Table I

sample label	temp/°C	$\tau_{1/2}$/min	$k_{obsd} \times 10^{-4}$ (σ)/s^{-1}
A	90.4	7.01	16.47 (0.10)
B	90.4	7.00	16.50 (0.21)
C	90.4	6.98	16.54 (0.19)
D	80.4	14.72	7.85 (0.07)
E	80.4	14.64	7.89 (0.13)
F	80.4	14.75	7.83 (0.11)
G	75.4	21.6	5.35 (0.03)
H	75.4	21.8	5.30 (0.03)
I	75.4	21.6	5.34 (0.02)
J	70.4	33.4	3.46 (0.03)
K	70.4	33.5	3.45 (0.02)
L	70.4	32.8	3.52 (0.06)

Table II

substituent	σ	$k_{obsd} \times 10^{-4}$ (σ)/s^{-1}
CF_3	0.54	8.45 (0.22), 8.54 (0.14), 8.29 (0.17)
Cl	0.23	5.89 (0.02), 6.09 (0.08), 6.25 (0.12)
H	0.0	5.35 (0.03), 5.30 (0.03), 5.34 (0.02)
OMe	−0.27	3.64 (0.06), 3.83 (0.03), 4.11 (0.06)
NMe_2	−0.83	2.48 (0.02), 2.25 (0.03), 2.31 (0.04)
$\rho = +0.39$ (0.02)		

observed rate compared to the thermolyses that employed 2 equiv of phosphine (Table I).

Thermolysis of 2b in the Absence of Trimethylphosphine. An NMR sample of **2b** in C_6D_6 was prepared as above, with no trimethylphosphine, and the sample was heated in the NMR probe to 80.4 °C. The rate of disappearance of **2b** was monitored, using the combined signal of the cyclopentadienyl resonances as an internal standard. The observed rate constant ($k_{obsd} = 7.82$ (0.09) $\times 10^{-4}$/s) was identical with the rate observed with 2 equiv of PMe_3. The resulting mixture exhibited resonances attributable to methane (δ 0.15 (s)), unreacted Cp_2ZrMe_2 (δ −0.12 (s, 3 H), 5.72 (s, 10 H)), $Cp_2Zr(SCH_2Ph)_2$ (δ 4.20 (s, 4 H), 5.79 (s, 10 H), aryl signals obscured), and zirconocene thiobenzaldehyde oligomers $[Cp_2Zr(HCSPh)]_n$ (δ 3.69, 3.77, 3.83, 4.10 (s, ca. 3:1:3:3 ratio, total of 1 H), 5.28, 5.31, 5.55, 5.57, 5.63, 5.71, 5.94, 5.95 (s, ca. 3:3:3:1:1:3:3:3 ratio, total of 10 H), aryl signals obscured). To this sample was added trimethylphosphine (0.020 mL, ca. 2 equiv), and the tube was heated to 60 °C in the NMR probe. After 15 min, no resonances attributed to oligomeric $[Cp_2Zr(HCSPh)]_n$ remained, and only resonances due to the thiobenzaldehyde trimethylphosphine complex **1b**, Cp_2ZrMe_2, CH_4, free PMe_3, and $Cp_2Zr(SCH_2Ph)_2$ were observed.

Determination of k_H/k_D. Two NMR samples of monodeuteriated **2b** in C_6D_6 containing PMe_3 were prepared as for **2b** above, with the benzenemethane-*d*-thiol prepared above. The samples were heated in an oil bath at 80 °C for 4 h. ^1H NMR showed signals attributable to the thiobenzaldehyde complex **1b**, with a depleted signal for the benzylic hydrogen. The observed signal was 15.82–16.65% of that observed for unlabeled **1b**, using the cyclopentadienyl resonances as an internal standard. This indicates a k_H/k_D of 5.2 (0.2).

Determination of Hammett ρ. NMR samples of **2c–f** in C_6D_6 containing PMe_3 were prepared as for **2b** above, with the appropriate thiol. Observed rate constants for the formation of **1c–f** (three samples for each compound) were measured at 75.4 °C (Table II).

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Registry No. 1a, 107272-32-2; **1b**, 107272-34-4; **1c**, 113686-33-2; **1d**, 113686-34-3; **1e**, 113686-35-4; **1f**, 113686-36-5; **2a**, 113686-37-6; **2b**, 113686-38-7; **2c**, 113686-39-8; **2d**, 113686-40-1; **2e**, 113686-41-2; **2f**, 113686-42-3; C_6H_5CHDSH, 113686-43-4; *p*-$(CF_3)C_6H_4CH_2SH$, 108499-24-7; *p*-$(Me_2N)C_6H_4CH_2SH$, 113686-44-5; Cp_2ZrMe_2, 12636-72-5; CH_3CH_2SH, 75-08-1; $C_6H_5CH_2SH$, 100-53-8; *p*-$ClC_6H_4CH_SH$, 6258-66-8; *p*-$(MeO)C_6H_4CH_2SH$, 6258-60-2; C_6H_5CHDCl, 79449-94-8; *p*-$(CF_3)C_6H_4CH_2Br$, 402-49-3; *p*-$(Me_2N)C_6H_4CH_2OH$, 1703-46-4.

Synthesis and Reactivity of Binuclear Tropocoronand and Related Organocopper(I) Complexes. Catalytic Enantioselective Conjugate Addition of Grignard Reagents to 2-Cyclohexen-1-one

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Abstract: The conjugate addition of Grignard reagents, RMgCl, where R = Ph, *n*-Bu, and Me, to 2-cyclohexen-1-one was promoted by a series of new catalysts (0.006–0.04, mol fraction) prepared from copper(I) species and either of two ligand systems. The first used the tropocoronand macrocycle, H_2(TC-5,5), while the second employed a new chiral ligand, H-(CHIRAMT), based on *N,N'*-dialkyl-substituted aminotroponeimines. Alkyl-bridged dicopper(I) compounds of both ligands are believed to form in solution, serving as catalysts for the production of racemic 3-substituted cyclohexanones or, in the latter homochiral system, optically active (4–14% ee) products. The regiospecificity, product yield, and enantioselectivity were determined for several reactions utilizing various catalysts. The best results were obtained with copper alkyl complexes freshly prepared in situ. The use of 12-crown-4 as complexing agent for lithium allowed the isolation and characterization of otherwise thermally unstable binuclear copper(I) compounds of the tropocoronands bearing bridged moieties. The structure of one, [Li(12-crown-4)$_2$][$Cu_2(\mu$-Br)(TC-5,5)] (**1**), was determined by X-ray crystallography. Crystal data for $C_{40}H_{62}BrN_4O_8Cu_2Li$ (**1**) is as follows: monoclinic, *Cc*, $a = 17.970$ (7) Å, $b = 16.243$ (4) Å, $c = 15.660$ (6) Å, $\beta = 111.44$ (3)°, $V = 4254.7$ Å^3, $Z = 4$. The structure was refined to $R_1 = 0.043$ by using 2122 data with $F_o > 3\sigma(F_o)$. The second compound, [Li(12-crown-4)$_2$][$Cu_2(\mu$-Ph)(TC-5,5)] (**2**), is thought to possess a similar structure on the basis of spectroscopic data and elemental composition. The synthesis and spectroscopic properties (IR, ^1H, and ^{13}C NMR) of the new compounds, including the chiral bidentate ligand, H(CHIRAMT), are reported. A possible catalytic mechanism consistent with the observed reactivity is discussed along with a proposed model for the transition state leading to chiral induction.

Recent work in our laboratory has demonstrated the versatility of tropocoronand, H_2(TC-*n,n'*), macrocycles as binucleating ligands.[1-5] These molecules, constructed by linking two aminotroponeimine groups with polymethylene chains to form macro-

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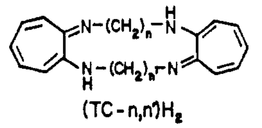

(TC-n,n')H$_2$
n,n' = 3,3; 4,4; 4,5; 5,5; 6,6

cyclic rings of variable size, bind low oxidation state late transition metals such as Cu(I) and Rh(I). Complexes characterized to date include alkyne-bridged dicopper(I),[2,4] dicopper(I) dicarbonyl,[5] and dirhodium(I) tetracarbonyl[1,5] derivatives. Although these neutral molecules exhibit interesting structural features, such as syn–anti stereoisomerism, they have limited synthetic utility.

