55
C14–C20	2.81	2.40	2.81	2.70	2.63
C13–C21	3.81	3.05	3.78	3.54	3.44
C12–C22	4.83	3.94	4.81	4.44	4.29
C11–C23	5.92	4.68	5.90	5.38	5.18
C10–C24	6.89	5.52	6.87	6.23	5.97

[a] Atomic numbering scheme given in Figure 1. [b] Estimated from an idealized Fieser model. [c] Calculated by the programs PC Model and MMX available from Serena Software, Bloomington, IN. The C16–C18 bridge in Figure 1, $(CH_2)_n$, is varied from 1 to 3 carbons.

in toluene under Dean–Stark conditions where water could be azeotropically removed from the system. The bis-Friedländer product **10a** was formed in 81% yield. Our ability to efficiently stop the reaction at the monoketone stage proved fortuitous since it allowed the preparation of unsymmetrical orthocyclophanes. It is noteworthy that methoxy substitution improves the Friedländer reaction either by increasing the nucleophilicity of the amine moiety or by hindering self-condensation of the aminoaldehyde.

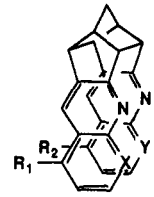
Lithium aluminum hydride reduction of **5a** provided the corresponding alcohol **7** in 80% yield. TCU-2-en-7-one (**8**) was prepared in three steps according to the procedure of Eaton.[16] Friedländer condensation of **8** with **4a** and **4b** provided the corresponding 2,3-fused quinoline **9a** and 1,8-naphthyridine **9b**, respectively.



7 **8**

9 a X = CH (54%)
b X = N (27%)

When the monoketones **5** were treated with 1 equiv of the *o*-aminoaldehydes **4a–d**, they provided the layered systems **10a–f**, which were characterized primarily by their ^1H and ^{13}C NMR spectra. The symmetrical systems evidenced clear patterns for their aromatic protons where $H_{4'}$ was a singlet and the resonances corresponding to $H_{5'}$–$H_{8'}$ could be assigned by their multiplicities and analogy to other known systems (see Table I). The protons of the TCU bridge were less readily assigned.



10 a X = Y = CH, $R_1 = R_2$ = H (57%)
b X = Y = N, $R_1 = R_2$ = H (60%)
c X = CH, Y = N, $R_1 = R_2$ = H (40%)
d X = Y = $COCH_3$, $R_1 = R_2$ = H (58%)
e X = $COCH_3$, Y = CH, $R_1 = OCH_3$, R_2 = H (78%)
f X = Y = $COCH_3$, $R_1 = R_2 = OCH_3$ (90%)

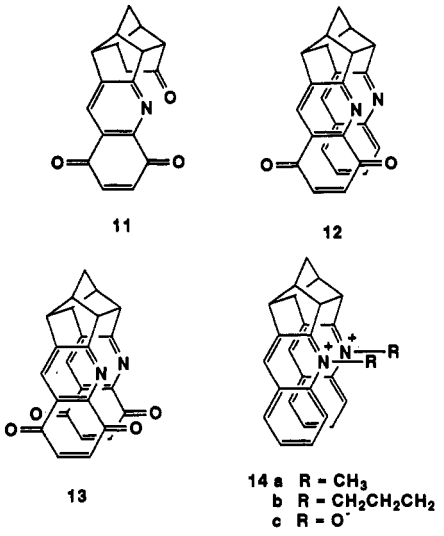
In their ^{13}C NMR spectra, the symmetrical systems, **10a,b,d,f** showed the expected eight or nine lines for the aromatic carbons and four lines for the TCU cage. The unsymmetrical systems **10c,e** showed twice the number of aromatic carbons and seven lines for the TCU cage. The methoxy signals for **10d–f** were also characteristic, appearing in the range of 59.5–60.4 for the 8-methoxy group. Eaton and co-workers have pointed out the utility of carbon versus proton NMR in identifying cage-type compounds.[16]

Direct oxidation of the dimethoxybenzo ring could be accomplished by treatment with ceric ammonium nitrate (CAN) catalyzed by 2,6-pyridinedicarboxylic acid *N*-oxide (PDANO).[17] The quinones were characterized by disappearance of the methoxy ^1H and ^{13}C NMR signals concurrent with the appearance of the quinone $^{13}C{=}O$ at about 185 ppm and a strong IR absorption at about 1660 cm^{-1}. These compounds were sensitive to heat and light, turning dark after a period of time. The N-alkylated layered systems **14a,b** were prepared by treating **10a** with

(16) Eaton, P. E.; Cassar, L.; Hudson, R. A.; Hwang, D. R. *J. Org. Chem.* **1976**, *41*, 1445.

(17) (a) Syper, L.; Kloc, K.; Mlochowski, J. *Synthesis* **1979**, 521. (b) Matsumoto, I.; Tomimoto, K. Japan Kokai Pat. No. 73-80, 570; *Chem. Abstr.* **1984**, *80*, 108385. (c) Lim, J.-L.; Chirayil, S.; Thummel, R. P., manuscript in preparation.

methyl iodide or 1,3-dibromopropane, and the di-*N*-oxide **14c** resulted from *m*-chloroperbenzoic acid oxidation of **10a**.



Properties of Fused TCU Derivatives

1. Structural Considerations. Our original intention had been to utilize the diketones **3a–c** to prepare *syn*-orthocyclophanes whose interdeck distances were controlled by the length of the bridge X. Utilizing MMX calculations[18] we were able to estimate the geometries of a series of layered quinolines as summarized in Table II. As expected, increasing the length of the polymethylene bridge forces the two decks closer together. In all three cases (n = 1–3) the two quinoline rings are canted slightly toward one another on the side bearing the nitrogen atom. For the system where n = 1 (**10a**) we also constructed a Fieser model and measured the interdeck distances. The canting of the two rings is absent in this model and the estimated interdeck distances are considerably less than those calculated by MMX. A similar analysis was employed by Prinzbach who prepared the dibenzofused analogues of **3a** and **3b** and examined their geometries by X-ray crystallography.[2c]

To test the validity of the two different models of **10a** we carried out a single-crystal X-ray analysis of this molecule. An ORTEP drawing is given in Figure 1, and the measured interdeck distances are given in Table II. The agreement of the experimental values with those predicted by MMX is extremely good with an average variation of only 0.024 Å. This close agreement lends confidence to calculations made for other similar systems such as those where n = 2, 3. The dihedral angle between the quinoline rings is 50.5° while the Fieser models would predict an angle of only 40°. The observed splaying of the molecule is due to considerable distortion at the "hinge" carbons (C_2, C_5 and C_{14}, C_{20}) of the cage. There are three C–C–C bond angles which center on each hinge carbon. The two angles contained in the cyclopentane rings measure 101.5° and 102.3°, while the one which is exocyclic to the cyclopentanes is 113.3°. It is the magnitude of this latter angle which causes the splaying of the two quinoline rings. For the systems where n = 2, 3 this angle becomes smaller and the splaying diminishes.

A second feature evidenced by the X-ray structure involves the incorporation of a hydrogen-bonded water molecule bridging the two quinoline nitrogens with N–H

(18) The programs PC MODEL and MMX were obtained from Serena Software, Bloomington, IN.

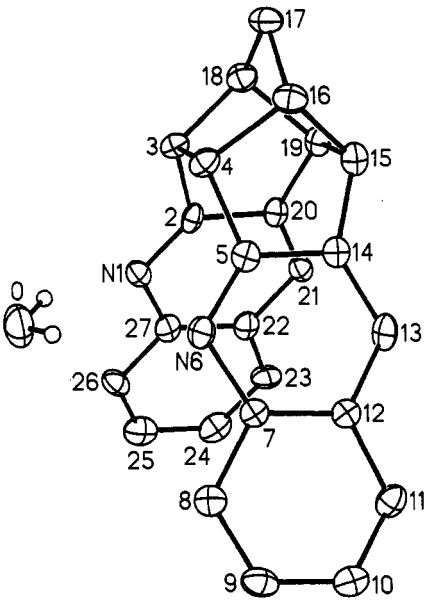


Figure 1. ORTEP drawing for 2,3:7,6-bis(2′,3′-quinolino)TCU (**10a**) with the atomic numbering scheme, used for crystallographic analysis only.

bond lengths of 2.12 and 2.19 Å. This tightly bound water molecule is also evidenced by a signal at 2.61 ppm in the proton NMR. The molecular mechanics calculations do not include the water molecule, yet they still predict the two quinoline rings to be slightly canted toward one another. One possible explanation is that the dipoles of the quinolines are trying to partially cancel by orienting toward each other. This dipole-induced canting would be more pronounced for **10b** and is consistent with the smaller upfield shifts seen in its ^{1}H NMR.

