C-6, 2 × Me), 33.8 (t, C-4), 33.8 (s, C-6), 37.2 (t, C-5), 51.4 (q, OMe), 130.6 (s, C-2), 154.4 (s, C-1), 168.2 (s, COOMe), 198.1 (s, CO). **2b**: ^{1}H NMR δ 1.08 and 1.11 (s, 6 H, C-6, 2 × Me), 1.15-1.90 (m, 5 H, H-4, H-5, OH), 1.76 (s, 3 H, C-2, Me), 3.76 (s, 3 H, OMe), 3.98 (t, 1 H, H-3).

3-Oxo-2,6,6-trimethylcyclohex-1-ene-1-carboxylic Acid (1a). To a stirred solution of a mixture of α- and β-cyclocitrals (5.5 g, 0.036 mol) containing 55% of the β-isomer[4] (GC) in purified dioxane[7] with 10% of H_2O (500 mL) were added finely divided $CaCO_3$ (14.6 g, 0.146 mol) and freshly crystallized NBS (15 g, 0.086 mol). The mixture was efficiently stirred while being irradiated with visible light from a 1000-W halogen lamp and heated gently just to start boiling. When the initial color faded away, an additional amount of NBS (17 g, 0.098 mol) in dioxane (270 mL) was added dropwise (approximately in 1 h). After the addition was complete, the reaction mixture remained colorless and a white solid stuck to the walls of the reaction flask. The solution was decanted and the solvent removed in vacuo. The residue was taken up with an aqueous saturated solution of $NaHCO_3$ (150 mL) and Et_2O (50 mL), cooled, and filtered, and the filtrate was extracted with Et_2O (3 × 100 mL). The aqueous layer was then cooled (0 °C), brought to pH 3 by addition of cold (0 °C) aqueous 50% HCl, and extracted with Et_2O (5 × 100 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), and evaporated. The residue (3.01 g) was recrystallized from benzene to give pure **1a** (2.33 g): mp 187.5-188 °C (lit.[1] mp 187-189 °C). From the mother liquors, after treatment with Jones reagent[8] in cooled (0 °C) acetone, followed by crystallization from benzene, an additional amount (276 mg) of **1a** (mp 187-189 °C) was obtained; total amount of **1a**: 2.6 g, 72% yield.

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Registry No. **1a**, 51823-74-6; **1b**, 28120-76-5; (±)-**2b**, 60078-94-6; (±)-**3**, 51820-11-2; (±)-α-cyclocitral, 59462-59-8; β-cyclocitral, 432-25-7.

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α-Methyl Functionalization of Electron-Poor Heterocycles:[1a] 2,9-Bis(chloromethyl)-1,10-phenanthroline. Synthesis of a [3.3]Cyclophane Containing the 1,10-Phenanthrolino Moiety

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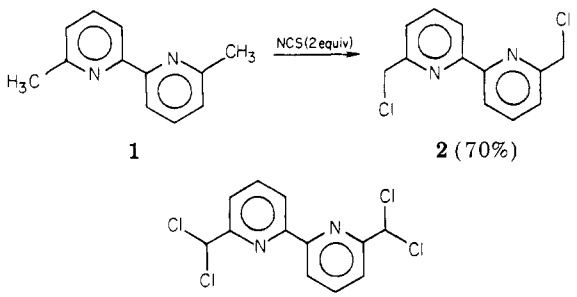
Introduction

It has been shown that electron-deficient heteroaromatics with 2,6-oxo substituents do not readily form transition-metal complexes.[2] In order to circumvent the major causes of the poor ligandophilicity, e.g., the inherent imidate moiety and diminished N electron density, inclusion of an α-methylene unit between the bridge oxygen atoms and heterocyclic ring has been deemed necessary. Numerous macrocycles containing the pyridino and dipyridino subunits have been reported;[3] however, only a few examples of macrocycles containing the related phenanthrolino moiety are known.[4] Further, no phenanthrolino macrocycles have yet been reported that contain α-methylene units. It was evident that reactions, which were applicable to the α-functionalization of 2,6-dimethylpyridine and 6,6′-dimethyl-2,2′-bipyridine (**1**),[1] could *not* be readily applied to 2,9-dimethyl-1,10-phenanthroline. We now describe the α-functionalization of 2,9-dimethyl-1,10-phenanthroline along with its incorporation into a [3.3]cyclophane.