Because of our interest in discovering new or useful chemistry mediated by bimetallic complexes of known structure,[6] we have extended these studies to the synthesis and characterization of binuclear copper(I) alkyl species. Recognizing the importance of organocopper compounds in organic synthetic methodology[7] and the availability of only limited solid-state structural information about these reagents,[8-11] we sought to prepare complexes that not only would mimic or improve upon existing reagents but would also lend themselves to structural characterization. In addition, the tremendous progress being made in asymmetric synthesis,[12] including the conjugate addition of chiral organocuprate reagents,[13] spurred us to investigate bimetallic catalysts of asymmetric reactions.

In this article we describe the preparation, characterization, and reactivity of new copper(I) alkyl and phenyl complexes of binucleating tropocoronand macrocycles and a related chiral N,N'-disubstituted aminotroponeiminate ligand. These compounds represent an initial approach to the development of catalysts for asymmetric conjugate addition of Grignard reagents to cycloalkenones, a reaction with many potential applications.[14]

Experimental Section

Methods and Materials. Tropocoronands were synthesized according to ref 15. The 2-(tosyloxy)tropone was prepared by a literature method[16] from commercially available tropolone (Lancaster Synthesis or Aldrich Chemical Company). Lithium and Grignard reagents were purchased and used as received from Aldrich except for *n*-butyllithium (*n*-BuLi), which was titrated by either of two methods to determine the active alkyllithium content.[17] Details of procedures for handling and storage of this reagent are described elsewhere.[5] Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl and flushed with argon for at least 15 min prior to use. Standard Schlenk techniques were used in handling all air-sensitive compounds and reaction mixtures.

Elemental analyses were performed by Schwarzkopf Microanalytical Laboratories (Woodside, NY) and Atlantic Microlab, Inc. (Atlanta, GA). Proton and carbon-13 NMR spectral analyses were carried out on a Bruker 250 or Varian XL-300 FT instrument, by using deuteriochloroform or tetrahydrofuran-d_8 distilled from sodium benzophenone ketyl and stored in small ampules (1 mL). Chemical shifts are reported in ppm downfield from tetramethylsilane (TMS). Infrared spectra (KBr) were recorded on an IBM Instruments IR/30S FTIR spectrophotometer.

Gas chromatographic analyses were performed by using a Hewlett-Packard (HP) Model 5890 gas chromatograph, equipped with a flame-ionization detector (FID) and an HP-3393A integrator. An HP-1 methylsilicone gum 0.53 mm × 10 m fused silica column was used for separations. Conditions included a column head pressure of 10 psig and a temperature gradient program which held the initial oven temperature at 80 °C for 2 min, followed by gradual heating at a rate of 20°/min to a final oven temperature of 200 °C. Products were identified by coinjection with authentic samples purchased commercially or prepared by unambiguous routes. Cyclohexenone, 12-crown-4, and (*R*)-α-methylbenzylamine were purchased from Aldrich and stored over 4 Å molecular sieves. Tetrakis(acetonitrile)copper(I) tetrafluoroborate, [Cu(NCCH$_3$)$_4$](BF$_4$), was prepared according to ref 18 and stored in a nitrogen-filled glovebox. CuBr·Me$_2$S was obtained from Aldrich and also stored in the drybox.

Preparative HPLC was carried out by using a Waters Associates PrepLC 500 instrument equipped with a refractive index detector and a PrepPAK/SILICA 500 cartridge.

Synthesis of [Li(12-crown-4)$_2$][Cu$_2$(μ-Br)(TC-5,5)] (1). Neat 12-crown-4 (130 μL, ~0.80 mmol) was added to a THF (8 mL) suspension of CuBr·Me$_2$S (92.4 mg, 0.45 mmol) under argon. The mixture was stirred, cooled to −78 °C, and treated with a THF (8 mL) solution of Li$_2$(TC-5,5), prepared from H$_2$(TC-5,5) (68.6 mg, 0.18 mmol) and *n*-BuLi (2.0 equiv). The initial yellow-green reaction mixture turned amber over the course of the next 0.5 h at −78 °C. The cooling bath was removed, and the mixture was allowed to warm up to 0 °C. After 0.5 h, a red-brown precipitate had formed. The mixture was concentrated in vacuo and transferred to a drybox. The solid was collected by filtration and washed a few times with ether/THF (1:1, v/v), leaving an orange powder contaminated with [Li(12-crown-4)$_2$]Br (190 mg, 111% yield), a cream-colored solid. Recrystallization from THF proved to be difficult since the product **1** is only sparingly soluble in this solvent. Mixtures of small red crystals and red amorphous powder were usually obtained from dilute THF solutions stored at −20 °F in the drybox, combined yield, 72.0 mg (42%). Spectroscopic data: IR (KBr, cm^{-1}) 2910 (m), 2842 (m), 2809 (m), 1585 (s), 1500 (s), 1470 (s), 1453 (s), 1416 (s), 1386 (s), 1365 (m), 1347 (m), 1304 (w), 1289 (m), 1266 (s), 1227 (m), 1208 (w), 1134 (s), 1097 (s), 1024 (s), 992 (w), 925 (m), 885 (w), 856 (m), 768 (w), 724 (s); ^{1}H NMR (300 MHz, THF-d_8, 296 K) δ 6.60 (4 H, dd, J = 9.8, 11.4 Hz), 6.16 (4 H, d, J = 11.4 Hz), 5.69 (2 H, t, J = 9.8 Hz), 3.58 partially obscured by solvent peaks (crown protons, s), 3.06 (4 H, t, J = 13.0 Hz), 2.45 (4 H, quartet, J = 13.0 Hz), 1.80 overlapping with solvent peaks (~12 H, complex m); ^{13}C NMR (75.5 MHz, THF-d_8, 295 K) δ 162.30, 132.80, 110.54, 108.76, 70.65, 51.84, 33.10, and 30.31 corresponding to carbons C11, C13, C14, C12, crown carbons, C31, C32, and C33, respectively (see Figure 1 for atom labeling scheme). Anal. Calcd for C$_{40}$H$_{62}$BrN$_4$O$_8$Cu$_2$Li: C, 51.06; H, 6.64; Br, 8.49. Found: C, 50.86; H, 6.75; Br, 8.11.

Synthesis of [Li(12-crown-4)$_2$][Cu$_2$(μ-Ph)(TC-5,5)] (2). A THF (8 mL) suspension of [Cu(NCCH$_3$)$_4$](BF$_4$) (137.6 mg, 0.437 mmol) was cooled to −78 °C and treated with PhLi (0.384 mmol) under argon. The mixture was stirred for 10 min, treated with neat 12-crown-4 (270 μL, ~1.67 mmol), and allowed to warm up gradually to 0 °C. The light red solution was stirred at 0 °C for 10 min and recooled to −78 °C whereupon a THF (8 mL) solution of Li$_2$(TC-5,5), prepared from H$_2$(TC-5,5) (72.1 mg, 0.191 mmol) and *n*-BuLi (0.384 mmol), was added dropwise via syringe. The burgundy mixture was allowed to warm up to room temperature with stirring (10 min), filtered, and concentrated in vacuo.

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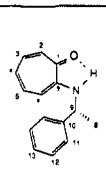
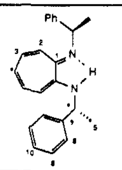
Table I. ^{13}C NMR Chemical Shift Data for Chiral Ligands[a]

carbon		
1	*b*	152.00
2	122.38	111.58
3	137.08	132.99
4	128.80	118.20
5	135.99	25.10
6	110.06	55.06
7	154.34	145.56
8	24.34	126.12
9	52.77	128.55
10	142.44	126.70
11	125.56	
12	129.12	
13	127.35	

[a] Observed at 67.9 MHz by using $CDCl_3$ solutions. [b] Not observed.