We hoped that this hydrogen bonding site might be useful in the complexation of other guests such as primary amines. To test this hypothesis, we examined the interaction of **10a** with 3-phenylpropylamine. Our hope was that the amino group would hydrogen bond to the quinoline nitrogens while the phenyl ring would intercalate between the layered aromatic rings of the host. By NMR we did not observe any appreciable change in the aromatic protons of **10a** in the presence of the amine. It appears that there is insufficient room in the cleft of **10a** to accomodate a benzenoid guest. To test this theory we compared the ^{1}H NMR spectrum in C_6D_6 of **10a** with its appropriate model compound **15a**. The upfield shifts which we observed in C_6D_6 were then compared with those in $CDCl_3$ (see Table I). Little change is found for H_4 and H_8 but H_5, H_6, and H_7 experience considerably larger shifts in C_6D_6. We interpret this to mean that some intercalation of the benzene solvent is occurring in the region of these three protons. As expected, it is most pronounced at H_6 and H_7, which are held the furthest apart. Intercalation in the vicinity of H_8 is unfavorable, explaining why the relatively short tether on our 3-phenylpropylamine prohibits such binding. We are currently exploring ways of making this cleft more accessible to these types of guests.

Examination of the crystal packing diagram of **10a** (Figure 2) brings to light several other interesting features. The crystal packing occurs in layers where the orientation of adjacent molecules are 180° out of phase: ΛVΛVΛV. This packing allows the quinoline rings to align themselves in a more or less parallel array although the stacking is in an oblique fashion. The quinoline nitrogens, and hence the H-bonded water molecules, are oriented on the same side for each individual layer (see top 4 molecules) but alternate from one layer to the next (compare with lower

Table III. Ultraviolet Adsorption Data[a] for Annelated TCU's and Model Compounds

compd	λ_{max} (ϵ)				
10a	295 (33500)	302 (34400)	308 (54100)	314 (44900)	322 (72800)
10b	297 (30900)	303 (39500)	309 (53700)	315 (48700)	323 (56500)
10c	297 (32400)	303 (35400)	309 (44500)	315 (40900)	324 (49500)
15a	292 (8500)	298 (12600)	304 (22300)	311 (21400)	318 (34200)
15b	293 (6000)	299 (9000)	306 (12500)	312 (12500)	319 (14500)

[a] Wavelength in nanometers for 10^{-5} M solutions in 95% EtOH.

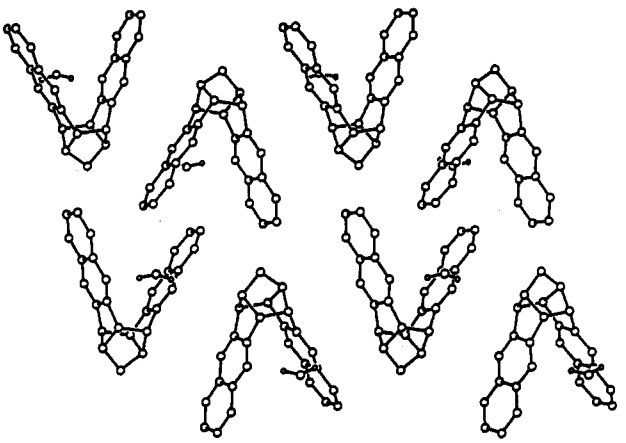
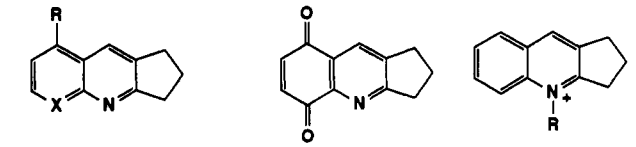


Figure 2. Crystal packing diagram for 2,3:7,6-bis(2′,3′-quinolino)TCU (10a).

4 molecules). Finally, we note that pairs of molecules in adjacent layers are beginning to "sandwich" each other so that one benzo ring of each partner is nudging slightly into the cleft of the opposite molecule. It will be interesting to see how further changes in the geometry of the cyclophane, especially the cleft, will influence the crystal packing.

2. NMR Analysis. Table I contains the ^{1}H NMR chemical shift data for the annelated TCU derivatives **9–13**. In order to better analyze this data we have also prepared a series of model compounds **15a–c**[19,20] and **16** and included their ^{1}H NMR chemical shifts in Table I.



15 a X = CH, R = H
b X = N, R = H
c X = $COCH_3$, R = OCH_3

16

17

Of principal interest are changes in NMR properties resulting from through-space electronic interaction between the decks of the layered compounds. Several effects are clearly evident. With respect to **15a–c**, we find that the protons of the layered systems are shifted upfield and hence shielded by the opposing ring. These shielding effects are clearly distance related. For **10a** as compared to **15a** we find $\Delta\delta$ values ranging from 0.21 to 0.33 ppm. The shift is the largest for $H_{4'}$ which would be held closest to the opposing ring (see Table I) and the smallest for $H_{6'}$ and $H_{7'}$ which would be held the furthest away. Intermediate behavior is observed for $H_{5'}$ and $H_{8'}$ whose changes are nearly identical.

For the layered 1,8-naphthyridine system **10b** the shielding effects are diminished (0.11–0.22 ppm). It is doubtful that the geometry of this molecule is much different from **10a** but more likely that the anisotropic deshielding effect is simply less for this ring system. The greater difference between $H_{6'}$ and $H_{7'}$ in **10b** implies that the canting of these two rings towards each other may be more pronounced such that $H_{7'}$ is held closer to the opposing ring than $H_{6'}$. This hypothesis is in accord with our earlier observation that similar canting in **10a** results from the elimination of an $H_{1'}$–$H_{1''}$ interaction. The mixed system **10c** shows a very consistent effect for the $\Delta\delta$ values of the quinoline ring protons and increased shielding for protons on the 1,8-naphthyridine ring. The tetramethoxy derivative **10f** shows the largest shielding effect as compared with **15c**. These effects are more pronounced in the electron-rich dimethoxybenzo ring where the upfield shift averages 0.74 ppm. The layered quinone system **13** shows only moderate shielding as compared with the analogous **16**.

3. Ultraviolet Spectra. Table III summarizes some pertinent UV absorption data for the annelated TCU's **10a–c** and the appropriate model compounds **15a,b**. In general, the quinoline systems show a long-wavelength band in the region 295–322 nm, which evidences some fairly well resolved vibrational structure. For the 1,8-naphthyridines, the same band is evident but shifted about 1 nm to longer wavelength and less well resolved. These features result from the presence of the second nitrogen whose additional lone pair electrons broadens the n-π^* vibrational transitions.

In comparison with the model compounds, the absorption maxima of the TCU derivatives are shifted 3–4 nm to longer wavelength while the intensities are at least doubled. The shift is indicative of a small interring delocalization and concomitant with a decrease of the n-π^* excitation energy. Tashiro and co-workers have observed a similar bathochromic shift in [3.3]orthocyclophanes with facing benzene and naphthalene rings.[7] The intensity increase is expected for a molecule possessing two chromophores.

4. Reduction Potentials. Quinoline quinones are known to undergo reversible two-electron reductions to the corresponding hydroquinone dianions.[21] By cyclic voltammetry we observe a clear reduction wave for **16** at $E_{1/2}$ = 0.6 V versus SCE. The TCU derivatives **11** and **12** show essentially the same reduction potential. The layered quinone **13** also shows a single reduction wave at 0.6 V, indicating that both quinone rings are reduced concurrently at the same potential.