Results and Discussion

A. α-Methyl Functionalization. Treatment of **1** with 2 equiv of *N*-chlorosuccinimide (NCS) under appropriate free-radical conditions gives primarily the desired *sym*-chloromethyl derivative **2**;[1] in contrast, however, **4** experiences enhanced reactivity under identical conditions. Thus, treatment of **4** with 2 equiv of NCS and benzoyl peroxide initiator gave the hexachloro derivative **5** and a complex mixture of chloro derivatives. Attempts to obtain the desired *sym*-chloromethyl **8** in one step, as the major product and in pure form by NCS chlorination have been unsuccessful. The trichloromethyl intermediate **5** was prepared (100%) when 6 equiv of NCS was utilized.[5] A one-pot hydrolysis of **5** in concentrated sulfuric acid and subsequent esterification afforded **6** in quantitative overall yield.[6] Reduction of **6** with $LiAlH_4$ resulted in low yields of the biscarbinol **7**, whereas with $NaBH_4$, **6** was quantitatively transformed to **7**.[7]



The chloromethyl derivative **8** was obtained (72%) by the use of PCl_3;[8,9] when $SOCl_2$ was used for this conversion,

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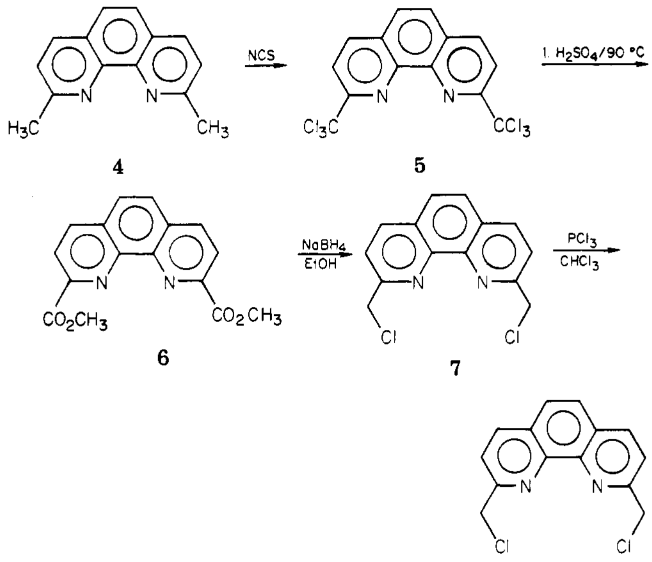
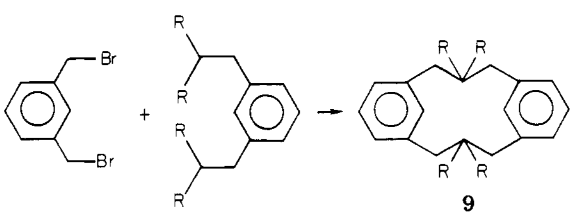


4 5 6 7 8

a yet unknown compound containing four sulfur atoms was isolated.

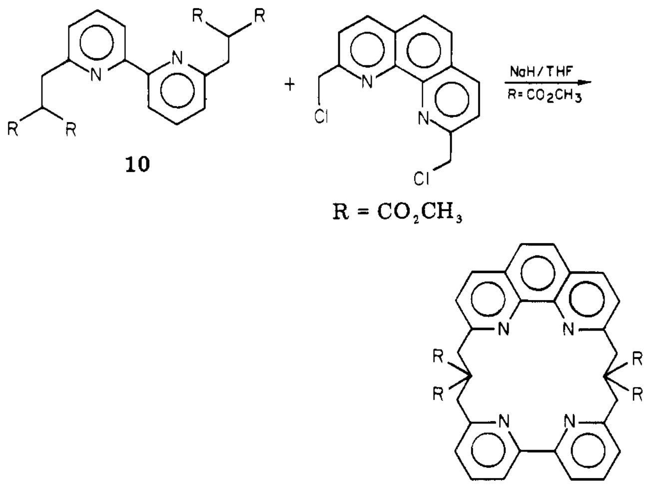
B. Cyclophane Formation and Characterization. In order to synthesize macrocycles possessing two different bonding loci within a cavity, the synthesis of [3.3]-cyclophanes was explored through the combination of 1 and 4. Shinmyozu et al.[10] successfully prepared 9 via condensation of *m*-bis(bromomethyl)benzene and the bis anion of tetraethyl *m*-diethylbenzene-$\alpha,\alpha,\alpha',\alpha'$-tetracarboxylate. Since 10 was available from previous stud-



