conversion of $Co(CO)_4^{\bullet}$ to $Co(CO)_3L^{\bullet}$ minimizes the energy wasting back electron transfer

$$Cp_2Co^{\bullet} + Co(CO)_3L^{\bullet} \xrightarrow{\text{slow}} Cp_2Co^{+}Co(CO)_3L^{-} \quad (6)$$

owing to the significantly enhanced oxidation potential of the phosphine-substituted radical.[14] Indeed the high quantum yield ($\Phi = 0.3$) for the photoredox process (eq 4) indicates that $Co(CO)_4^{\bullet}$ is scavenged by phosphine half as fast as it undergoes back electron transfer in eq 3. Furthermore the interception of $Co(CO)_4^{\bullet}$ must follow cage escape from $Cp_2Co^{\bullet}$ (see eq 3) since the ligand substitution of 17ϵ carbonylmetal radicals ($k_s \sim 10^7$ M^{-1} s^{-1})[15] is generally slower than diffusive separation of radical pairs ($\tau \sim 10^{-9}$ s).[16]

When phosphites such as $L' = P(OMe)_3$ and $P(OPh)_3$ are employed as scavengers, the stoichiometry of the photoinduced process is

$$Cp_2Co^{+}Co(CO)_4^{-} \xrightarrow[L']{h\nu_{CT}} Cp_2Co^{+}Co(CO)_3L'^{-} + CO \quad (7)$$

which corresponds to an overall ligand substitution of the tetracarbonylcobalt anion. Such a transformation also derives from an initial CT excitation of the CIP in eq 3 and ligand substitution by phosphite (cf. eq 5). Independent experiments demonstrate that the subsequent thermal reduction of the phosphite-substituted carbonylcobalt dimer is rapid and quantitative, i.e.

$$2Cp_2Co + Co_2(CO)_6L'_2 \rightarrow 2Cp_2Co^{+}Co(CO)_3L'^{-} \quad (8)$$

The latter illustrates the ligand dependence of the redox properties of carbonylmetals since the *phosphine* analogues are inert, i.e.[19]

$$2Cp_2Co + Co_2(CO)_6L_2 \not\rightarrow 2Cp_2Co^{+}Co(CO)_3L^{-} \quad (9)$$

These photoinduced processes of CIP thus provide a novel mode for the activation of ionic species in solution. We hope that further elaborations with a variety of other organometallic and organic ions will establish the generality of the charge-transfer methodology.

Acknowledgment. We thank J. D. Korp for crystallographic assistance and the National Science Foundation and Robert A. Welch Foundation for financial support.

Supplementary Material Available: Tables of bond distances and angles and anisotropic thermal parameters for $Cp_2Co^{+}Co(CO)_4^{-}$ (1 page); table of structure factor amplitudes (4 pages). Ordering information is given on any current masthead page.

(13) (a) Mugnier, Y.; Reeb, P.; Moise, C.; Laviron, E. *J. Organomet. Chem.* **1983**, *254*, 111. (b) Reeb, P.; Mugnier, Y.; Moise, C.; Laviron, E. *J. Organomet. Chem.* **1984**, *273*, 247. (c) Wegman, R. W.; Brown, T. L. *Inorg. Chem.* **1983**, *22*, 183. (d) Cf. also: Lee, K. Y.; Kuchynka, D. J.; Kochi, J. K. *Organometallics* **1987**, *6*, 1886.

(14) For $Co(CO)_4^{\bullet}$, $Co(CO)_3PMe_2Ph^{\bullet}$, and $Co(CO)_3[P(OPh)_3]^{\bullet}$, E°_{red} are estimated to be +0.4, -0.4, and 0.0 V, respectively.

(15) (a) Fox, A.; Malito, J.; Poë, A. *J. Chem. Soc., Chem. Commun.* **1981**, 1052. (b) Hershberger, J. W.; Klingler, R. J.; Kochi, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 61. (c) Herrinton, T. R.; Brown, T. L. *J. Am. Chem. Soc.* **1985**, *107*, 5200. (d) Summers, D. P.; Luong, J. C.; Wrighton, M. S. *J. Am. Chem. Soc.* **1981**, *103*, 5238. (e) Meyer, T. J.; Caspar, J. V. *Chem. Rev.* **1985**, *85*, 187.