The red solid was transferred to the drybox and washed with anhydrous ether (3 × 10 mL). The orange solid was very soluble in THF, and dark red irregularly shaped crystals were obtained from THF solutions stored at −20 °F (85.4 mg, 47.7%). Like compound **1**, crystals of **2** are air-sensitive and turn black within seconds of exposure. Sealed solutions of **2** kept at room temperature also turn brown, eventually forming a dark precipitate. Spectroscopic data: IR (KBr, cm^{-1}) 3040 (w), 2918 (m), 2840 (m), 1586 (s), 1503 (s), 1471 (m), 1452 (s), 1417 (s), 1384 (m), 1360 (m), 1302 (m), 1287 (m), 1264 (s), 1224 (m), 1135 (m), 1097 (s), 1024 (s), 926 (m), 885 (w), 855 (w), 717 (m); ^{1}H NMR (300 MHz, THF-d_8, 295 K) δ 8.23 (2 H, complex m), 6.92–6.82 (3 H, complex m), 6.54 (4 H, dd, J = 8.8, 11.6 Hz), 6.14 (4 H, d, J = 11.6 Hz), 5.63 (2 H, t, J = 8.8 Hz), 3.77 (4 H, complex m), 3.44 (crown protons, s), 2.87 (2 H, doublet of triplets, J = 13.1, 8.2 Hz), 2.43 (4 H, complex m), 1.96–1.76 overlapping with solvent peaks (8 H, complex m), and 0.96 (2 H, complex m); ^{13}C NMR (75.5 MHz, THF-d_8, 295 K) δ 162.07, 145.35, 132.33, 129.04, 126.24, 125.36, 110.67, 107.92, 70.39, 50.77, 31.74, and 26.89, tentatively assigned to carbons C11, phenyl-ipso, C13, phenyl-meta, phenyl-para, phenyl-ortho, C14, C12, crown carbons, C31, C32, and C33, respectively (see Figure 1 for tropocoronand carbon labeling scheme). Anal. Calcd for $C_{46}H_{67}N_4O_8Cu_2Li$: C, 58.90; H, 7.20; N, 5.97. Found: C, 58.81; H, 7.36; N, 6.05.

Synthesis of 2-[(*R*)-α-Methylbenzylamino]tropone (3). A flame-dried, 500-mL, three-necked, round-bottomed flask equipped with a Teflon-coated magnetic stirrer bar, reflux condenser, and rubber septa was charged with 2-(tosyloxy)tropone (15.6 g, 56.5 mmol), triethylamine (9.0 mL, ~65 mmol), (*R*)-α-methylbenzylamine (8.0 mL, ~62 mmol), and anhydrous ethanol (150 mL). The mixture was heated under reflux for 18 h. The resulting dark solution was allowed to cool to room temperature and concentrated under vacuum. The residual dark brown oil was dissolved in diethyl ether (300 mL), washed consecutively with aqueous saturated ammonium chloride solution (1 × 100 mL) and aqueous sodium chloride solution (half-saturated, 1 × 100 mL), and dried ($MgSO_4$). The solution was diluted to one-third of its original volume with pentane and filtered through a two-tiered column of activated alumina over silica gel (0.5-in. height × 3.0-in base diameter of each). A small upright watch glass was placed over the top layer to help prevent disruption of the column materials during filtration. Concentration of the yellow filtrate gave a yellow solid which was recrystallized from hot ether/pentane (~2:1, v/v) to give bright yellow needles of **3** (7.4 g, 58% yield), mp 84–85 °C, $[\alpha]^{25}{}_D$ ($CDCl_3$) = −626.1°. Spectroscopic data: IR (KBr, cm^{-1}) 3289 (s, N-H), 2967 (w), 1604 (s), 1590 (s), 1544 (s), 1508 (s), 1475 (s), 1459 (s), 1448 (s), 1404 (s), 1389 (m), 1377 (m), 1361 (m), 1263 (m), 1208 (m), 1136 (m), 1087 (w), 1067 (w), 767 (w), 727 (s), 698 (s), 608 (w); ^{1}H NMR (250 MHz, $CDCl_3$, 296 K) δ 7.57 (1 H, br), 7.37–7.14 (7 H, complex m), 7.02 (1 H, t, J = 10 Hz), 6.60 (1 H, complex m), 6.34 (1 H, d, J = 10 Hz), 4.66 (1 H, quintet, J = 6.8 Hz), and 1.64 (3 H, d, J = 6.8 Hz); ^{13}C NMR spectral data are listed in Table I. Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.53; H, 7.30; N, 5.83.

Preparation of 1-[(*R*)-α-Methylbenzylamino]-7-[(*R*)-α-methylbenzylimino]-1,3,5-cycloheptatriene (4, H(CHIRAMT)). Compound **3** (4.80 g, 21 mmol) dissolved in 50 mL of toluene was heated under reflux and treated with neat dimethyl sulfate (2.2 mL, ~1.1 equiv, *exercise extreme care*) dropwise via syringe. The mixture was heated and stirred under N_2 for 1.5 h, after which time a dark oil had separated. The toluene was decanted, and the oil was allowed to cool to room temperature. Water (150 mL) was added, and the aqueous solution was transferred to a separatory funnel. The solution was made basic by the addition of aqueous 5% sodium bicarbonate (10 mL) and was extracted with methylene chloride (3 × 75 mL). The combined organic phases were dried (Na_2CO_3), filtered, and concentrated to give a dark oil (3.1 g, 60%). The oil was dissolved in anhydrous ethanol (150 mL) and treated with neat (*R*)-α-methylbenzylamine (1.75 mL, ~1.05 equiv). The dark solution was stirred at room temperature for 110 h. The reaction was concentrated in vacuo to yield a dark oil which was dissolved in ether (250 mL), washed with an aqueous saturated ammonium chloride solution (1 × 50 mL), diluted with hexane (80 mL), and dried (Na_2CO_3). The mixture was filtered through a two-tiered alumina/silica column similar to that used for the preparation of **3**. TLC analysis of the filtrate (ether/hexane eluent, 3:1 v/v) showed two spots corresponding to **4** (R_f 0.7) and unreacted **3** (R_f 0.3). The product was purified by preparative liquid chromatography (PrepPAK/Silica 500; Et_2O/hexane eluent, 3:1 v/v) to give **4** as an oil (2.75 g, 65%). The crude oil was dissolved in a minimum quantity of methanol, and water was added until the solution just became turbid. After standing overnight at room temperature, the solution deposited yellow-gold needles of **4**, Mp 74 °C, $[\alpha]^{22}{}_D$ ($CDCl_3$) = −919.7°. Compound **4** is henceforth abbreviated H(CHIRAMT). Spectroscopic data: IR (neat liquid, cm^{-1}) 3220 (br, N-H), 3085 (sh, w), 3065 (m), 3030 (m), 2975 (s), 2930 (m), 2870 (m), 1600 (s), 1545 (s), 1520 (s), 1480 (sh, s), 1477 (s), 1464 (s), 1430 (m), 1400 (s), 1390 (s), 1288 (s), 1230 (s), 1159 (m), 1103 (m), 1046 (m), 901 (m), 781 (sh, s), 770 (s), 720 (s), 576 (m); ^{1}H NMR (250 MHz, $CDCl_3$, 296 K) δ 7.41–7.28 (8 H, complex m), 7.27–7.19 (2 H, complex m), 6.61 (2 H, dd, J = 9.7, 12.0 Hz), 6.23 (2 H, d, J = 11.7 Hz), 6.06 (1 H, t, J = 10.0 Hz), 4.76 (2 H, quartet, J = 7.0 Hz), and 1.59 (6 H, d, J = 7.0 Hz); ^{13}C NMR spectral data are listed in Table I; MS, *m/e* (rel intensity) 328 (M^+, 43), 313 ($M - CH_3$, 38), 223 (M − PhMeCH, 100). Anal. Calcd for $C_{23}H_{24}N_2$: C, 84.11; H, 7.37; N, 8.53. Found: C, 83.94; H, 7.39; N, 8.50.