9

R = CO_2Et

ies,[11] the heterocyclophane 11 was prepared (>50%) by the treatment of the dianion of 10 with 8 under high dilution conditions.[12] The ^1H NMR spectrum of 11 showed two spikes at δ 3.55 and 3.84 for the two different α-methylene groups and a singlet at δ 3.67 for the methoxycarbonyl groups, indicative of the symmetrical nature of the cyclophane. The aromatic region for the rigid phenanthroline moiety remains invariant, but the dipyridine H-3 shifts upfield ($\Delta\delta$ = 0.20), suggestive of a syn conformation imposed by the macrocyclic structure. Selective decoupling at H-5 (δ 7.88) transforms the H-4 (δ 8.10) triplet into a doublet and simultaneously sharpens the H-3 (δ 8.11) doublet, confirming the assignment. The ^{13}C NMR of 11 further demonstrates the symmetry by the presence of exactly 16 resonances, as predicted. Interestingly, both ^1H and ^{13}C NMR spectra indicate that the methoxycarbonyl groups reside in magnetically equivalent envi-



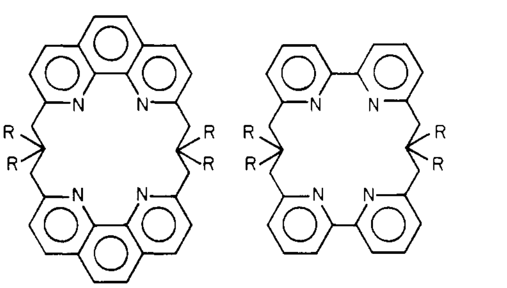
10

R = CO_2CH_3

11

ronments at 28 °C, supportive of a mobile conformational equilibrium at that temperature. Variable-temperature NMR showed a coalescence temperature of −56 °C as the singlet at δ 3.67 was slowly transformed into two broad singlets, thus supporting a conformational rigidity via the diastereotopic ester groups (see Figure 1).

Attempts to prepare the related 12 and 13 by this procedure were unsuccessful.[13] Several attempts to prepare



12, R = CO_2CH_3 **13**, R = CO_2CH_3

nickel and copper complexes of 11 were also unsuccessful, presumably as a result of either the steric constraints imposed by the ester groups at the site of complexation or an unfavorable orientation of the N electrons. In addition to cyclophane 11, the synthesis of a crown ether derivatives of phenanthroline has been completed.[14]

Experimental Section

General Comments. All melting points were taken in capillary tubes with a Thomas-Hoover Uni-Melt apparatus and are un-

(9) An alternate reaction sequence to obtain 2,9-bis(bromomethyl)-1,10-phenanthroline has been recently reported[5] after the completion of these studies. This involved transformation of 4 to the dialdehyde followed by reduction to 7 and subsequent treatment with hydrogen bromide to give the bromo derivative (37% yield). Attempts to reproduce their procedures on a larger scale resulted in reduced yields, whereas the herein reported reaction sequence was relatively independent of reaction size.

(10) Shinmyozu, T.; Inazu, T.; Yoshino, T. *Chem. Lett.* **1976**, 1405.

(11) Newkome, G. R.; Onishi, M.; Puckett, W. E.; Deutsch, W. A. *J. Am. Chem. Soc.* **1980**, *102*, 4551.

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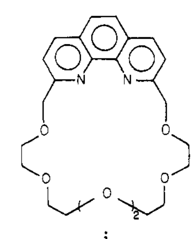
(13) Successful decarboxylation of 11 was conducted under basic conditions. Esterification of bis acid afforded a mixture of isomers, which could not be readily separated and thus were not characterized further.