For the diquaternary salt **14a**, on the other hand, we observe two separate irreversible reductions with cathodic peak potentials of −0.72 and −1.10 V versus SCE. These values bracket the single reduction wave observed for **17** at −0.90 V (see Figure 3). Two important observations can be made. At scan rates of up to 800 mV/s, the radicals formed by reduction of these *N*-methylquinolinium salts are unstable toward reoxidation and hence the waves are totally irreversible. Second, the two rings of **14a** influence one another's reduction potentials. The first reduction

(19) Thummel, R. P.; Kohli, D. K. *J. Heterocycl. Chem.* **1977**, *14*, 685.
(20) Braun, J. V.; Petzgold, A.; Schultheiss, A. *Chem. Ber.* **1923**, *56*, 1347.
(21) Evans, D. H.; Griffith, D. A. *Electroanal. Chem.* **1982**, *134*, 301.

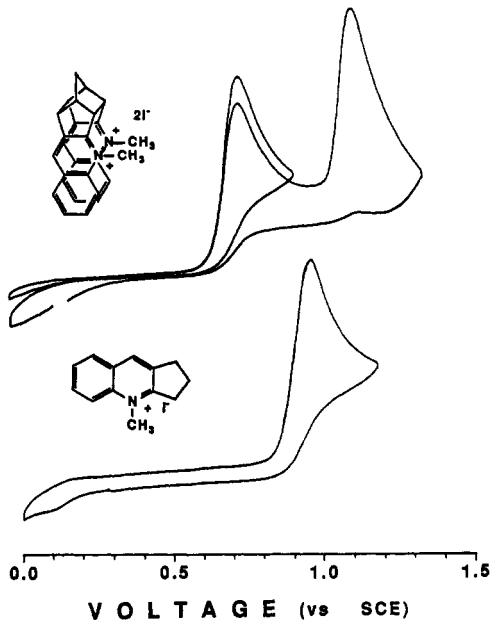


Figure 3. Cyclic voltammograms of *N,N*-dimethyl-2,3:7,6-bis-(2′,3′-quinolino)TCU diiodide (**14a**) and *N*-methylcyclopenta-[*b*]quinolinium iodide (**17**) in DMF containing 0.1 M TBAP at 25 °C at a sweep rate of 200 mV/s.

occurs more readily because of the dicationic nature of **14a** while the second reduction is more difficult. We know that the pyrido rings of these layered systems are closer together than their annelated benzo counterparts (see Table II). The disparate observations for **13** and **14a** are thus in qualitative agreement with the relative distance between the sites undergoing reduction.

In conclusion, we have demonstrated that the TCU ring system can be annelated to a variety of aromatic heterocycles in a stepwise fashion by employment of the Friedländer condensation. These layered aromatic rings show readily predictable structural characteristics as well as physical properties consistent with electronic interaction between the decks. Further studies on related annelated TCU derivatives are underway with particular emphasis on the design of cleftlike host systems and charge-transfer mediators.

Experimental Section

Nuclear magnetic resonance spectra were recorded on a General Electric QE-300 spectrometer. ^{1}H NMR chemical shifts are reported in ppm downfield from Me_4Si or from 3-(trimethylsilyl)propionic-2,2,3,3-d_4 acid, sodium salt (TSP) when deuterium oxide (D_2O) was used as solvent. ^{13}C NMR chemical shifts are reported in ppm downfield from Me_4Si referenced to the central line of $CDCl_3$. Infrared spectra were recorded on a Perkin-Elmer 1330 spectrophotometer. Ultraviolet spectra were obtained on a Perkin-Elmer 330 spectrophotometer. Mass spectra were obtained on a Hewlet-Packard 5970A GC–mass spectrometer operating at 70 eV. Cyclic voltammograms were recorded in acetonitrile and DMF according to a procedure which has been previously described.[22] Melting points were obtained on a Fisher-Johns melting point apparatus and were uncorrected. All solvents were freshly distilled reagent grade. Elemental analyses were performed by Canadian Microanalytical Service, Ltd., Delta, B.C., and HRMS were obtained on a CEC-Dupont 21-110B spectrometer by peak matching at 70 eV.

7,6-(2′,3′-Quinolino)TCU-2-one (5a). A mixture of TCU-2,7-dione[12] (0.88 g, 5 mmol), 2-aminobenzaldehyde[23] (1.32 g, 10.1 mmol), and one pellet of potassium hydroxide in 15 mL of absolute ethanol was refluxed under nitrogen for 48 h. After evaporation of the solvent, the crude product was purified by chromatography on silica gel (30 g), eluting with 1:1 hexane–EtOAc, and crystallized upon slow evaporation of the eluent to give 0.7 g (55%) of **5a**: mp 145–146 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, $H_{8'}$, $J_{7',8'}$ = 8.3 Hz), 7.74 (s, $H_{4'}$), 7.68 (d, $H_{5'}$, $J_{5',8'}$ = 7.8 Hz), 7.61 (t, $H_{7'}$), 7.45 (t, $H_{6'}$), 3.5 (2 overlapping m, 3 H), 2.9 (2 overlapping m, 3 H), 2.1 (m, 2 H), 1.65 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) 218.0 (CO), 169.1, 147.1, 138.0, 129.9, 128.7, 128.2, 127.1, 126.9, 125.7. 56.3, 53.4, 49.8, 47.1, 41.8, 40.2, 34.9 ppm; IR (KBr) 3030, 2900, 2940, 1715 (C=O), 1610, 1560, 1490, 1450, 1390, 1295, 1232, 1120 cm^{-1}; mass spectra, *m/e* (relative intensity) 261 (100, M$^+$), 232 (45), 218 (28), 180 (34), 179 (35), 167 (50), 109 (20).

7,6-(2′,3′-[1,8]Naphthyridino)TCU-2-one (5b). A mixture of TCU-2,7-dione[12] (0.88 g, 5 mmol), 2-aminonicotinaldehyde[24] (0.73 g, 6 mmol), and one pellet of KOH in 20 mL of absolute ethanol was stirred at room temperature under nitrogen for 12–16 h. Upon formation of a precipitate, the reaction mixture was refluxed for 48 h. Water (5 mL) and charcoal (1 g) were then added, and the mixture was refluxed for an additional hour. After filtration, the solvent was evaporated and the crude product was chromatographed on alumina (40 g) eluting with 19:1 EtOAc–MeOH to afford 0.65 g (50%) of **5b** as a white solid: mp 195 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.96 (d, $H_{7'}$, $J_{6',7'}$ = 4 Hz), 8.05 (d, $H_{5'}$, $J_{5',6'}$ = 8 Hz), 7.77 (s, $H_{4'}$), 7.39 (dd, $H_{6'}$, $J_{6',7'}$ = 4.2 Hz, $J_{5',6'}$ = 7.8 Hz), 3.55 (2 overlapping m, 3 H), 2.95 (2 overlapping m, 3 H), 2.1 (2 overlapping m, 3 H), 1.60 (d, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) 216.9 (CO), 173.3, 155.8, 152.0, 139.6, 136.4, 130.6, 121.5, 96.0, 57.4, 56.8, 53.9, 50.1, 47.4, 42.0, 40.5, 35.3 ppm; IR (KBr) 2960, 2940, 2920, 2826, 1737 (C=O), 1600, 1560, 1488, 1404, 1380, 1285, 1246, 1130, 1100, 950, 822, 810 cm^{-1}.