The Conjugate Addition of Grignard Reagents to Cyclohexenone Using Copper(I) Tropocoronand Catalysts Prepared in situ. A suspension of $CuBr{\cdot}Me_2S$ (38.3 mg, 0.186 mmol) in THF (5 mL) was treated at −78 °C with PhLi (1.0 equiv) under an atmosphere of argon. The mixture was allowed to stir above the cooling bath for a few minutes and then recooled to −78 °C. A THF (7 mL) solution of Li_2(TC-5,5), prepared from H_2(TC-5,5) (35.0 mg, 0.093 mmol) and *n*-BuLi (2.0 equiv), was then added dropwise via syringe. The slurry was allowed to warm up until a clear homogeneous burgundy solution was obtained (2–3 min). The solution was then recooled to −78 °C. Two THF (8 mL each) solutions, one containing 2-cyclohexen-1-one (0.4444 g, 4.623 mmol) and the other containing phenylmagnesium chloride (4.62 mmol), were then added dropwise and simultaneously via syringe. After the additions were complete, the mixture was stirred at −78 °C for 10 min and quenched with a saturated aqueous ammonium chloride solution (7 mL). The mixture was diluted with ether (50 mL) and transferred to a 250-mL separatory funnel. The aqueous layer was extracted with fresh ether (2 × 20 mL), and the combined organic layers were washed with aqueous saturated sodium bicarbonate (25 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was mixed with ether/hexane (2:5, v/v) to precipitate the macrocycle (methanol may also be used for this purpose). Passage through a short silica gel column and removal of the solvents provided a dark liquid (0.684 g, 85% yield, based on cyclohexenone) which was >97% 3-phenylcyclohexanone by GLC. Traces of biphenyl and the product from 1,2-addition were also detected.

By using the same method, a red-brown solution was obtained from the complexation of $(CuBu)_n$[19] and Li_2(TC-5,5). Treatment of the catalyst solution with cyclohexenone and *n*-BuMgCl (25 equiv each/Cu) at −78 °C and subsequent workup as above provided 3-butylcyclohexanone (79% isolated yield), free of any 1,2-addition product.

The Michael-like addition of methylmagnesium chloride to cyclohexenone in the presence of catalytic amounts of "Li[Cu_2Me(TC-5,5)]" prepared as above from $(CuMe)_n$ and Li_2(TC-5,5) proceeds with a regioselectivity of only ~4:1 (1,4- versus 1,2-addition) although the stoichiometric reaction between the reagent formed by the addition of 2.0 equiv of MeLi to Li[Cu_2Me(TC-5,5)] and 2.0 equiv of cyclohexenone is regiospecific in favor of the Michael adduct. The poor results obtained in the former, catalytic mode of reaction may reflect unfavorable rates of formation and reactivity of the active molecular species when R is methyl.

[Li(12-crown-4)$_2$][Cu_2(μ-Br)(TC-5,5)] (1) as Catalyst. Solid **1** (20 mg, ~0.02 mmol) was placed in flame-dried, 50-mL, round-bottomed flask equipped with a Teflon-coated magnetic stir bar. After the addition of THF (5 mL), the amber mixture was cooled to −78 °C and treated with 1.0 mL of a THF solution (9.0 mL total) of *n*-BuMgCl (3.2 mmol). After 10 min at −78 °C, the mixture was treated with a THF (9.0 mL) solution of cyclohexenone (0.298 g, 3.1 mmol) added dropwise and concurrently with the remainder of the Grignard reagent. After an additional 10 min, the mixture was quenched with a saturated aqueous ammonium chloride solution (10 mL) and worked up as before (vide supra). The product mixture (0.2455 g, 51%) was analyzed by GLC and found to contain the 1,2-addition product (~20%) as well as the desired 3-butylcyclohexanone (~80%).

$[Li(12\text{-crown-}4)_2][Cu_2(\mu\text{-}Ph)(TC\text{-}5,5)]$ (2) as Catalyst. Red crystals of **2** (4.0 mg, 4.3 μmol) were dissolved in THF (4 mL) under an argon atmosphere. The light red solution was cooled to −78 °C and treated with THF (250 μL each) solutions of cyclohexenone and *n*-BuMgCl (0.213 mmol each) added dropwise and simultaneously. The reaction mixture was stirred at −78 °C for an additional 10 min, quenched, and worked up in the usual manner (see above) to yield 0.0203 g (62%) of a mixture shown by GLC analysis to be composed of the 1,4- and 1,2-addition (R = Bu) products in a 6:1 ratio.

Conjugate Addition Utilizing Chiral Catalysts. The following is a typical procedure for the synthesis of 3-substituted cyclohexanones using catalytic amounts of alkylcopper(I) complexes of the lithium salt of compound **4**, Li[CuR(CHIRAMT)] (R = Ph, Bu, and Me).

A THF (5 mL) suspension of $CuBr{\cdot}Me_2S$ (26.3 mg, 0.128 mmol) was treated with 1.0 equiv of *n*-BuLi at −78 °C under an argon atmosphere. The mixture was allowed to warm up slightly with the formation of a bright yellow solid. The mixture was again cooled to −78 °C and treated with Li(CHIRAMT) formed from **4** (85.8 mg, 0.261 mmol) and *n*-BuLi (1.0 equiv). The yellow slurry was stirred with gradual warming until a homogeneous burgundy solution was obtained. In the case of R = Me, a homogeneous burgundy mixture was not obtained even after prolonged stirring at room temperature, and it was evident that unreacted $(CuMe)_n$[19] was still present. The solution was cooled to −78 °C, and THF (8 mL each) solutions of *n*-BuMgCl (25.0 equiv) and cyclohexenone (0.3068 g, 3.19 mmol) were added dropwise and simultaneously over a 5-min period. The resulting reaction mixture was stirred for an additional 10 min at −78 °C, quenched with saturated aqueous NH_4Cl solution (7 mL), and worked up as described in the previous section. Pure 3-butylcyclohexanone (0.4617 g, 94%) was obtained as checked by GLC.

3-Phenylcyclohexanone (93% yield) was obtained by this method with use of a PhMgCl/Li[CuPh(CHIRAMT)] ratio of 25:1. The reaction involving the methyl derivative again proved to be sluggish, giving a product mixture (28% combined yield) comprised of ~20% 1,2-addition product and the remainder, 3-methylcyclohexanone. Owing to the catalytic nature of the reaction, the alkyl groups of the Grignard and copper(I) species need not be the same.

Li[CuBr(CHIRAMT)] as Catalyst. A THF (8 mL) suspension of $CuBr{\cdot}Me_2S$ (13.1 mg, 0.064 mmol) was treated with a THF (7 mL) solution of Li(CHIRAMT), prepared from **4** (21.0 mg, 0.064 mmol) and *n*-BuLi (1.0 equiv), at −78 °C under argon. The mixture was allowed to warm up with stirring until a homogeneous red-brown solution was obtained (~20 min). The solution was cooled to −78 °C, and THF (8 mL each) solutions of cyclohexenone (0.308 g, 3.20 mmol) and *n*-BuMgCl (3.20 mmol) were then added dropwise and simultaneously. The resulting yellow-green solution was stirred at −78 °C for an additional 5 min, quenched with a saturated aqueous ammonium chloride solution, and worked up in the usual manner. The product mixture (0.3585 g, 73%) contained some 1,2-addition product (~5%) along with the desired 3-butylcyclohexanone. Conversion to the ketal (see below) and analysis by ^{13}C NMR showed an enantiomeric excess of 14.5%.