(14) The pentaethylene glycol crown ether derivative (i) was prepared



i

by previously described procedures.[15] The macrocycle was characterized spectroscopically: ^1H NMR δ 3.64–3.95 (m, CH_2O, 20 H), 5.15 (s, α-CH_2, 4 H), 7.72 (d, 3,8-phen H, J = 8.5 Hz, 2 H), 7.76 (s, 5,6-phen H, 2 H), 8.50 (d, 4,7-phen H, J = 8.5 Hz, 2 H); MS m/e 442 (M^+, 8), 383 (9), 339 (14), 311 (12), 237 (24), 223 (100), 208 (75).

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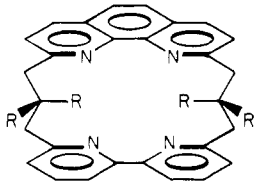

Figure 1. Perspective drawing of cyclophane **11** (R = CO_2CH_3).

corrected. ^1H and ^{13}C NMR spectra were determined on a Bruker WP-200 NMR spectrometer with $CDCl_3$ as solvent and Me_4Si as the internal standard. IR spectra were recorded on a Perkin-Elmer 621 grating-infrared spectrophotometer. Mass spectral (MS) data (70 eV) [reported as assignment, relative intensity] were determined by D. Patterson on a Hewlett-Packard HP 5985 GC/mass spectrometer. Reported R_f values were ascertained by a standardized thin-layer chromatographic (TLC) procedure: Baker-flex silica gel IB2-F plates by eluting with the stipulated solvent system. For preparative thick-layer chromatography (ThLC), 2-mm silica gel PF-254-366 plates were used. Elemental analyses were performed by R. Seab in these laboratories.

2,9-Bis(trichloromethyl)-1,10-phenanthroline (5). A stirred suspension of **4** (10 g, 50 mmol), NCS (39 g, 300 mmol), and benzoyl peroxide (50 mg) in CCl_4 (400 mL) was refluxed for 6 h. The mixture was cooled, filtered, and concentrated in vacuo to give a solid, which was dissolved in $CHCl_3$. The organic fraction was washed with a saturated aqueous Na_2CO_3 solution, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo to give **5**, as a pale yellow solid: 19.9 g (100%); mp 212–214 °C (lit.[5] mp 212–214 °C).

2,9-Bis(methoxycarbonyl)-1,10-phenanthroline (6). A stirred mixture of **5** (59 g, 140 mmol) and concentrated H_2SO_4 (27 mL) was heated to 90 °C for 2 h.[6] [*HCl gas was liberated*!] After cooling of the mixture, MeOH (65 mL) was *cautiously* added with rapid stirring, and then the solution was refluxed for 1 h. The mixture was cooled and neutralized *cautiously* with a saturated aqueous Na_2CO_3 solution and filtered to give (100%) **6**, as a light tan solid: mp 190–200 °C. The product was purified by sublimation to give (95%) the pure ester as colorless microcrystals: mp 210–212 °C (lit.[5] mp 213–214 °C).

2,9-Bis(hydroxymethyl)-1,10-phenanthroline (7). Solid $NaBH_4$ (3 g, 80 mmol) was slowly added to a solution of **6** (5 g, 20 mmol) in absolute EtOH (500 mL).[7] The solution was refluxed for 3 h, cooled, and concentrated to give a solid, which was dissolved in H_2O (200 mL) and continuously extracted with $CHCl_3$ for 6 h. The organic extract was concentrated in vacuo to give diol **7**, as light yellow microcrystals: 3.9 g (95%); mp 195–197 °C (lit.[5] mp 197–198 °C).

2,9-Bis(chloromethyl)-1,10-phenanthroline (8). To a solution of diol **7** (3 g, 12.5 mmol) in $CHCl_3$ (200 mL) was slowly added PCl_3 (12 mL) in $CHCl_3$ (20 mL) with constant stirring.[8] After addition was completed, the mixture was refluxed for 1 h and then concentrated in vacuo to give a viscous oil, which was neutralized with a saturated aqueous Na_2CO_3 solution. After filtration and washing with cold water, the bis chloride was isolated as a light yellow solid (which was further purified by passing through a short silica gel column eluting with CH_2Cl_2): 2.5 g (72%); mp 178–180 °C dec; ^1H NMR δ 5.11 (s, CH_2, 4 H), 7.83 (s, 5,6-phen H, 2 H), 7.95 (d, 3,8-phen H, J = 8.5 Hz, 2 H), 8.32 (d, 4,7-phen H, J = 8.5 Hz, 2 H); ^{13}C NMR δ 47.41 (CH_2Cl), 122.50 (C-3), 126.58 (C-5), 128.28 (C-4A), 137.35 (C-4), 144.77 (C-10B), 157.43 (C-2); IR (CsI) 1620, 1590, 1360, 1270, 1140, 850 cm^{-1}; MS, m/e 276 (M^+, 100), 241 (36.1), 205 (42.9). Anal. Calcd for $C_{14}H_{10}N_2Cl_2$: C, 60.69; H, 3.61; N, 10.11. Found: C, 60.32; H, 3.94; N, 9.88.