7,6-(2′,3′-(8′-Methoxyquinolino))TCU-2-one (5c). The same procedure described above for **5a** was followed using TCU-2,7-dione[12] (0.54 g, 3.1 mmol) and 3-methoxy-2-aminobenzaldehyde[25] (0.57 g, 3.8 mmol) to yield 0.8 g (90%) of **5c** as a white solid after chromatography on alumina (40 g), eluting with EtOAc: mp 223–225 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.7 (s, $H_{4'}$), 7.36 (dd, $H_{6'}$, J = 7.8, 8 Hz), 7.24 (d, $H_{5'}$), 6.97 (d, $H_{7'}$), 4.03 (s, 3 H, OCH_3), 3.65 (d, 1 H, J = 11 Hz), 3.39 (2 overlapping m, 2 H), 2.97 (m, 1 H), 2.82 (2 overlapping m, 2 H), 2.05 (s, overlapping quartet, 3 H), 1.60 (d, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) 207.6 (CO), 168.1, 155.6, 138.8, 130.1, 128.4, 126.1, 119.3, 107.7, 57.2, 56.8, 55.9, 53.9, 50.2, 47.6, 42.0, 40.4, 35.3 ppm; IR (KBr) 2917, 2880, 1710 (C=O), 1478, 1451, 1247, 1112, 1073, 898, 723 cm^{-1}.

7,6-(2′,3′-(5′,8′-Dimethoxyquinolino))TCU-2-one (5d). The procedure described above for **5a** was followed using TCU-2,7-dione[12] (0.2 g, 1.14 mmol) and 3,6-dimethoxy-2-aminobenzaldehyde[17c] (0.25 g, 1.4 mmol) to give 0.28 g (80%) of **5d** after chromatography on alumina (30 g), eluting with EtOAc: mp 211–212 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (s, $H_{4'}$) 6.87 (d, $H_{6'}$ or $H_{7'}$, $J_{6',7'}$ = 7.5 Hz), 6.72 (d, $H_{6'}$ or $H_{7'}$), 3.99 (s, OCH_3), 3.93 (s, OCH_3), 3.70 (d, 1 H, J = 10 Hz), 3.41 (2 overlapping m, 2 H), 2.98 (s, 1 H), 2.85 (2 overlapping m, 2 H), 2.07 (s overlapping q, 3 H), 1.61 (d, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) 218.3 (C=O), 168.5, 149.5, 148.5, 139.2, 138.0, 125.1, 120.2, 106.7, 103.8, 57.2, 56.9, 55.9, 55.7, 53.9, 50.2, 47.5, 42.2, 40.3, 35.2 ppm; IR (KBr) 2960, 2930, 1732 (C=O), 1669, 1481, 1402, 1372, 1260, 1157, 1090, 1076, 801, 722 cm^{-1}.

7-Hydroxy-2,3-(2′,3′-quinolino)TCU (7). To a solution of $LiAlH_4$ (0.3 g, 7.9 mmol) in 20 mL of anhydrous THF was added a solution of **5a** (1 g, 3.8 mmol) in 30 mL of anhydrous THF under N_2, and the mixture was refluxed for 16 h. After cooling, excess $LiAlH_4$ was destroyed by the successive addition of 0.3 mL of H_2O, 0.3 mL of aqueous KOH, and 1 mL of H_2O. The granular inorganic precipitate was filtered, and evaporation of the filtrate yielded a white solid which was recrystallized from 1:1 EtOAc–hexane to give 0.8 g (80%) of **7**: mp 175–177 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, $H_{8'}$, $J_{7',8'}$ = 8.1 Hz), 7.76 (s, $H_{4'}$), 7.71 (d, $H_{5'}$, $J_{5',6'}$ = 7.8 Hz), 7.61 (d of d, $H_{7'}$, $J_{6'7'}$ = 7 Hz), 7.47 (dd, $H_{6'}$, $J_{5',6'}$ = 7.7 Hz), 4.42 (m, 1 H), 3.32 (2 overlapping m, 2 H), 3.21 (m, 1 H), 2.67 (m, 1 H), 2.59 (m, 1 H), 2.45 (m, 1 H), 2.13 (m, 2 H), 2.01 (m, 1 H), 1.81 (AB quartet, 2 H), 0.75 (m, 1 H); ^{13}C NMR

(22) Thummel, R. P.; Goulle, V.; Chen, B. *J. Org. Chem.* **1989**, *54*, 3057.

(23) (a) Opie, J. W.; Smith, L. I. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol III, p 56. (b) Kalir, A. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol V, p 825.

(24) Caluwe, P.; Majewicz, T. *J. Org. Chem.* **1979**, *44*, 531.

(25) Tröger, J.; Gerö, St. *J. Prakt. Chem.* **1926**, *113*, 293.

(75 MHz, $CDCl_3$) 173.5 ($C_{2'}$), 141.5, 129.9, 128.8, 128.5, 127.4, 126.1, 76.4 (C_7), 55.9, 51.9, 49.9, 49.8, 49.3, 43.8, 37.2, 33.8 ppm; IR (KBr) 3200 (b), 2890, 1400, 1310, 1154, 1098, 737 cm^{-1}. Anal. Calcd for $C_{18}H_{17}NO \cdot H_2O$: C, 76.86; H, 6.76; N, 4.98. Found: C, 76.55; H, 6.86; N, 5.01.

2,3-(2',3'-Quinolino)TCU-6-ene (9a). The procedure described above for **5a** was followed using TCU-6-en-2-one[16] (0.12 g, 0.75 mmol) and 2-aminobenzaldehyde[23] (1.2 g, 0.99 mmol). After evaporation of the solvent, the crude product was chromatographed on alumina (40 g), eluting with EtOAc to give a yellow oil (0.1 g, 54%): ^1H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, $H_{8'}$, $J_{7',8'}$ = 8.3 Hz), 7.67 (d, $H_{5'}$, $J_{5',6'}$ = 8 Hz), 7.62 (s, $H_{4'}$), 7.58 (dd, $H_{7'}$, $J_{6',7'}$ = 7 Hz), 7.42 (dd, $H_{6'}$), 5.61 (d, 1 H, =CH), 5.48 (d, 1 H, =CH), 3.40 (s, 1 H), 3.23 (overlapping m, 3 H), 2.91 (m, 1 H), 2.77 (m, 1 H), 1.92 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) 172.7, 146.6, 141.6, 136.7, 136.4, 128.5, 128.0, 127.9, 127.4, 125.4, 125.0, 62.1, 60.9, 51.6, 50.2, 49.2, 47.1, 34.2 ppm; IR ($CHCl_3$) 2948m 1634, 1576, 1500, 1400, 1336, 1284, 905, 857, 832, 750 cm^{-1}; HRMS m/e calcd for $C_{18}H_{15}N$ 245.12045; observed 245.12076.

2,3-(2',3'-[1,8]Naphthyridino)TCU-6-ene (9b). The procedure described above for **5a** was followed using TCU-6-en-2-one[16] (0.12 g, 0.75 mmol) and 2-aminonicotinaldehyde[24] (0.12 g, 0.98 mmol). After evaporation of the solvent, the crude product was chromatographed on alumina (35 g) eluting with 95:5 EtOAc–MeOH to give **9b** (50 mg, 27%) as a yellow oil: ^1H NMR (300 MHz, $CDCl_3$) δ 8.93 (br s, $H_{7'}$), 8.03 (d, $H_{5'}$, $J_{5',6'}$ = 7.3 Hz), 7.61 (s, $H_{4'}$), 7.36 (dd, $H_{6'}$, $J_{6',7'}$ = 4.3 Hz), 5.63 (m, 1 H, =CH), 5.46 (m, 1 H, =CH), 3.43 (s, 1 H), 3.22 (overlapping m, 3 H), 2.94 (m, 1 H), 2.79 (m, 1 H), 1.96 (m, 2 H); ^{13}C NMR (300 MHz, $CDCl_3$), 176.8, 155.6, 151.2, 142.9, 137.0, 136.4, 136.1, 127.9, 121.7, 120.9, 62.2, 61.0, 51.9, 50.4, 49.3, 47.0, 34.3 ppm; IR ($CHCl_3$) 2958, 1596, 1567, 1402, 1260, 1097, 1004, 908, 833, 815 cm^{-1}; HRMS m/e calcd for $C_{17}H_{14}N_2$ 246.11569, observed 246.11516.