(16) (a) Noyes, R. M. *Prog. React. Kinet.* **1961**, *1*, 129. (b) The unexpectedly slow rate of back electron transfer in spite of the driving force[14,17] may arise from a sizeable reorganization energy for $Co(CO)_4^{\bullet}$ resulting from a configurational change.[18]

(17) $E^{\circ}_{ox} = -0.95$ V for Cp_2Co. Koelle, U. *J. Organomet. Chem.* **1978**, *152*, 225.

(18) Hanlan, L. A.; Huber, H.; Kündig, E. R.; McGarvey, B. R.; Ozin, G. A. *J. Am. Chem. Soc.* **1975**, *97*, 7054. See, also: Elian, M.; Hoffmann, R. *Inorg. Chem.* **1975**, *14*, 1058.

(19) (a) The irreversible cathodic CV peak potential for $Co_2(CO)_6[P(OPh)_3]_2$ is 300 mV more *positive* than that for $Co_2(CO)_6[PMe_2Ph]_2$. (b) It is also possible[14] that $Co(CO)_3[P(OPh)_3]^{\bullet}$ is reduced by $Cp_2Co^{\bullet}$ prior to dimerization in eq 5.

An Iron-Activated Alcohol Dehydrogenase: Metal Dissociation Constants and Magnetic and Spectroscopic Properties

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Two alcohol dehydrogenases (ADH) have been isolated from the fermenting bacterium *Zymomonas mobilis*.[1] One is a "normal" zinc enzyme while the second contains iron (α_4; 150000 Da). The presence of naturally occurring iron at the active center of an ADH or of any NAD^+-linked dehydrogenase has not been reported previously. In striking contrast to the four-coordinate ZnN_2S_2 site in horse liver ADH,[2] this communication shows the center to be a mononuclear six-coordinate high spin ferrous site bound to oxygen and nitrogen ligand atoms. Preliminary spectroscopic and magnetic properties of the active Fe^{2+} and Co^{2+} forms are presented as well as those of the inactive Mn^{2+}, Fe^{3+}, Ni^{2+}, Cu^{2+}, and Zn^{2+} forms.

The Fe^{II}–ADH is not very stable as isolated ($t_{1/2}$, 2–5 h; 4 °C). Inclusion of Co^{2+} in the isolation buffer provides Co^{2+}-substituted enzyme, Co–ADH, which is more stable and also active.[3] Treatment of Co–ADH with 1,10-phenanthroline leads to metal-free apoenzyme[3] which may be stored indefinitely at 77 K. Fe^{2+} and Co^{2+} reactivate apo–ADH completely[3] upon addition of a single equivalent, while Zn^{2+} is ineffective under the same conditions.

Apparent dissociation constants determined by metal buffer or competition experiments[4] are listed below

M:	Mn^{2+}	Fe^{2+}	Fe^{3+}	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}
pK_M:	7.4	7.5	5.8	7.8	8.3	8.5	9.0

All the bivalent metals are tightly bound with pK_M increasing monotonically but slowly across the first transition series, a property generally associated with the presence of oxygen ligands.[5] The slope is even lower than those observed[6] for glyoxalase I and phosphoglucomutase, two enzymes thought to involve six-coordinate N_2O_4 coordination spheres.

The tight metal binding and availability of apoenzyme to act as reference and as diagmagnetic correction has facilitated spectral

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(3) Conditions: KMes (10 mM); pH 6.5. The specific activities of Fe-, Co-, and apo–ADH were 750, 300, and <3 IU mg^{-1}. Content (g atoms per subunit) of Fe, Co, and Zn, in the three forms were (0.96 ± 0.15, <0.05, <0.01), (<0.08, 1.16 ± 0.03, <0.01), and (<0.02, <0.05, <0.01), respectively. Enzyme concentrations in the range 0.6–1.2 mM were employed in the physical measurements.