Conversion to the Diastereomeric Ketals and Analysis by ^{13}C NMR. A toluene (5 mL) solution of the 3-substituted cyclohexanone (2.0 mmol), (*R*,*R*)-2,3-butanediol (3.4 mmol), tosic acid monohydrate (0.1 mmol), and solid magnesium sulfate (~10 mg) was heated under reflux (3–5 h). The mixture was cooled and concentrated under vacuum. The residue was dissolved in ether and chromatographed through a disposable pipette containing activated alumina (~3 cm). The filtrate was concentrated in vacuo, and the liquid (usually >90% isolated yield) was dissolved in deuteriochloroform. A ^{13}C NMR spectrum was recorded, and a comparison of the integrated carbon resonances (C3 of the ketal) provided an estimate for the relative amounts of diastereomers present.[20]

X-ray Structural Work. $[Li(12\text{-crown-}4)_2][Cu_2(\mu\text{-}Br)(TC\text{-}5,5)]$ (1). An irregularly shaped red crystal grown from THF at −20 °F of approximate dimensions 0.1 mm × 0.16 mm × 0.3 mm was mounted under hydrocarbon grease in a capillary. The tip of the capillary was sealed with a small flame prior to mounting on the diffractometer. The crystal quality was checked by open counter ω scans of several low-angle reflections and showed no unusual features ($\overline{\Delta\omega_{1/2}} = 0.20°$). Study on the diffractometer revealed a *C*-centered monoclinic system with systematic absences consistent with either space group *Cc* (C_s^4, no. 9) or *C*2/*c* (C_{2h}^6, no. 15).[21] Crystal data are as follows: $a = 17.970$ (7) Å, $b = 16.243$ (4) Å, $c = 15.660$ (6) Å, $\beta = 111.44$ (3)°, $V = 4254.7$ Å^3, $Z = 4$. The structure was refined to $R_1 = 0.043$ by using 2122 data with $F_o > 3\sigma(F_o)$. Further details of data collection, reduction, and refinement are summarized in Table S1 (Supplementary Material); typical procedures in our laboratory are described in ref 22. Standard reflections monitored every 3600 s of exposure time showed no crystal decay over a period of 6 days.

The structure was solved and refined in the acentric space group by standard Patterson and difference Fourier techniques. Refinement was carried out by using the SHELX-76 package of crystallographic programs.[23] All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were placed in fixed, calculated positions (C–H = 0.95 Å) and allowed to "ride" on their respective carbon atoms. Each group of hydrogen atoms was given a common isotropic temperature factor, which converged at $U = 0.363$ (10) Å^2 for the aminotroponeiminate ring hydrogen atoms, $U = 0.042$ (6) Å^2 for the methylene linker chain protons, and $U = 0.23$ (2) Å^2 for the crown ether hydrogen atoms. The structure was divided into anionic and cationic blocks, each containing fewer than 280 variables, which were then refined separately with the cycles of refinement alternating between the two blocks. The function minimized was $\sum w(|F_o| - |F_c|)^2$, where $w = 1.0165/[\sigma(F_o) + 0.000625(F_o)^2]$. Scattering factors for neutral atoms and corrections for anomalous dispersion were taken from ref 24; hydrogen atom scattering factors were obtained from ref 25.

Results

Syntheses. The reaction of $Li_2(TC\text{-}5,5)$ with 2.0 equiv of $CuBr{\cdot}Me_2S$ and excess 12-crown-4 produces a compound of limited solubility consistent with its ionic nature (eq 1). This compound, **1**, which represents the first anionic complex of the tropocoronand macrocycles that we have been able to isolate and characterize, is air- and temperature-sensitive. Red solutions of **1** in THF, in which it is only sparingly soluble, quickly turn dark brown upon exposure to oxygen or upon standing for extended periods at room temperature, even in sealed tubes. Compound **1** is stabilized by the crown ether, a class of molecule previously employed to isolate and crystallize sensitive species.[26] Without 12-crown-4, the chemistry proceeds as indicated by eq 2, in which

$$2\ CuBr{\cdot}Me_2S \xrightarrow[\substack{\text{THF} \\ \text{12-crown-4} \\ \text{(4.0 equiv)} \\ -78°\text{ - r.t.}}]{Li_2(TC\text{-}5,5)} \begin{array}{c}]Li(12\text{-crown-}4)_2][Cu_2(\mu\text{ -}Br)(TC\text{-}5,5)] \\ \underset{\sim}{1}\text{, red solid} \\ + \\ [Li(12\text{-crown-}4)_2]Br \\ \text{cream-colored solid} \end{array} \qquad (1)$$

the principal products are metallic copper and the known mononuclear cupric complex, [Cu(TC-5,5)].[27] This disproportionation reaction has been previously observed for binuclear copper(I) tropocoronands.[5]

$$2\ CuBr{\cdot}Me_2S \xrightarrow[\substack{\text{THF} \\ -78°\text{ - r.t.}}]{Li_2(TC\text{-}5,5)} [Cu(TC\text{-}5,5)] + Cu(0) + 2\ LiBr \qquad (2)$$

Compound **1** is also produced indirectly and is present as a contaminant in product mixtures obtained from chemistry designed to form $[Li(12\text{-crown-}4)_2][Cu_2(\mu\text{-}R)(TC\text{-}5,5)]$, **2** (eq 3). This

$$CuBrMe_2S \xrightarrow{RLi} \begin{array}{c} (CuR)_n \\ + \\ LiBr \end{array} \xrightarrow[\text{12-crown-4}]{Li_2(TC\text{-}5,5)} \underset{\sim}{1} \text{ and } \underset{\sim}{2} \qquad (3)$$

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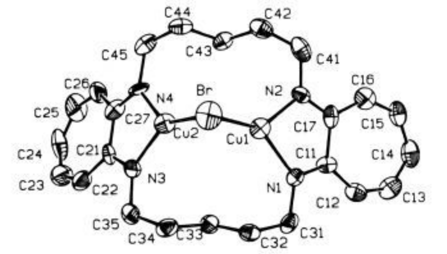

Figure 1. The structure of $[Cu_2(\mu\text{-}Br)(TC\text{-}5,5)]^-$, showing the 50% probability thermal ellipsoids and atom labeling scheme.

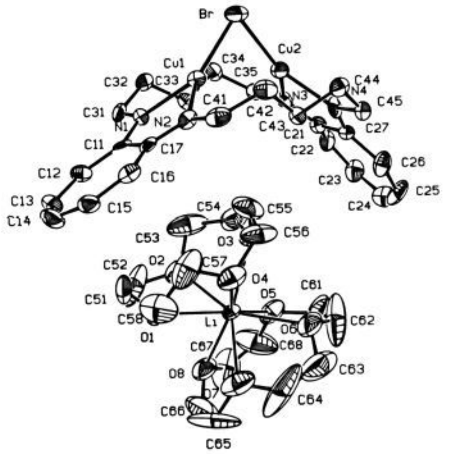

Figure 2. Structure of both the $[Li(12\text{-crown-}4)_2]^+$ cation and $[Cu_2(\mu\text{-}Br)(TC\text{-}5,5)]^-$ anion (alternative view from Figure 1).

result indicated that, in order to isolate pure samples of complexes such as **2**, halide-free solutions were necessary. A tetrakis(acetonitrile)copper(I) salt having a noncoordinating counterion was therefore employed. Although commonly used as a copper(I) source in inorganic chemistry, $[Cu(NCCH_3)_4](BF_4)$ has not enjoyed the popularity of the cuprous halides in the preparation of copper-based reagents in organic synthesis.[28] Possibly, side reactions involving the RLi or RMgCl reagents and the CH_3CN groups of the copper(I) precursor were a concern. As demonstrated by the successful synthesis of the putative phenyl-bridged dicopper(I) tropocoronand, however, the metal atom is apparently more reactive toward phenyllithium, at least, than are the coordinated acetonitrile groups (eq 4). This fact, together with the

$$[Cu(NCCH_3)_4](BF_4) + PhLi \xrightarrow[-78°]{THF} (CuPh)_n + LiBF_4$$

$$\xrightarrow[12\text{-crown-}4]{Li_2(TC\text{-}5,5)} \underset{\mathbf{2}\text{, red solid}}{[Li(12\text{-crown-}4)_2][Cu_2(\mu\text{-}Ph)(TC\text{-}5,5)]} \qquad (4)$$

ease of preparation[18] and storage of $[Cu(NCCH_3)_4](BF_4)$, may make it a viable alternative to the cuprous halides where the absence of potentially coordinating ligands is desired.

Crystal and Molecular Structure of 1. Figures 1 and 2 present two views of the structure of the anionic portion of complex **1**. Table S2 (Supplementary Material) reports final non-hydrogen atom positional parameters, while Table II lists mean values of interatomic distances and angles. Non-hydrogen atom thermal parameters, hydrogen atom positional parameters, a complete listing of bond lengths and angles, and observed and calculated structure factors are available as Tables S3–S6 (Supplementary Material), respectively.