2,3:7,6-Bis(2',3'-quinolino)TCU (10a). Method A. A mixture of monoketone **5a** (0.5 g, 1.9 mmol), 2-aminobenzaldehyde[23] (0.32 g, 2.6 mmol), and one pellet of KOH in 20 mL of toluene was refluxed under nitrogen for 18 h using a Dean–Stark trap. The reaction was monitored by TLC (silica gel, EtOAc). After cooling, the solvent was evaporated and the crude product was chromatographed on silica gel (20 g), eluting with 9:1 EtOAc–MeOH. Subsequent crystallization from EtOAc–MeOH yielded 0.31 g (57%) of **10a**: mp 295 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, $H_{8'}$, $J_{7',8'}$ = 8.3 Hz), 7.43 (s, $H_{4'}$), 7.39 (d, $H_{5'}$, $J_{5',6'}$ = 8.2 Hz), 7.34 (t, $H_{7'}$), 7.19 (t, $H_{6'}$), 3.71 (br s, 2 H), 3.58 (br s, 4 H), 2.61 (s, exchanges with D_2O), 2.19 (quartet, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) 170 ($C_{2'}$), 147 ($C_{8a'}$), 140 ($C_{3'}$), 129, 128.7, 128.0, 127.1, 126.8 ($C_{4a'}$), 125.5, 59.2, 53.2, 49.4, 35.7 ppm; IR (KBr) 3030, 2910, 2840, 1630, 1570, 1500, 1460, 1410, 1310, 1160, 1100, 900, 750 cm^{-1}; GC–MS m/e (relative intensity) 346 (100, M^+), 331 (18), 180 (96), 167 (20).

Method B. A mixture of TCU-2,7-dione[12] (0.22 g, 1.25 mmol) and 2-aminobenzaldehyde[23] (0.35 g, 2.9 mmol) in 20 mL of toluene with 0.5 mL of a 50% KOH solution in MeOH was refluxed for 7 h using a Dean–Stark water separator. After cooling, the toluene was evaporated and the crude product was chromatographed on silica gel (15 g), eluting with 9:1 EtOAc–MeOH to give 0.35 g (81%) of **10a**; recrystallization from EtOAc provided pure material, mp 291 °C: spectral properties identical with those obtained by method A.

2,3:7,6-Bis(2',3'-[1,8]naphthyridino)TCU (10b). To a mixture of 0.13 g (0.5 mmol) of **5b** and 0.08 g (0.6 mmol) of 2-aminonicotinaldehyde[24] in 15 mL of absolute ethanol was added 7 drops of 50% methanolic KOH, and the reaction was stirred under nitrogen at room temperature for 6 h and then refluxed for 8 h. After cooling, slow evaporation of the solvent provided a white precipitate which was collected by filtration and washed with cold CH_2Cl_2. The filtrate was concentrated slowly to provide a second crop for a combined yield of 0.1 g (60%): mp >300 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.79 (d, $H_{7'}$, $J_{6',7'}$ = 3.2 Hz), 7.89 (d, $H_{5'}$, $J_{5',6'}$ = 8.1 Hz), 7.58 (s, $H_{4'}$), 7.22 (dd, $H_{8'}$), 3.87 (s, 2 H), 3.68 (s, 2 H), 3.65 (s, 2 H), 2.26 (AB quartet, 2 H, J_{gem} = 25.6, J_{vic} = 11.5 Hz), 2.09 (s, exchanges with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$)[26] 151.3, 136.7, 129.5, 112.2, 59.7, 53.7, 49.3, 35.9 ppm; IR (KBr) 2955, 2920, 1630, 1602, 1560, 1482, 1405, 1243, 1103, 800, 794 cm^{-1}. HRMS m/e calcd for $C_{23}H_{16}N_4$ 348.13748, observed 348.13727.

2,3-(2',3'-Quinolino)-7,6-(2'',3''-[1,8]naphthyridino)TCU (10c). Method A. To a mixture of **5a** (0.1 g, 0.38 mmol) and 2-aminonicotinaldehyde[24] (0.04 g, 0.33 mmol) in 20 mL of acetic acid was added 4 drops of sulfuric acid, and the mixture was refluxed under nitrogen for 18 h. After cooling, the reaction was poured into a mixture of 20 mL of ammonium hydroxide and 20 g of ice and extracted with 3 × 15 mL of CH_2Cl_2. After drying over $MgSO_4$ and evaporation of the solvent, the crude product was chromatographed on 10 g of silica gel, eluting with 9:1 EtOAc–MeOH to provide material which was recrystallized from EtOAc to give **10c** (15 mg, 9%): mp 296–300 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.69 (d, $H_{7''}$), 7.74 (2 d, $H_{8'}$ and $H_{5''}$), 7.45 (s, $H_{4'}$ and $H_{4''}$), 7.39 (d, $H_{5'}$, $J_{5',6'}$ = 8.3 Hz), 7.33 (t, $H_{7'}$), 7.18 (t, $H_{6'}$), 7.1 (dd, $H_{6''}$, J = 4, J = 7.6 Hz), 3.77 (br s, 2 H), 3.6 (s, 4 H), 3.08 (br s, exchanges with D_2O), 2.21 (AB quartet, 2 H, J_{gem} = 21.5, J_{vic} = 11.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$), 173.9, 169.5, 155.1, 151.3, 146.6, 140.8, 139.2, 136.1, 129.2, 128.9, 128.7, 128.6, 127.9, 126.7, 125.3, 120.8, 59.3, 59.2, 53.4, 53.3, 49.2, 49.1, 35.7 ppm; IR (KBr) 2950, 1635, 1597, 1565, 1488, 1405, 927, 820 cm^{-1}. Anal. Calcd for $C_{24}H_{17}N_3 \cdot H_2O$: C, 78.88; H, 5.25; N, 11.50. Found: C, 78.89; H, 5.24; N, 11.56.

Method B. To a mixture of **5b** (0.12 g, 0.5 mmol) and 2-aminobenzaldehyde[23] (0.08 g, 0.75 mmol) in 20 mL of toluene was added 5 drops of 50% methanolic KOH, and the mixture was refluxed under nitrogen using a Dean–Stark trap. After 16 h the reaction was cooled, the solvent was evaporated, and the crude product was chromatographed on 30 g of alumina, eluting with 9:1 EtOAc–MeOH to provide 0.6 g (40%) of **10c**, mp 297–298 °C: NMR spectra (^1H and ^{13}C) were identical with those described in method A.

2,3:7,6-Bis(2',3'-(8'-methoxyquinolino))TCU (10d). The same procedure described above for **10a** was followed using monoketone **5c** (0.16 g, 0.55 mmol) and 3-methoxy-2-aminobenzaldehyde[25] (0.1 g, 0.66 mmol) to give 0.13 g (58%) of **10d** after chromatography on alumina (30 g), eluting with 9:1 EtOAc–MeOH: mp >300 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.41 (s, 2 H, $H_{4'}$), 7.06 (dd, 2 H, $H_{6'}$, J = 7.8, 7.4 Hz), 6.97 (d, 2 H, $H_{5'}$), 6.68 (d, 2 H, $H_{7'}$), 3.82 (s, 6 H, OCH_3), 3.78 (s, 2 H), 3.54 (s, 2 H), 3.52 (s, 2 H), 2.15 (AB quartet, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$), 169.0, 155.2, 148.5, 140.3, 129.1, 128.0, 125.5, 119.2, 107.7, 59.6 (OCH_3), 55.9, 53.4, 49.1, 35.7 ppm; IR (KBr) 2960, 2940, 1610, 1502, 1477, 1406, 1359, 1265, 1100, 1082, 762, 750, 718 cm^{-1}. Anal. Calcd for $C_{27}H_{22}N_2O_2 \cdot H_2O$: C, 76.41; H, 5.66; N, 6.60. Found: C, 76.35; H, 5.56; N, 6.28.