(4) pK_{Co} was determined employing nitrilotriacetic acid as metal buffer.[6a] The concentration of Co–ADH was estimated via the activity assay. Fe^{2+} oxidized under the above conditions. pK_M for the inactive M–ADH (M = Mn^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}) were determined via competition with Co^{2+}. Complementary experiments in which total Co^{2+} and then total M^{2+} concentrations were kept constant were employed to maximize precision. The constant for Fe^{2+} was established via competition with Zn^{2+} and that for Fe^{3+} via competition with Fe^{2+}.

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and magnetic characterization of the system.

Fe^{II}–ADH (95.4 atom% ^{57}Fe) shows a single, asymmetric quadrupole doublet in its Mossbauer spectrum at 4.2 K. The isomer shift (δ, 1.24 mm s^{-1}) and quadrupole splitting (ΔE_Q, 3.43 mm s^{-1}) are typical of high spin $S = 2$ ferrous centers in a ligand field of symmetry close to octahedral.[7] In the presence of a 3.2 T magnetic field, a broad, poorly resolved spectrum was obtained. The spin state is confirmed by the temperature dependence of the magnetic susceptibility measured in the range 4.3–50 K on a SQUID susceptometer (Figure 1): A Curie–Weiss dependence is observed (θ, −3.5 K) with $\mu_{Fe} \sim 5.4\ \mu_B$ in the range 50–20 K and decreasing to 4.1 μ_B at 4.3 K. The behavior is that expected for a $^5T_2(d^6)$ ground state, whose orbital degeneracy has been raised by moderate spin-orbit coupling and by a lower symmetry ligand field.[8]

Active Co^{II}–ADH features a well-resolved electronic spectrum (Figure 2; λ_{max} 510 nm, ϵ 31.5 M^{-1} cm^{-1}) whose molar absorptivity is characteristic of a high spin $S = {}^3/_2$ six-coordinate center of symmetry less than octahedral.[9] The spectrum is similar to those[10] of Co^{2+}-substituted glyoxalase I, conalbumin, and phospholipase C. The magnetic moment shows a gradual decrease from 5.9 μ_B at 52.3 K to 3.9 μ_B at 4.2 K, behavior expected[8] for a $^4T_1(d^7)$ ground state influenced by similar spin-orbit coupling and ligand field effects to those acting in Fe^{II}–ADH. The ESR spectrum (g_1, 5.60; g_2, 3.98; g_3, 2.55; g_{av} 4.04)[11] at 9.5 K supports the presence of a distortion away from octahedral symmetry. The absence of strong absorptions above 350 nm in the electronic and MCD[12] spectra indicates that cysteine is not a ligand.

Each of these physical techniques detect changes at the cobalt site in the binary Co^{II}–ADH–NAD^+ and ternary Co^{II}–ADH–NAD^+–*i*–PrOH complexes[13] (e.g., Figure 2). *i*-PrOH has no effect in the absence of NAD^+. Subtle changes only are apparent in the 4.2 K Mossbauer parameters of the Fe^{II}-binary and -ternary complexes.

The data for Mn^{II}-, Ni^{II}-, and Cu^{II}–ADH support the presence of high spin $S = {}^5/_2$, 1, and ${}^1/_2$ sites, respectively. In particular, the ESR spectrum of Cu^{II}–ADH (Figure 3)[11,14] exhibits a well-resolved nine-line hyperfine pattern in the $g_\perp$ region, characteristic of the presence of four ^{14}N ($I = 1$) ligand atoms, probably supplied by histidine residues.[15] Mn^{II}–ADH shows a strict Curie temperature dependence with μ_{Mn}, 5.9 μ_B, and a high spin Mn^{II} ESR spectrum[14] similar to that of manganese(II)-phosphoglucomutase.[16]

It is apparent from the existing data that the metal binding site contains a mixture of nitrogen and oxygen ligand atoms and that, for the native enzyme, a mononuclear high spin ferrous site is present. Certain oxygenase systems,[17] such as lipoxygenase I and catechol 2,3-dioxygenase, exhibit similar structural features: a closer comparison with those systems and with the zinc-based ADHs[2] will emerge from continuing work.