The most noteworthy features of compound **1** are the bridging bromide ligand in the anion and the complexation of the lithium cation by two 12-crown-4 molecules. The tropocoronand complex bears an overall negative charge, in contrast to several other structurally characterized tropocoronand complexes,[1] all of which are neutral, extremely soluble species. Compound **1** is insoluble in nonpolar solvents such as ether and toluene and only sparingly soluble in THF.

Table II. Mean Values of Bond Lengths and Angles of **1**[a]

	min	max	mean
Cu1–Cu2	2.975 (3)		2.975 (3)
Cu–Br	2.308 (2)	2.320 (2)	2.314 (6)
Cu–N	1.994 (10)	2.029 (7)	2.009 (9)
N–C (tropo)	1.29 (1)	1.33 (2)	1.32 (1)
N–C (linker)	1.44 (1)	1.46 (1)	1.452 (5)
C–C (tropo)	1.35 (2)	1.54 (2)	1.41 (2)
C–C (linker)	1.49 (2)	1.53 (2)	1.505 (5)
Li–O	2.26 (3)	2.45 (2)	2.34 (2)
O–C (crown)	1.32 (3)	1.48 (2)	1.39 (1)
C–C (crown)	1.19 (4)	1.45 (3)	1.34 (3)
N–Cu–N	80.6 (3)	81.1 (3)	80.9 (3)
N–Cu–Br	138.1 (2)	140.3 (3)	139.1 (5)
Cu–Br–Cu	80.0 (1)		80.0 (1)
C–N–C	118.7 (8)	120.0 (10)	119.4 (4)
C–N–Cu	114.5 (7)	126.2 (7)	120.1 (20)
N–C–C (tropo)	113.6 (9)	124.4 (9)	118.8 (17)
N–C–C (linker)	111.6 (8)	113.0 (10)	112.2 (3)
C–C–C (tropo)	121.0 (10)	136.0 (10)	128.3 (14)
C–C–C (linker)	112.6 (9)	116.3 (8)	113.9 (7)
C–O–C (crown)	113.0 (10)	123.0 (20)	115.8 (13)
O–C–C (crown)	106.0 (20)	131.0 (20)	117.3 (22)

[a] Standard deviation of the mean: $S_m = \{(\sum X_i)^2 - [(\sum X_i)^2/N]/N(N-1)\}^{1/2}$.

The average Cu–Br bond length in **1** is 2.314 (6) Å, significantly shorter than the corresponding average values of 2.56 (4) Å in the $[(Ph_3P)CuBr]_4$ "cubane" structure,[29] which features triply bridging bromide ions, and 2.45 (2) Å in $[Cu_2(CO)_2(tmen)_2(\mu\text{-}Br)](BPh_4)$ (**5**),[30] a bromide-bridged binuclear complex. The shorter Cu–Br distance in **1** is consistent with the lower coordination number of copper(I).[31] The Cu–Br–Cu angle of 80.0 (1)° in **1** is considerably more acute than that in **5**, 102.8 (1)°, resulting in a shorter distance between copper atoms in **1** (2.975 (3) Å) compared to **5** (3.827 (2) Å). The average Cu–N bond length of 2.009 (9) Å and N–Cu–N bite angle of 80.9 (3)° in **1** compares with respective values of 1.911 (5)° and 84.1 (2)° found in (μ-alkyne)dicopper tropocoronands[2,4] and 1.934 (6) Å and 83.2 (3)° observed for $[Cu_2(CO)_2(TC\text{-}5,5)]$.[5] The coordination geometry of the copper atoms can best be described as trigonal-planar with the sums of the bond angles about Cu1 and Cu2 being 358.3° and 359.9°, respectively. The tropocoronand ligand conformation is saddle-shaped (Figure 2) and is similar to previous tropocoronand structures in which the metals are held in a syn relationship.[2,5]

The cationic portion of compound **1** is comprised of an eight-coordinate lithium atom encapsulated by two 12-crown-4 molecules in approximate D_{4d} symmetry (Figure 2). One may consider the lithium ion as residing in the center of a square antiprism with oxygen atoms occupying the corner positions. The Li–O bond lengths fall between 2.26 (3)–2.45 (2) Å, well within the range of 2.21–2.56 Å found in previous studies.[8a] Thus, the present $[Li(12\text{-crown-}4)_2]^+$ structure bears no significant differences from those found in the literature.

The structure of compound **2** is most likely analogous to that of **1**, with a bridging phenyl group in place of the μ-Br ligand. This proposal is supported by elemental analyses, proton NMR spectral data, which indicate the presence of only one kind of phenyl group and 1 equiv of $[Li(12\text{-crown-}4)_2]^+$, carbon-13 NMR spectral data which support a symmetrical structure, and the well-documented ability of aryl groups to bridge multiple copper centers.[9] Efforts to find conditions suitable for growing X-ray

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Table III. Product Distribution of the Conjugate Addition of Grignard Reagents to Cyclohexenone Using Various Catalysts[a]

entry	catalyst	R	catalyst, mol fract	1,4/1,2[b]	%[c]	% ee[d]
1	Li[Cu_2R(TC-5,5)]	Ph	0.02	97	85	
2	Li[Cu_2R(TC-5,5)]	Bu	0.02	>100	79	
3	Li[Cu_2R(TC-5,5)]	Me	0.02	4	*e*	
4	[Li(12-crown-4)$_2$]-[Cu_2(μ-Br)(TC-5,5)]	Bu	0.006	4	51	
5	[Li(12-crown-4)$_2$]-[Cu_2(μ-Ph)(TC-5,5)]	Bu	0.02	6	62	
6	Li[CuR(CHIRAMT)]d	Ph	0.04	>100	93	4.0 (*S*)
7	Li[CuR(CHIRAMT)]	Bu	0.04	>100	94	14.0 (*S*)
8	Li[CuR(CHIRAMT)]	Me	0.04	4	28	*e*
9	Li[CuR(CHIRAMT)]	Bu	0.02	19	73	14.5 (*S*)

[a] Reactions were carried out by adding equimolar THF solutions of RMgCl and cyclohexenone to a −78 °C THF solution of the catalyst. [b] The regioselectivity was estimated from the relative integrated areas of GLC peaks corresponding to these products (the dehydration of the tertiary alcohol during analysis was assumed). [c] Combined yield after chromatography. [d] As determined by the ratio of diastereomeric ketals (see text). [e] Not determined.

quality crystals are continuing. Of the compounds of general formula [Li(12-crown-4)$_2$][Cu_2(μ-R)(TC-5,5)], where R = Ph, Bu, and Me, the phenyl derivative is the most robust, retaining its orange-red color over weeks at −20 °F in the drybox. The *n*-butyl compound turns brown over just a couple of days under these conditions.

Catalytic Activity. Table III summarizes the product distribution and other features of the conjugate addition of Grignard reagents to cyclohexenone catalyzed by aminotroponeiminate copper(I) alkyl, phenyl, and bromide complexes. Of the catalysts listed, the ones prepared in situ perform the best with respect both to regiospecificity (~100:1 favoring 1,4-addition) and chemical yield (>85% isolated yield). These findings, excluding the poor performance in the case of R = Me, compare favorably with the results of recent work by others.[32]

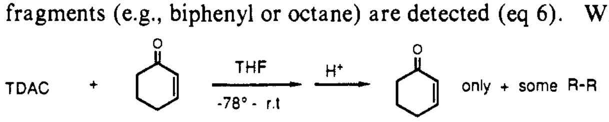
Entries 4 and 5 in Table III also reveal that compounds **1** and **2** are active as catalysts for the conjugate addition reaction. In the case of **1**, reaction with excess Grignard reagent probably displaces bromide ion to give species analogous to **2**. Displacement of bridging halide ion by excess alkyllithium reagent was recently demonstrated to occur in a Ti–Rh heterobimetallic complex.[33] The use of less nucleophilic Grignard reagents in our case, however, may result in incomplete conversion of the μ-bromo complex to the copper(I) alkylating agent under the conditions of the experiment. Under such circumstances, accumulation of unconverted Grignard reagents produces significant amounts of the product expected from its direct reaction with cyclohexenone, the 1,2-adduct. The performance of compound **2** (entry 5, Table III) shows some improvement over that of **1**, lending support to the preceding arguments. Past studies have shown, however, that the factors affecting the ultimate outcome of organocopper-mediated reactions are, in general, quite complex.[7,13,34] The fact that compound **2** still performs well below the level of activity displayed by catalysts prepared in situ may point to the importance of free lithium in these reactions. Little or no free lithium is present in solution under the conditions of entries 4 and 5. By contrast, there are at least two lithium ions per copper in the reactions where catalysts prepared in situ were employed.