2,3-(2',3'-Quinolino)-7,6-(2'',3''-(5'',8''-dimethoxyquinolino))TCU (10e). The procedure described above for **10a** was followed using monoketone **5d** (0.21 g, 0.65 mmol) and 2-aminobenzaldehyde[23] (0.11 g, 0.91 mmol) to give 0.21 g (78%) of **10e** after chromatography on alumina (40 g), eluting with 95:5 EtOAc–MeOH: mp 119–121 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.86 (s, $H_{4''}$), 7.76 (d, $H_{8'}$, $J_{7',8'}$ = 8.4 Hz), 7.47 (s, $H_{4'}$), 7.41 (d, $H_{5'}$, $J_{5',6'}$ = 8.0 Hz), 7.32 (dd, $H_{7'}$, $J_{6',7'}$ = 7 Hz), 7.17 (dd, $H_{6'}$), 6.51 (d, $H_{7''}$, $J_{6'',7''}$ = 8.5 Hz), 6.35 (d, $H_{6''}$), 3.82 (s, 3 H, OCH_3), 3.79 (br s, 2 H), 3.76 (s, 3 H, OCH_3), 3.56 (br s, 4 H), 2.16 (AB quartet, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) 170.0, 169.1, 149.2, 148.4, 146.4, 139.7, 139.2, 138.6, 128.9, 128.6, 127.8, 127.0, 126.7, 125.3, 123.7, 119.7, 106.8, 103.4, 59.6, 59.5, 56.1, 55.5, 53.3, 53.0, 49.4, 49.1, 35.6 ppm; IR (KBr) 2950, 2940, 1610, 1480, 1402, 1370, 1320, 1260, 1160, 1150, 1185, 1175, 1165, 820, 800, 754, 722 cm^{-1}. Anal. Calcd for $C_{27}H_{24}N_2O_3 \cdot {}^1/_2H_2O$: C, 78.07; H, 5.54; N, 6.75. Found: C, 78.20; H, 5.41; N, 6.89.

2,3:7,6-Bis(2',3'-(5',8'-dimethoxyquinolino))TCU (10f). A mixture of monoketone **5d** (0.2 g, 0.62 mmol), 3,6-dimethoxy-2-aminobenzaldehyde[17c] (0.17 g, 0.94 mmol), and five drops of methanolic KOH in 30 mL of toluene was refluxed for 18 h using a Dean–Stark trap. The crude product, obtained after the same workup used for **10a**, was chromatographed on 30 g of alumina, eluting with 95:5 EtOAc–MeOH to give 0.27 g (90%) of **10f**: mp 268–270 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.89 (s, 2 H, $H_{4'}$), 6.07 (d, 2 H, $H_{7'}$, $J_{6',7'}$ = 8.5 Hz), 6.00 (d, 2 H, $H_{6'}$), 3.82 (s, 2 H), 3.72 (s, 6 H, OCH_3), 3.70 (s, 6 H, OCH_3), 3.55 (s, 2 H), 3.52 (s, 2 H), 2.83 (br s, 2 H, H_2O), 2.14 (AB quartet, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$), 169.3, 148.5, 148.4, 139.7, 124.1, 119.8, 111.7, 108.9, 103.6, 60.4, 56.1, 55.6, 53.1, 49.3, 35.7 ppm; IR (KBr) 2950, 2938, 1670,

(26) Too dilute to observe quaternary carbons.

1661, 1612, 1503, 1480, 1372, 1324, 1262, 1158, 1093, 1072, 900, 804, 723 cm^{-1}; HRMS m/e calcd for $C_{29}H_{26}N_2O_4$ 466.18923, observed 466.18911.

7,6-(2′,3′-(5′,8′-Dioxoquinolino))TCU-2-one (11). A solution of ceric ammonium nitrate (CAN, 1.28 g, 2.34 mmol) in acetonitrile–water (1:1, 15 mL) was added dropwise to a stirred, ice-cold suspension of **5d** (0.25 g, 0.78 mmol) in acetonitrile–water (2:1, 15 mL) to which had been added a solution of 2,6-pyridinedicarboxylic acid *N*-oxide[17b] (PDANO) (0.43 g, 2.34 mmol) in 5 mL of 2:1 acetonitrile–water. After the addition was complete, the reaction mixture was kept at 0 °C for 30 min and stirred for an additional 30 min at room temperature. The reaction was followed by TLC (silica gel, ETOAc). Since the reaction was not yet complete, additional CAN (0.85 g, 1.55 mmol) and PDANO (0.25 g, 1.37 mmol) were added at once to the mixture, and it was stirred for an additional 1 h at room temperature. The mixture was then diluted with water and extracted with CH_2Cl_2 (3 × 30 mL). The combined extracts were washed with brine and water, dried over $MgSO_4$, and concentrated at room temperature to give a yellow solid (180 mg, 80%), which turned brown upon exposure to light: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (s, $H_{4'}$), 7.08 (d, $H_{6'}$ or $H_{7'}$, $J_{6,7}$ = 10.4 Hz), 6.98 (d, $H_{6'}$ or $H_{7'}$), 3.64 (d, 1 H, J = 11 Hz), 3.44 (2 overlapping m, 2 H), 3.05 (s, 1 H), 2.88 (2, overlapping m, 2 H), 2.09 (s overlapping m, 3 H), 1.53 (d, 1 H, J = 19 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) 216.9 (CO, ketone), 184.9 (CO, quinone), 183.1 (CO, quinone), 175.2, 146.3, 146.2, 138.6, 137.3, 128.7, 127.8, 57.9, 57.2, 53.6, 50.7, 47.7, 42.2, 40.4, 35.2 ppm; IR (KBr) 2940, 1725 (C=O), 1660, 1558, 1353, 1290, 1121, 1058, 844, 815 cm^{-1}.

2,3-(2′,3′-Quinolino)-7,6-(2″,3″-(5″,8″-dioxoquinolino))TCU (12). The procedure described above for **11** was followed using **10e** (0.1 g, 0.25 mmol), CAN (0.94 g, 1.7 mmol), and PDANO (0.32 g, 1.7 mmol) to give **12** (87 mg, 94%) as a red solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 (d, $H_{8'}$, $J_{7',8'}$ = 7.9 Hz), 8.01 (d, $H_{5'}$, $J_{5',6'}$ = 8.1 Hz), 7.83 (s, $H_{4'}$ or $H_{4''}$), 7.81 (s, $H_{4'}$ or $H_{4''}$), 7.62 (dd, $H_{7'}$, $J_{6',7'}$ = 7.8 Hz), 7.47 (dd, $H_{6'}$), 6.84 (d, $H_{7''}$, $J_{6'',7''}$ = 10.4 Hz), 6.75 (d, $H_{6''}$), 4.00 (AB quartet, 2 H), 3.73 (m, 4 H), 2.28 (AB quartet, 2 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 184.8, 182.8, 175.5, 169.1, 147.2, 146.7, 145.4, 138.9, 138.4, 136.8, 129.1, 128.8, 128.3, 127.5, 127.2, 126.7, 125.7, 60.4, 59.9, 53.3, 53.2, 49.6, 49.0, 35.6 ppm; IR (KBr) 2960, 1660, 1590, 1400, 1360, 1300, 837, 818, 764, 722 cm^{-1}.

2,3:7,6-Bis(2′,3′-(5′,8′-dioxoquinolino))TCU (13). The procedure described for **11** was followed using **10f** (70 mg, 0.15 mmol), CAN (0.75 g, 1.37 mmol), and PDANO (0.25 g, 1.37 mmol) to give **13** (55 mg, 90%) as a yellow solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (s, $H_{4'}$), 6.87 (d, $H_{6'}$ or $H_{7'}$, $J_{6'7'}$ = 10.3 Hz), 6.78 (d, $H_{6'}$ or $H_{7'}$), 3.73 (s, 2 H), 3.62 (s, 2 H), 3.53 (s, 2 H), 2.16 (AB quartet, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$), 184.7, 182.8, 175.1, 146.7, 138.7, 137.1, 127.7, 127.6, 61.6, 53.1, 49.1, 35.6 ppm; IR (KBr) 2948, 1678 (CO), 1660 (CO), 1595, 1356, 1300, 1261, 1062, 845, 813, 797 cm^{-1}.

