of a 90:10 mixture of silyl ketene acetals (*Z*/*E*)-**1a** and completely converted within 40 min into the dioxetanes (*Z*/*E*)-**2a** (90:10, determined by NMR). On warming a sample of the dioxetane mixture (*Z*/*E*)-**2a** from −20 to +20 °C, both (*Z*)- and (*E*)-dioxetane rearranged into the α-silylperoxy ester **3a**. At −20 °C as shown by NMR, the time of rearrangement was about 1 d for the isomer (*Z*)-**2a** and several weeks for the (*E*)-**2a** isomer. (*Z*)-**2a**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.10 (s, 3 H, SiMe), 0.12 (s, 3 H, SiMe), 0.89 (s, 9 H, SitBu), 1.02 (s, 9 H, CtBu), 3.71 (s, 3 H, OMe), 4.86 (s, 1 H, CH); ^{13}C NMR (50 MHz, $CDCl_3$) δ −3.5 (2 × q, $SiMe_2$), 18.1 (s, SitBu), 24.4 (q, CtBu), 25.6 (q, SitBu), 29.6 (s, CtBu), 51.6 (q, OMe) 94.4 (d, C-4), 109.6 (s, C-3).

Photooxygenation of (*E*)-*tert*-Butylketene Methyl Trimethylsilyl Acetal ((*E*)-1b). The above general procedure was followed by employing 0.410 g (2.00 mmol) of silyl ketene acetal (*E*)-**1b**, which was completely converted within 50 min into a 70:30 mixture of dioxetane (*E*)-**2b** and α-silylperoxy ester **3b**.[9,21] ^{1}H NMR monitoring of the reaction progress revealed that the latter was formed by rearrangement of the dioxetane (*E*)-**2b**. A sample of the reaction mixture was allowed to stand at 20 °C for 1 d and all the dioxetane rearranged into the α-silylperoxy ester **3b**. (*E*)-**2b**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.29 (s, 9 H, $SiMe_3$), 0.99 (s, 9 H, tBu), 3.27 (s, 3 H, OMe), 4.74 (s, 1 H, CH). **3b**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.19 (s, 9 H, $SiMe_3$), 0.98 (s, 9 H, tBu), 3.75 (s, 3 H, OMe), 4.12 (s, 1 H, CH); ^{13}C NMR (50 MHz, $CDCl_3$) δ −1.4 (q, $SiMe_3$), 26.5 (q, tBu), 34.6 (s, tBu), 51.4 (q, OMe), 91.5 (d, C-2), 171.0 (s, C=O).

Photooxygenation of *tert*-Butylketene Bis(trimethylsilyl) Acetal (1c). The above general procedure was followed by employing 0.780 g (3.00 mmol) of silyl ketene acetal **1c**, which was completely converted within 30 min into a 60:40 mixture (determined by ^{1}H NMR) of dioxetane **2c** and α-silylperoxy ester **3c**.[6,22] On rotaevaporation (0 °C (15 Torr)) the dioxetane was completely converted into the known[6,22] α-silylperoxy ester **3c**. **2c**: ^{1}H NMR (80 MHz, CCl_4) δ 0.1 (s, 9 H, $SiMe_3$), 0.2 (s, 9 H, $SiMe_3$), 0.9 (s, 9 H, tBu), 4.4 (s, 1 H, CH). **3c**: ^{1}H NMR (80 MHz, CCl_4) δ 0.1 (s, 9 H, $OSiMe_3$), 0.2 (s, 9 H, $OOSiMe_3$), 0.9 (s, 9 H, tBu), 3.9 (s, 1 H, CH).

Trapping Experiments with Acetaldehyde. In the Photooxygenation of (*E*)-*tert*-Butylketene Methyl *tert*-Butyldimethylsilyl Acetal ((*E*)-1a). The above general procedure was followed by using 0.240 g (1.00 mmol) of silyl ketene acetal (*E*)-**1a**, 5 mL of acetaldehyde, and 2 mg of TPP in 5 mL of CCl_4. The experiments were run at −20, −10, 0, 10, and 20 °C, and by ^{1}H NMR monitoring no trapping product was detected.