It should be noted that, owing to the catalytic nature of the reaction, the R group in the final product is determined solely by the identity of the Grignard reagent (entry 5) and that the sluggishness of methyl group transfer may make that species the ideal general catalyst where Me is retained. This conclusion is similar to that reached previously following studies of mixed-heteroorganocuprate chemistry.[7a,35]

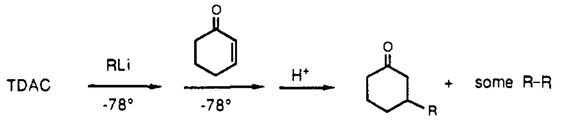
Stoichiometry of the Conjugate Addition. It is useful at this stage to review stoichiometric details of the conjugate addition reaction. First, when a yellow THF solution of Li_2(TC-5,5) (0.5 equiv) and a yellow suspension of $(CuR)_n$[19] in THF are combined at −78 °C and allowed to warm up gradually, an air-sensitive burgundy solution of a tropocoronand dicopper(I) alkyl complex (TDAC) forms (eq 5). The homogeneous solution of the TDAC,

$$\mathrm{CuBr{\cdot}Me_2S} \xrightarrow[0^\circ]{\mathrm{RLi}} (\mathrm{CuR})_n \xrightarrow[-78^\circ\text{ - r.t}]{1/2\ \mathrm{Li_2(TC\text{-}5,5)}} \mathrm{TDAC} \qquad (5)$$

when treated with cyclohexenone (1.0 equiv per Cu), produces no conjugate addition products. Only unreacted cyclohexenone and small amounts of products resulting from coupling of R fragments (e.g., biphenyl or octane) are detected (eq 6). When the TDAC is pretreated at −78 °C with RLi (1.0 equiv per Cu), a reaction accompanied by a slight darkening of the burgundy solution, and then allowed to react with cyclohexenone (1.0 equiv) at −78 °C, 3-alkylcyclohexanone product is produced immediately after quenching of the reaction mixture (eq 7). The intensity of the burgundy color returns to its original shade after addition of the cycloalkenone, and no solids are observed over the course of the fast reaction. A small amount of coupled product, R–R, is still present. The persistence of the deep burgundy color and the absence of any precipitate are taken as evidence that a TDAC is present throughout the course of the reaction and is responsible for the observed conjugate addition product in the presence of added alkyllithium or Grignard reagent. The possible identity of the TDAC is discussed in the following section.

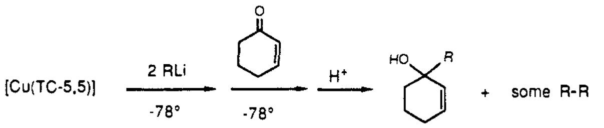


(6)



(7)

Solutions of the mononuclear complex, [Cu(TC-5,5)], yield only 1,2-addition products under conditions that produce only 1,4-addition with the TDAC (eq 8). The RLi-pretreated TDAC's, with R = Ph, Bu, and Me, undergo the "stoichiometric" reaction with cyclohexenone smoothly except that significant amounts (up to 20%) of the 1,2-addition product are obtained with R = Me. This result parallels the behavior of the catalytic system (entry 3, Table III).



(8)

Asymmetric Induction by Chiral Complexes. In order to assess further the significance of binuclear complexes as catalysts for eq 7, we undertook the synthesis of nonmacrocyclic N,N′-disubstituted aminotroponeimines, the chelating and metal-binding abilities of which are well-documented.[36] Although the coordination chemistry of these molecules dates back over 25 years, the aminotroponeimines have been utilized primarily for the synthesis of mononuclear bis(aminotroponeiminato) complexes of divalent first-row transition metals.[37] These under-utilized ligands may be generally useful in forming three-coordinate copper alkyl complexes.[38] Our initial success with the tropocoronands

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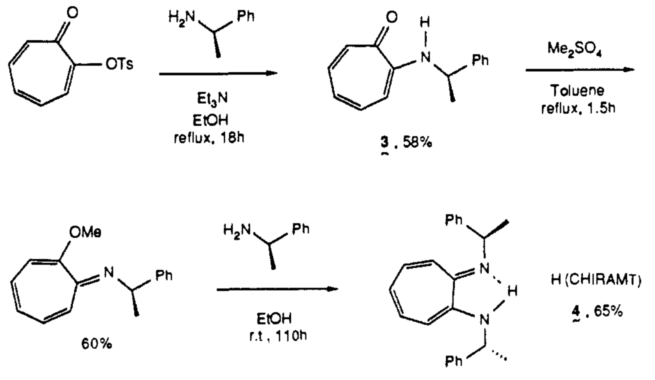
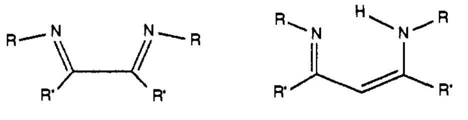
Scheme I



suggested that the aminotroponeimines (AMT's) may also stabilize organocopper compounds where other nitrogen donor ligands have failed.[39] Moreover, other ligand systems employing imine-type donor functionalities, such as the diazabutadiene (DAB) or diazadiene and a number of imine–enamine (ImEn) derivatives, have been used in the synthesis of low-oxidation state metal alkyl and carbonyl compounds.[40] Unlike these other ligand systems, however, the aminotroponeimines possess a highly delocalized electron distribution[41] and are more resistant to attack by nucleophiles[42] or electrophiles[43] that may be present or added to the reaction medium. Not only can the AMT ligands be expected to maintain their chemical integrity in reaction media, but the wide variety of chiral amine carbon fragments[44] that may be incorporated in the AMT adds to their potential synthetic utility as auxiliary ligands. Imine-type ligands have been employed with some success in asymmetric synthesis.[45]

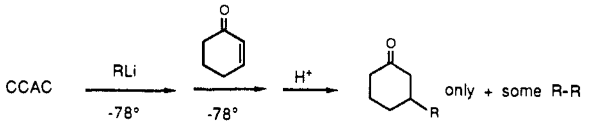


(DAB) (ImEn)

Scheme I outlines the three-step sequence employed to synthesize the first chiral derivative, H(CHIRAMT). The synthesis parallels the procedure used to prepare tropocoronands,[15] but without the final low yield cyclization step, multigram quantities of pure H(CHIRAMT) are readily obtained.

The behavior of the copper alkyl complexes derived from the AMT ligand parallels that of the tropocoronand-derived TDAC so closely that their chemical compositions are most likely very similar. A yellow mixture of $(CuR)_n$ and Li(CHIRAMT) at −78 °C in THF forms a homogeneous burgundy solution upon warming (eq 9). The species in solution, which we refer to as the chiral copper alkyl complex (CCAC), is unreactive toward added cyclohexenone. Pretreatment with RLi (1.0 equiv per Cu) followed by addition of the cycloalkenone at −78 °C, however, leads to the instantaneous and regiospecific production of the Michael-like adduct (eq 10). Once again, a small amount of R–R coupled product is detected, but the reaction produces little, if any, 1,2-addition product. As documented in Table III, fresh solutions of the CCAC are efficient catalysts for the conjugate addition of Grignard reagents (R = Ph, Bu) to cyclohexenone. Even a complex formed from $CuBr{\cdot}Me_2S$ and Li(CHIRAMT) (entry 9) provides useful amounts of product.

$$\underset{\text{yellow slurry}}{(CuR)_n} + Li(CHIRAMT) \xrightarrow[-78^\circ - r.t.]{THF} \underset{\text{burgundy solution}}{CCAC} \tag{9}$$



(10)