***N,N*-Dimethyl-2,3:7,6-bis(2′,3′-quinolino)TCU Diiodide (14a).** A mixture of **10a** (61 mg, 0.17 mmol) and CH_3I (0.26 g, 1.8 mmol) in 5 mL of CH_3CN was sealed in a heavy wall glass tube and heated at 140 °C for 20 h. The tube was then cooled and opened, and the solution was concentrated to half of its volume. A yellow-brown precipitate was collected by filtration and washed with 2 × 10 mL of cold hexane to afford 70 mg (63%) of **14a**: ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.69 (s, 2 H, $H_{4'}$), 8.23 (d, 2 H, $H_{8'}$, $J_{7',8'}$ = 8.9 Hz), 8.10 (d, 2 H, $H_{5'}$, $J_{5',6'}$ = 8.1 Hz), 8.02 (t, 2 H, $H_{7'}$), 7.80 (t, 2 H, $H_{6'}$), 4.57 (s, 6 H, *N*-methyl), 4.03 (s, 2 H), 3.9 (s, 2 H), 2.5 (s, 2 H), 2.32 (quartet, 2 H); ^{13}C NMR (75 MHz, DMSO-d_6), 168.3, 141.9, 139.5, 137.0, 133.8, 129.7, 129.6, 127.6, 119.6, 61.5, 52.7, 48.6, 41.7, 35.1 ppm; IR (KBr) 2940, 1595, 1510, 1460, 1190, 1150, 1115, 1080, 950, 940, 770 cm^{-1}.

1′,1″-Trimethylene-2,3:7,6-bis(2′,3′-quinolino)TCU Dibromide (14b). A mixture of **10a** (50 mg, 0.14 mmol) and 1,3-dibromopropane (5 mL) was heated at 120 °C for 36 h. Upon cooling a precipitate was formed, collected by filtration, and washed thoroughly with cold CH_2Cl_2 to provide 80 mg (100%) of **14b**: ^{1}H NMR (300 MHz, D_2O) δ 8.44 (s, 2 H, $H_{4'}$), 8.11 (d, 2 H, $H_{8'}$, $J_{7',8'}$ = 9 Hz), 7.89 (t overlapping d, 4 H, $H_{5'}$ and $H_{7'}$, $J_{5',6'}$ = 7.8 Hz), 7.68 (t, 2 H, $H_{6'}$), 5.59 (dt, 2 H, CH_2N, J = 15, 1.5 Hz), 5.23 (dd, 2 H, CH_2N), 4.66 (s, 2 H), 4.17 (s, 2 H), 4.11 (s, 2 H), 2.90 (m, 2 H), 2.65 (AB quartet, 2 H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6), 168.5, 142.0, 140.4, 134.7, 134.3, 130.3, 129.7, 128.1, 118.0, 58.4, 54.4, 53.0, 50.1, 35.0 ppm; IR (KBr) 2930, 1618, 1580, 1500, 1490, 1421, 1385, 1240, 1130, 742 cm^{-1}.

2,3:7,6-Bis(2′,3′-quinolino)TCU Di-*N*-oxide (14c). A mixture of **10a** (0.1 g, 0.3 mmol) and *m*-chloroperbenzoic acid (0.17 g, 1.0 mmol) in 20 mL of $CHCl_3$ was stirred at room temperature under nitrogen for 18 h. The solution was then washed with 200 mL of 5% $NaHCO_3$, dried over $MgSO_4$, and concentrated. Chromatography on silica gel (15 g), eluting with 1:1 MeOH–EtOAc, gave 80 mg (70%) of **14c**: mp >300 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (d, $H_{8'}$, $J_{8',7'}$ = 8.6 Hz), 7.47 (d, $H_{5'}$, $J_{5',6'}$ = 8 Hz), 7.40 (t, $H_{7'}$, $J_{6',7'}$ = 7.4 Hz), 7.29 (t, $H_{6'}$), 7.19 (s, $H_{4'}$), 4.42 (s, 2 H), 3.62 (s, 4 H), 2.18 (quartet, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$), 157.3, 140.8, 129.3, 129.1, 127.9, 127.4, 120.2, 120.1, 119.7, 59.6, 49.9, 47.5, 34.9 ppm; IR (KBr) 2940, 1740, 1572, 1495, 1396, 1355, 1320, 1292, 1220, 1090 cm^{-1}.

5,8-Dimethoxycyclopenta[*b*]quinoline (15c). The procedure described above for **5a** was followed using cyclopentanone (0.168 g, 2 mmol) and 2-amino-3,6-dimethoxybenzaldehyde[17c] (0.362 g, 2 mmol) to yield 0.24 g (52%) of **15c**: mp 98–100 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (s, H_4), 6.86 (d, H_6 or H_7, $J_{6,7}$ = 8.5 Hz), 6.69 (d, H_6 or H_7) 4.03 (s, 3 H, OCH_3), 3.94 (s, 3 H, OCH_3), 3.25 (t, 2 H), 3.09 (t, 2 H), 2.19 (quintet, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$), 167.0, 149.0, 148.5, 139.4, 135.1, 124.9, 120.3, 105.4, 102.6, 55.6, 55.5, 34.7, 30.4, 23.4 ppm; IR (KBr) 2980, 2920, 2820, 1600, 1468, 1380, 1360, 1310, 1248, 1199, 1122, 1080, 1045, 960, 897, 800, 797, 782, 718 cm^{-1}.

Cyclopenta[*b*]quinoline-5,8-quinone (16). The procedure described above for **11** was followed using **15c** (0.172 g, 0.75 mmol), CAN (1.65 g, 3 mmol), and PDANO (0.550 g, 3 mmol) to give **16** (81 mg, 54%) as a yellow solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.11 (s, H_4), 7.12 (d, H_6 or H_7, $J_{6,7}$ = 10.4 Hz), 6.93 (d, H_6 or H_7), 3.15 (t, 2 H), 3.04 (t, 2 H), 2.17 (quintet, 2 H); IR (KBr) 3005, 2940, 1675 (C=O), 1645 (C=O), 1580, 1442, 1410, 1390, 1340, 1290, 1248, 1135, 1090, 1050, 1020, 850, 790 cm^{-1}.

***N*-Methylcyclopenta[*b*]quinolinium Iodide (17).** A mixture of **15a**[19] (0.2 g, 1.2 mmol) and CH_3I (0.51 g, 3.6 mmol) in 20 mL of acetone was stirred for 18 h at room temperature under a nitrogen atmosphere. The reaction mixture was then concentrated to half of its volume, and the dark green preciptitate was collected by filtration and washed with cold acetone (20 mL) and cold acetonitrile (2 × 15 mL) to yield of 350 mg (93%) of **17**: ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.95 (s, H_4), 8.50 (d, H_8, $J_{7,8}$ = 8.9 Hz), 8.33 (d, H_5, $J_{5,6}$ = 8 Hz), 8.14 (t, H_7), 7.95 (t, H_6), 4.46 (s, 3 H, NCH_3), 3.64 (t, 2 H), 3.29 (t, 2 H), 2.32 (quintet, 2 H); IR (KBr) 2900, 2860, 1430, 1390, 1220, 1090, 890, 770, 745 cm^{-1}.

X-ray Structure Analysis. A clear colorless crystal of **10a** with the shape of a prismatic column having dimensions 0.50 × 0.25 × 0.15 mm was mounted on a glass fiber in a random orientation on an Enraf-Nonius CAD-4 automatic diffractometer. The radiation used was Mo Kα monochromatized by a dense graphite crystal assumed for all purposes to be 50% imperfect. Final cell constants, as well as other information pertinent to data collection and refinement, are listed in Table 4 of the supplementary material. The Laue symmetry was determined to be mmm, and from the systematic absences noted the space group was shown unambiguously to be *Pbca*. Intensities were measured using the θ–2θ scan technique, with the scan rate depending on the net count obtained in rapid pre-scans of each reflection. Two standard reflections were monitored periodically during the course of the data collection as a check of crystal stability and electronic reliability, and these did not vary significantly. In reducing the data, Lorentz and polarization factors were applied; however, no correction for absorption was made due to the small absorption coefficient.