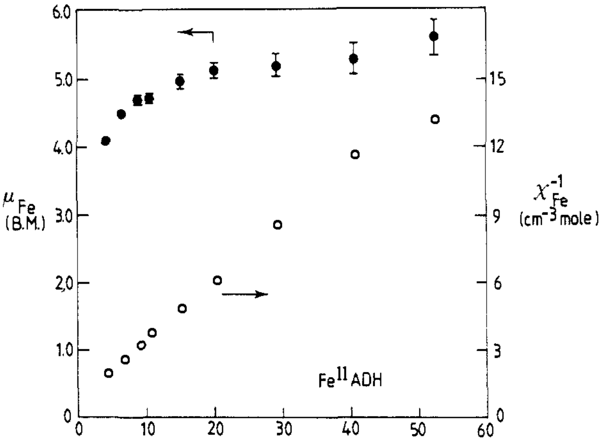

Figure 1. Temperature dependence of the reciprocal magnetic susceptibility (O) and of the magnetic moment (●) per iron atom for Fe^{II}–ADH.

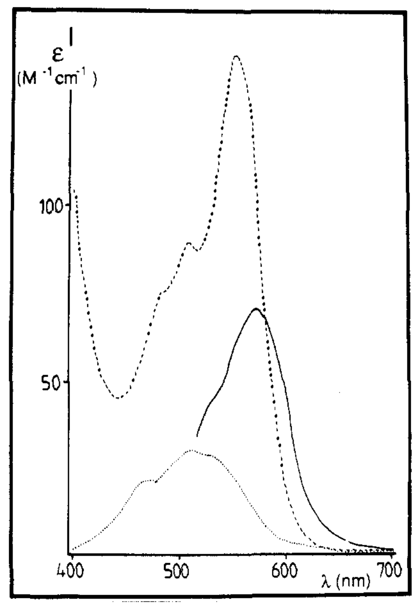

Figure 2. Limiting electronic spectra of Co^{II}–ADH:[3,13] no additives, (···); enzyme plus NAD^+ (3.4 equiv), (—); enzyme plus NAD^+ (3.4 equiv) and *i*-PrOH (2600 equiv), (- - -).

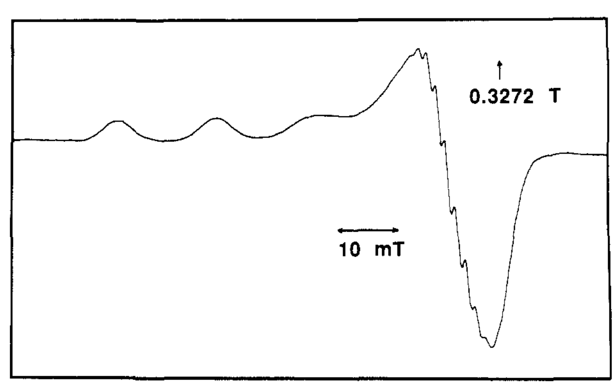

Figure 3. ESR spectrum of Cu^{II}–ADH.[3]

(7) (a) Johnson, C. E. *Topics Appl. Phys.* **1975**, *5*, 139–161. (b) Huynh, B. H.; Kent, T. A. *Adv. Inorg. Biochem.* **1985**, *6*, 163–223.

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(11) Hanson, G. R.; Pilbrow, J. R. are thanked for assistance.

(12) Bicknell, R.; Holmquist, B.; Scopes, R. K., unpublished observations.

(13) The molar ratios of oxidizing substrate NAD^+ and inhibitor *i*-PrOH of 3.4 and 2600 per subunit are those which generate limiting vis-UV and ESR spectra in the Co^{II} system. Note that *i*-PrOH causes dissociation of the tetrameric enzyme into a dimer form.

(14) ^{63}Cu-ADH: $g_\parallel$, 2.275; $g_\perp$, 2.057; $A_\parallel$, 173 × 10^{-4} cm^{-1}; $A_\perp$, 15.3 × 10^{-4} cm^{-1}; $A_\parallel$(N), 1.6 × 10^{-4} cm^{-1}; $A_\perp$(N), 14 × 10^{-4} cm^{-1}. Mn-ADH: g_0, 2.04; A_0, 86 × 10^{-4} cm^{-1}; ZFS < 0.014 cm^{-1}.