[3.3]Cyclophane (11). To a refluxing mixture of anhydrous THF (200 mL) and NaH (216 mg, 50% dispersion in oil) were added simultaneously over 3 h tetraester **10**[11] (500 mg, 1.7 mmol) in THF (100 mL) and **8** (311 mg, 1.1 mmol) in THF (100 mL) under an inert atmosphere, using high-dilution conditions.[12] After an additional 12 h of reflux, the excess NaH was cautiously neutralized with MeOH and then the mixture was concentrated in vacuo to give a solid, which was continuously extracted with $CHCl_3$. After concentration in vacuo the crude product (>50% yield, 90% purity) was chromatographed (ThLC) on alumina, eluting with $CHCl_3$/EtOAc (5:4), to give (45%) pure **11** as white crystals: mp 200 °C; ^1H NMR δ 3.55, 3.84 (2 s, Py/phen CH_2, 4 H each), 3.67 (s, OCH_3, 12 H), 7.35 (d, 3,8-phen H, J = 8.0 Hz, 2 H), 7.72 (s, 5,6-phen H, 2 H), 7.88 (d, 5-Py H, J = 7.0 Hz, 2 H), 8.10 (dd, 4-Py H, J = 7.0, 7.0 Hz, 2 H), 8.11 (d, 3-Py H, J = 7.0 Hz, 2 H), 8.43 (d, 4,7-phen H, J = 8.0 Hz, 2 H); ^{13}C NMR δ 38.9 (Py CH_2), 40.7 (phen CH_2), 52.5 (OCH_3), 58.3 [$C(CO_2CH_3)_2$], 119.5 (Py C-3), 123.3 (phen C-3,8), 123.8 (Py C-5), 126.0 (phen C-5,6), 127.5 (phen C-4a,4b), 136.0 (Py C-4), 137.7 (phen C-4 and C-7), 146.1 (phen C-10a and 10b), 156.0 (Py C-6), 156.6 (Py C-2), 157.7 (phen C-2,9), 171.5 (C=O); IR (CsI) 1720, 1550, 1430, 1200, 790 cm^{-1}. Anal. Calcd for $C_{36}H_{32}N_4O_8 \cdot CH_3OH$ (methanol found to be incorporated by TGA—approximately 4% loss of mass between 150 and 200 °C): C, 65.29; H, 5.33; N, 8.23. Found: C, 65.28; H, 4.98; N, 8.11.

Acknowledgment. We thank the National Science Foundation for partial support of this work.

Registry No. **4**, 484-11-7; **5**, 78831-41-1; **6**, 78831-35-3; **7**, 78831-36-4; **8**, 87518-61-4; **10**, 87518-62-5; **11**, 87518-63-6; i, 87518-64-7.

Solvolysis of [4.2.2]Propellan-7-yl Derivatives

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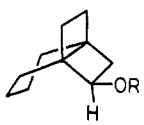
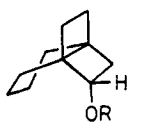
The solvolysis of constrained polycyclic cyclobutane derivatives has held considerable interest in recent years, because the geometry of the cyclobutane ring is of major importance in determining the solvolysis reactivity.[1] In this respect and in connection with the study on the carbocationic rearrangement of the propellanes involving a cyclobutane ring,[1f,2] we report here the solvolysis of tricyclic cyclobutane derivatives **1a** and **2a** having a highly strained [4.2.2]propellane framework.[3]





1a R = DNB **1b** R = H **1c** R = Ac

2a R = Ts **2b** R = H **2c** R = Ac

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