The chemistry of the CCAC differs from that of the TDAC in that the 3-alkylcyclohexanone products are optically active with an enantiomeric purity of 4% and 14% observed for the phenyl and butyl derivatives, respectively. These values, while low but comparable to early results in this field,[13c] are nevertheless significant because they were achieved in a system where the chiral ligand-to-substrate ratio is 0.04, about 200 times less than in recently published work where values of 88% ee (six times our result) were observed.[13a] To the best of our knowledge, this is the first time that asymmetric induction in a highly regiospecific catalytic conjugate addition of Grignard reagents to cyclohexenone has been reported. These results suggest the potential utility of chiral AMT-based catalysts in organic synthesis.[50]

Discussion

Addition of 12-crown-4 to reaction mixtures produced by complexation of 2 equiv of either CuBr or CuR with the dilithium salt of $(TC\text{-}5,5)^{2-}$ allows for the isolation of dinuclear anionic tropocoronand complexes with well-separated lithium cations. An X-ray diffraction study of compound **1** confirmed the presence of a single bromide ion bridging two copper(I) atoms. The copper(I) atoms are in a trigonal-planar geometry. This three-coordinate configuration of the copper atoms is characteristic of all dicopper(I) tropocoronand complexes structurally examined to date. These compounds include neutral alkyne-bridged arrangements as well as carbon monoxide adducts in which the {Cu–CO} moieties are located on opposite faces of the macrocycle.[2,4,5] The trigonal-planar geometry appears to be preferred by dicopper(I) tropocoronand complexes, whether neutral or ionic.

With this pattern of coordination, the well-recognized ability of aryl groups to bridge metal ions, and on the basis of spectroscopic evidence, we conclude that compound **2** has the same overall structure as **1**. The carbon-13 NMR spectral data are particularly interesting. The two most downfield resonances in the spectrum, at δ 162.07 and 145.35, are assigned to the imine (C11) carbons of the tropocoronand and the ipso carbon of the bridging phenyl group, respectively. The chemical shift of carbon C11 of the ligand, whenever observed, has been remarkably constant over the range of complexes studied, including **1**, appearing at 163 ppm ± 1.5 ppm. The value of ~145 ppm for the ipso carbon chemical shift is not unreasonable in a system devoid of any deshielding interaction with lithium ions. A chemical shift of 157.1 ppm (C_6D_6) was reported for a copper aryl compound where the ipso carbon may bridge more than two copper atoms.[46a] Also, a chemical shift of 169.9 ppm was observed for the ipso carbon in Ph_2CuLi (10% C_6D_{12} in Me_2S).[46b] The structure of the TDAC produced in the reaction between CuR and $Li_2(TC\text{-}5,5)$ (eq 5) is probably also similar to that of compound **1**. We postulate that a species formulated as $Li[Cu_2(\mu\text{-}R)(TC\text{-}5,5)]$ (the TDAC) forms directly at the elevated temperatures (i.e., above −30 °C) needed for complexation, characterized by a yellow-to-burgundy color change, to take place. The alkyl-bridged dicopper(I) core may be sufficiently stable to account for its inertness toward cyclohexenone. In the presence of excess nucleophilic reagent at −78 °C, however, a new species, containing perhaps two trigonal-planar

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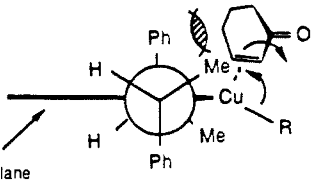
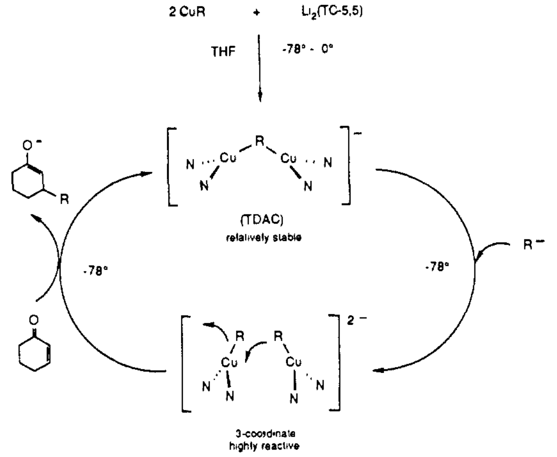


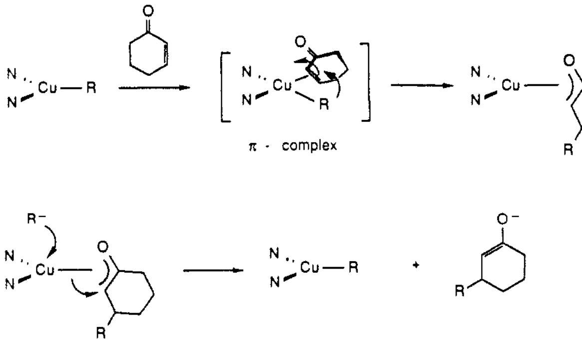
Figure 3. A possible configuration of a diastereotopic π-complex between cyclohexenone and the CCAC.

Scheme II



copper(I) atoms bearing terminal alkyl groups, forms that reacts readily with enone. Scheme II outlines a proposed catalytic mechanism.

Once the bridging mode of the TDAC is broken by excess nucleophile, the resulting copper centers may accommodate the π-donor (enone), forming an intermediate 18e⁻ π-complex from which the Michael-like adduct may emerge (eq 11). Spectroscopic and other evidence has been accumulating in support of a coordination complex which immediately precedes the conjugate addition of cuprates to enones.[47] The proposed mechanism for our system, however, does not invoke the commonly assumed intermediacy of copper(III) β-adducts.[48]



(11)

The same alkyl-bridged binuclear complex may result from the reaction of CuR with the chiral aminotroponeiminate, Li(CHIRAMT), to form Li[(CHIRAMT)Cu(μ-R)Cu(CHIRAMT)] (designated CCAC, eq 9). The same overall mechanism may then apply to account for the system's efficient catalytic property. Solution studies of organocopper compounds support the formation of polynuclear complexes with bridging R groups.[19,49] Chiral induction may take place in the π-complex, perhaps involving an interaction illustrated in Figure 3. Further mechanistic studies of this reaction and the synthesis of catalysts to produce higher enantiomeric selectivity are in progress.[50]

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Registry No. 1, 113548-24-6; **2**, 113584-16-0; **3**, 113548-32-6; **4**, 113548-33-7; 12-crown-4, 294-93-9; Li_2(TC-5,5), 113548-30-4; [Cu(N-CCH_3)$_4$](BF_4), 15418-29-8; *n*-BuMgCl, 693-04-9; Li(CHIRAMT), 113548-31-5; PhMgCl, 100-58-3; Li[Cu_2Ph(TC-5,5)], 113567-61-6; Li[Cu_2Bu(TC-5,5)], 113548-25-7; Li[Cu_2Me(TC-5,5)], 113548-26-8; Li[CuPh(CHIRAMT)], 113548-27-9; Li[CuBu(CHIRAMT)], 113548-28-0; Li[CuMe(CHIRAMT)], 113548-29-1; 2-(tosyloxy)tropone, 38768-08-0; (*R*)-α-methylbenzylamine, 3886-69-9; 2-cyclohexen-1-one, 930-68-7; 3-phenylcyclohexanone, 20795-53-3; 3-butylcyclohexanone, 39178-69-3; 2-butylcyclohexanone, 1126-18-7; 2-methylcyclohexanone, 583-60-8; 3-methylcyclohexanone, 591-24-2; (*S*)-3-phenylcyclohexanone, 57344-86-2; (*S*)-3-butylcyclohexanone, 72746-41-9.

Supplementary Material Available: Tables S1–S6 reporting experimental details of the X-ray study, non-hydrogen atom positional parameters, non-hydrogen atom thermal parameters, hydrogen atom parameters, and a complete listing of non-hydrogen interatomic distances and angles for **1** (6 pages); listing of observed and calculated structure factors for **1** (13 pages). Ordering information is given on any current masthead page.

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(50) **Note Added in Proof**: Substantially higher ee values (~80%) have recently been obtained with use of an improved catalyst system (Ahn, K.-H.; Lippard, S. J., to be submitted for publication).