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Carbocupration of Cyclopropene. A Novel Synthon of Cyclopropanone Enolate and Its Application to [3 + 2] and [3 + 2 + 2] Annulation

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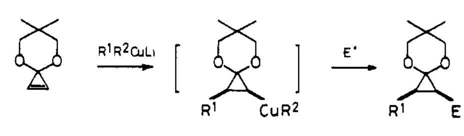
We report here that organocuprates undergo extremely rapid addition across the double bond of the cyclopropenone ketal **1**[1] to produce a previously inaccessible synthon of cyclopropanone enolate **2**. The resultant cuprio cyclopropane **2** then reacts with various electrophiles to produce substituted cyclopropanone ketals **3**. The virtue of this carbocupration/trapping reaction, besides its novelty,[2] stems from its ability to quickly assemble functional groups on the cyclopropane ring[2c] that are useful for further transformation. Thus, the reaction has been developed into a two-step transformation of **1** to a five-membered ring in a [3 + 2] manner as well as to a remarkably efficient single-pot [3 + 2 + 2] constructuion of a seven-membered ring (Scheme I).

Success of such an addition/trapping sequence primarily depends on the efficiency of the addition of the organometallics to the cyclopropene double bond. Of various species examined,[3a] organocuprates were found suitable for the desired reaction scheme.[3b] For instance, quantitative addition of Me_2CuLi (1.1 equiv) to the cyclopropene **1** occurred at −70 °C in 1 min (in ether, terminated by addition of MeOH) to afford the 2-methylcyclopropanone ketal **3a** (96% yield by quantitative GLC analysis; 71% isolated yield). When the reaction was quenched by D_2O, a deuteriated cyclopropane **3b** was obtained. A characteristic high field ^1H NMR signal of the protio 2-methylcyclopropane **3a** (0.30 ppm), assigned to the C-3 proton cis to the C-2 methyl group,[4] was absent in the deuteriated product **3b**, indicating the cis disposition of the metal and the methyl group (i.e., R^1) in the cuprio cyclopropane **2**.

Given the evidence of clean cis addition of the cuprate, we examined the trapping of the cuprio cyclopropane with carbon electrophiles. Thus, treatment of **1** with Me_2CuLi (1.0 equiv) followed by addition of MeI (2.1 equiv)/HMPA (1.05 equiv) gave, after warming to 0 °C, cis-2,3-disubstituted cyclopropane **3c** in 88% yield as a single product. Symmetry elements in the product, established by NMR spectroscopy,[5] unambiguously demonstrated the cis dimethyl structure. These experiments showed that the overall reaction (eq 1) involves the cis addition followed by the trapping with retention of the configuration.



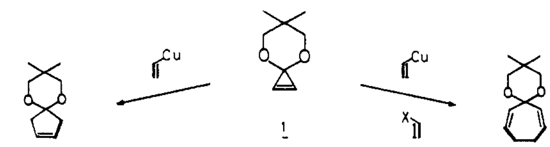
	R^1	E
3a	CH_3	H
3b	CH_3	D
3c	CH_3	CH_3
3d	CH_3	$CH_2CH{=}CH_2$

(1)

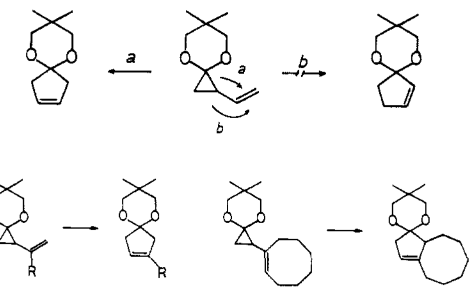
1 2 3

The reaction proceeded smoothly for several combinations of cuprates and alkylating reagents. Table I summarizes the results of the addition/trapping sequence. Addition of Bu_2CuLi followed by trapping with BuI afforded *cis*-dibutylcyclopropanone ketal (entry 6).[5] Allyl bromide reacted with the intermediary cuprio

Scheme I



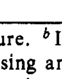
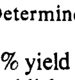
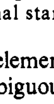
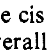
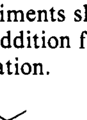
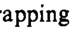
Scheme II[a]



4 R = H 57%
5 R = n-C_7H_{15} 51%
6 R = Ph 56%
7 78%
240–290 °C 1–5h

[a] Carried out in toluene containing 1 equiv of bis(trimethylsilyl)acetamide.