The structure was solved by MULTAN,[27] which revealed the positions of all non-hydrogen atoms in the asymmetric unit, with the exception of the water of solvation. The usual sequence of isotropic and anisotropic refinement was followed, after which all hydrogens except those on water were entered in ideally calculated positions. The water hydrogens were located in difference Fourier syntheses. In the final cycles of full-matrix least-squares, none of the hydrogen parameters were varied, except the coordinates of those on water. Temperature factors were estimated based on the thermal motion of the associated atoms. After all shift/esd ratios were less than 0.3, convergence was

(27) Germain, G.; Main, P.; Woolfson, M. M. *Acta Crystallogr., Sect. A* **1971**, *A27*, 368.

reached at the agreement factors listed in Table 4 (supplementary material). No unusually high correlations were noted between any of the variables in the last cycle of least-squares refinement, and the final difference density map showed no peaks greater than 0.20 e/Å^3. All calculations were made using Molecular Structure Corporation's TEXRAY 230 modifications of the SDP-PLUS series of programs.

Acknowledgment. Financial support from the Robert A. Welch Foundation and the National Science Foundation (Grant CHE-8607935) is gratefully acknowledged. The NMR spectrometer was partially funded by the NSF (Grant CHE-866352). We thank Dr. James Korp for assistance with the X-ray crystal analysis and J.-L.L. would like to thank Prof. A. Emran for his generous assistance.

Registry No. **3a**, 25282-60-4; **4a**, 529-23-7; **4b**, 7521-41-7; **4c**, 70127-96-7; **4d**, 126522-16-5; **5a**, 113258-54-1; **5b**, 131251-68-8; **5c**, 131251-69-9; **5d**, 131251-70-2; **7**, 131251-63-3; **8**, 58228-96-9; **9a**, 131251-64-4; **9b**, 131251-71-3; **10a**, 113258-55-2; **10b**, 131251-74-6; **10c**, 131251-75-7; **10d**, 131251-76-8; **10e**, 131251-77-9; **10f**, 131251-78-0; **11**, 131251-65-5; **12**, 131251-72-4; **13**, 131251-66-6; **14a**, 113258-57-4; **14b**, 131251-79-1; **14c**, 113258-56-3; **15a**, 5661-06-3; **15c**, 131251-73-5; **16**, 131251-67-7; **17**, 35005-74-4; cyclopentanone, 120-92-3.

Supplementary Material Available: Four tables of data collection and processing parameters, positional parameters and ESD's, bond distances, and bond angles and the ^{1}H and ^{13}C NMR spectra of compounds **5a-d**, **9a,b**, **10b,f**, **11-13**, **14a-c**, **15c**, **16**, and **17** (22 pages). Ordering information is given on any current masthead page.

Chiral Synthesis via Organoboranes. 29. A General Synthesis of α-Chiral Monosubstituted Acetylenes and Their Trimethylsilyl Derivatives from Enantiomerically Pure Boronic Esters

Herbert C. Brown,* Verinder K. Mahindroo,[1a] N. G. Bhat,[1b] and Bakthan Singaram

H. C. Brown and R. B. Wetherill Laboratories of Chemistry, Purdue University, West Lafayette, Indiana 47907

Received August 23, 1990

The procedure for the synthesis of RC≡CH by the iodination of $[R_3BC{\equiv}CH]^-Li^+$ is impractical for the synthesis of the corresponding chiral derivatives, R*C≡CH, due to the unavailability of the required R^*_3B compounds. RThxBOMe and $R^*ThxBOCH_3$, now readily available by established procedures, serve handily for the syntheses of RC≡CR′ and R*C≡CR respectively from LiC≡CR, but fail for the syntheses of either RC≡CH or R*C≡CH, in reasonable yield, from LiC≡CH. Fortunately, this difficulty can be circumvented by utilizing $LiC{\equiv}CSiMe_3$. Indeed, treatment of enantiomerically pure monoalkylthexylborinates, $R^*ThxBOCH_3$, readily prepared from enantiomerically pure boronic esters, with $LiC{\equiv}CSiMe_3$ forms an ate complex which readily undergoes the desired iodine-induced rearrangement, forming α-chiral (trimethylsilyl)acetylenes, $R^*C{\equiv}CSiMe_3$. The (trimethylsilyl)acetylenes are easily desilylated to afford the corresponding α-chiral terminal acetylenes, R*C≡CH, in yields of ~70% and essentially 100% enantiomeric excess (≥99%). These intermediates, $R^*C{\equiv}CSiMe_3$ and R*C≡CH, can be readily converted by simple procedures into a wide variety of pure enantiomers: $R^*CH{=}CH_2$, R^*CH_2CHO, R^*CO_2H, $R^*CH_2CO_2H$, R^*COCO_2R, etc. Since both (+)- and (-)-alkylboronic esters are now readily available in essentially 100% enantiomeric purity, it is now possible to synthesize (+)- and (-)-α-chiral monosubstituted acetylenes and their trimethylsilyl derivatives in very high enantiomeric purities. This provides the first general, efficient synthesis of these valuable synthons in such high enantiomeric purities.

In 1961, asymmetric hydroboration marked a milestone in achieving chiral synthesis approaching 100% ee by a nonenzymatic process.[2] Since then, we[3] and others[4] have refined this method to the point where many functional groups of interest to the organic chemist are now readily accessible in essentially enantiomerically pure form. Among the chiral organoboranes attainable via this process, enantiomerically pure boronic esters,[5] $R^*B(OR)_2$, have emerged as particularly versatile reagents. They have been converted into enantiomerically pure alcohols,[6] aldehydes,[7] acids,[7] and homologated alcohols,[7] as well as borohydrides,[8] diols,[9] and amines.[10] As part of our continuing research efforts to develop simple, practical methods for enantioselective synthesis via optically pure boronic esters, we undertook to find an efficient, general synthesis of α-chiral monosubstituted acetylenes, R*C≡CH. Previous syntheses of such acetylenes have utilized optically active precursors. α-Chiral 1-alkynes have been also prepared earlier, in moderate optical purities, by applying Wittig-type reaction of the reagent, (dichloromethylene)tris(dimethylamino)phosphorane, $(Me_2N)_3P{=}CCl_2$, to α-chiral aldehydes, followed by elimination of the intermediate with *n*-butyllithium.[11] A conventional method for preparing these compounds is the bromination-dehydrobromination of α-chiral olefins.[12] The former approach suffers from substantial racemization of the product, while the latter

(1) (a) Postdoctoral research associate on Grant GM 10937-26 from the National Institute of Health. (b) Postdoctoral research associate on Grant CHE 87-06102 from the National Science Foundation.
(2) Brown, H. C., Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 486.
(3) For a detailed review of asymmetric hydroboration, see: Brown, H. C.; Jadhav, P. K. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2, Chapter 1.
(4) Masamune, S.; Kim, B. M.; Petersen, J. S.; Sato, T.; Veenstra, S. J.; Imai, T. *J. Am. Chem. Soc.* **1985**, *107*, 4549.
(5) Brown, H. C., Singaram, B. *J. Am. Chem. Soc.* **1984**, *106*, 1797.
(6) For leading references, see: Srebnik, M.; Ramachandran, P. V. *Aldrichimica Acta* **1987**, *20*, 9.
(7) Brown, H. C.; Imai, T.; Desai, M. C.; Singaram, B. *J. Am. Chem. Soc.* **1985**, *107*, 4980.
(8) Brown, H. C.; Singaram, B.; Cole, T. E. *J. Am. Chem. Soc.* **1985**, *107*, 460.
(9) Matteson, D. S.; Sadhu, K. M. *J. Am. Chem. Soc.* **1983**, *105*, 2077.
(10) Brown, H. C.; Kim, K. W.; Singaram, B.; Cole, T. E. *J. Am. Chem. Soc.* **1986**, *108*, 6761.
(11) Marcassi, F.; Giacomelli, G.; Menicagli, R. *Gazz. Chim. Ital.* **1980**, *110*, 195.
(12) Lardicci, C.; Botteghi, C.; Benedetti, E. *J. Org. Chem.* **1966**, *31*, 1534.

0022-3263/91/1956-1500$02.50/0