Table I. Carbocupration/Electrophilic Trapping of the Cyclopropenone **1**[a]

entry	cuprate (equiv)	electrophile (equiv)	product		%yield[b]
1	Me_2CuLi (1.10)	MeOH	3a		71, 96[c]
2	(1.0)	MeI (2.1)/HMPA (1.05)	3c		88[c]
3	(1.05)	$CH_2{=}CHCH_2Br$ (2.1)	3d		81[d]
4	$MeCu(Li){-}{\equiv}{-}SiMe_3$ (1.05)	$CH_2{=}CHCH_2Br$ (1.05)	3d		76[d]
5	$MeCu(Li)SPh$ (1.1)	MeI (1.0)/HMPA (1.1)	3c		78[c]
6	Bu_2CuLi (1.0)	BuI (2.1)/HMPA (1.05)			72
7	 R = H (1.3)	H_2O		R = H	54
8	R = Ph (1.3)	H_2O		R = Ph	78
9	 $-Cu(Li){-}{\equiv}{-}SiMe_3$ (1.0)	H_2O		R = H	72
10	 (1.1)	MeI (5)/HMPA (1.1)		R = Me	79

[a] See footnote 14 for experimental procedure. [b] Isolated yield except in entries 1–5. [c] Determined by GLC by using an internal standard. [d] Determined by ^1H NMR by using an internal standard.

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(2) (a) Carbometalation of simple olefins leading to stable organometallics has not been reported: Cf. Yamamoto, Y.; Yamada, J.-i.; Uyehara, T. *J. Am. Chem. Soc.* **1987**, *109*, 5820. (b) There have been reported a few examples of carbometalation of simple cyclopropenes by main group organometallics around or above room temperature: Grignard reagent: Lukina, M. Yu.; Rudashevskaya, T. Yu.; Nesmeyanova, O. A. *Dokl. Akad. Nauk SSSR* **1970**, *190*, 1109. Rudashevskaya, T. Yu.; Nesmeyanova, O. A. *Izv. Akad. Nauk SSSR Ser. Khim.* **1983**, 1821. Lehmkuhl, H.; Mehler, K. *Liebigs Ann. Chem.* **1978**, 1841. Allylic metals: Köster, R.; Arora, S.; Binger, P. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 205. Stoll, A. T.; Negishi, E.-i. *Tetrahedron Lett.* **1985**, *26*, 5671. (c) Elaborate preparation of substituted cyclopropanes directed toward synthesis of complex molecules has been achieved with low level of stereocontrol: cf. Piers, E.; Morton, H. E.; Nagakura, I.; Thies, R. W. *Can. J. Chem.* **1983**, *61*, 1226. Wender, P. A.; Essenstat, M. A.; Filosa, M. P. *J. Am. Chem. Soc.* **1979**, *101*, 2196. Yamamoto, H.; Kitatani, K.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 5816.

(3) (a) Reaction of alkyllithium, alkylmagnesium halide, and alkylcopper resulted either in recovery of **1** at low temperatures or in total decomposition at higher temperatures. (b) The cuprio cyclopropane **2** starts to decompose above −50 to −20 °C.

(4) The assignment was based on the characteristically high chemical shift and the coupling constant (200 MHz ^1H NMR/$CDCl_3$ 0.30 ppm, dd, $J = 5.4$, 5.9 Hz): Cf. Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, 2nd ed.; Pergamon Press: Oxford, 1969; pp 227 and 286.

(5) The appearance of only seven ^{13}C signals (equivalent ketal methyl groups as well as nonequivalent ketal methylene carbons) excluded the trans structure (C_2 symmetry). Same argument also proved the stereochemistry of the *cis*-dibutylcyclopropanone ketal. Further evidence of the cis addition/trapping is provided in the Supplementary Material. Cyclopropyl cuprates generally react with electrophiles with retention of configuration (ref 2c).

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