In the Rearrangement of (*E*)-4-*tert*-Butyl-3-[(*tert*-butyldimethylsilyl)oxy]-3-methoxy-1,2-dioxetane ((*E*)-2a). To a solution of 0.140 g (0.510 mmol) of dioxetane (*E*)-**2a** in 2 mL of CCl_4 was added 0.5 mL of acetaldehyde. The reaction mixture was allowed to stand at 35 °C while being monitored by ^{1}H NMR. After all the dioxetane was consumed, the solvent was rotaevaporated (20 °C (17 Torr)) and the residue chromatographed at −40 °C on Florisil by eluting with a 9:1 petroleum ether (bp 30–50 °C)/diethyl ether mixture to give α-silylperoxy ester **3a**, α-hydroperoxy ester **9**,[21] and the diastereomeric trioxanes **10a** and **10a′** in a total yield of 60% and the relative proportions of 35:25:23:17. Iodometry of the isomeric mixture of the trapping products gave a 88.6 ± 1.2% peroxide content. **10a**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.26 (s, 6 H, $SiMe_2$), 0.92 (s, 9 H, SitBu), 1.01 (s, 9 H, CtBu), 1.27 (d, $J = 6$ Hz, 3 H, CMe), 3.77 (s, 3 H, OMe), 4.34 (s, 1 H, 6-H), 5.46 (q, $J = 6$ Hz, 1 H, 3-H). **10a′**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.09 (s, 6 H, $SiMe_2$), 0.94 (s, 9 H, SitBu), 1.01 (s, 9 H, CtBu), 1.24 (d, 3 H, CMe), 3.79 (s, 3 H, OMe), 4.22 (s, 1 H, 6-H), 5.44 (q, 1 H, 3-H). **9**: IR (CaF_2) ν 3520, 3380, 2960, 2868, 1741, 1432, 1370, 1355, 1337, 1215, 1171, 1090 cm^{-1}; ^{1}H NMR (80 MHz, CCl_4) δ 0.89 (s, 9 H, tBu), 3.68 (s, 3 H, OMe), 4.05 (s, 1 H, CH), 8.9 (s, 1 H, OOH).

In the Rearrangement of (*Z*/*E*)-4-*tert*-Butyl-3-[(*tert*-butyldimethylsilyl)oxy]-3-methoxy-1,2-dioxetanes ((*Z*/*E*)-2a). Following the above procedure, a solution of 0.600 mmol of dioxetane (*Z*/*E*)-**2a** and 0.5 mL of acetaldehyde in 2 mL of CCl_4 was allowed to stand at 20 °C while being monitored by ^{1}H NMR. After all of the dioxetane was consumed, the solvent was rotaevaporated (20 °C (17 Torr)) and the residue chromatographed at −40 °C on Florisil by eluting with a 9:1 petroleum ether (bp 30–50 °C)/diethyl ether mixture to give α-silylperoxy ester **3a**, α-hydroperoxy ester **9**, and the diastereomeric trioxanes **10a** and **10a′** in a total yield of 65% and the relative proportions of 61:16:15:8.

Acknowledgment. We gratefully appreciate generous financial support from the Deutsche Forschungsgemeinschaft (SFB Nr. 172 "Molekulare Mechanismen Kanzerogener Primärveränderungen"), the Wilhelm-Sander-Stiftung, and the Fonds der Chemischen Industrie.

Supplementary Material Available: ^{1}H NMR spectra of the compounds (*E*)-**1a**, (*Z*)-**1a**, (*E*)-**1b,c**, (*E*)-**2a**, (*Z*)-**2a**, (*E*)-**2b,c**, **3a**, **3b**, **3c**, **9**, **10a**, **10a′** (14 pages). Ordering information is given on any current masthead page.

A Laser Flash Photolysis Derived Study of a Glycosylidene Carbene

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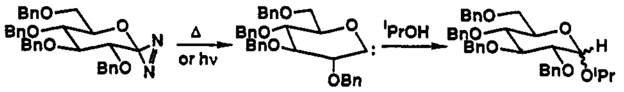
Laser flash photolysis of a glycosylidene-derived diazirine produces the corresponding carbene. The carbene can be intercepted with pyridine to form an ylide. The absolute rate constants for the reaction of the glycosylidene carbene with alcohols can be obtained by monitoring the absolute rate of formation of the pyridinium ylide. The kinetic data favors a mechanism involving a proton transfer from the alcohol to the carbene.

The preparation of the glycosylidene diazirine **1** and some of the chemistry of its corresponding carbene **2** have recently been reported.[1] Carbene **2** inserts into the OH bonds of alcohols and phenols to form mixtures of α- and β-D-glucopyranosides, such as **3**.



1 2 3

Because of the obvious potential of glycosylidene-derived diazirines as glycosyl donors, the mechanism of the reaction of carbene **2** with alcohols was investigated by laser flash photolysis (LFP) techniques.[2] LFP (XeF excimer laser,

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[1] (a) Briner, K.; Vasella, A. *Helv. Chim. Acta* **1989**, *72*, 1371. (b) Briner, K.; Vasella, A. *Helv. Chim. Acta* **1990**, *73*, 1764. (c) Vasella, A. *Pure Appl. Chem.* **1991**, *63*, 507.

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Table I. Absolute Rate Constants for the Reaction of Carbene 2 with Monomeric and Oligomeric ROH at Ambient Temperature[a]

carbene	ROH	pK_{HA}[j]	[ROH],[b] M	*k*, M^{-1} s^{-1} monomer	*k*, M^{-1} s^{-1} oligomer	solvent
2[e]	CH_3CH_2OH	15.90	0–0.5	1.2×10^{6}[d]	1.3×10^7	CH_3CN
2[e]	CH_3OH	15.54	0–0.6	1.1×10^{7}[d]	7.5×10^7	CH_3CN
2[e,f]	CH_3OH	15.54	0–0.3	1.7×10^{7}[d]	8.8×10^7	C_6H_6
2[e]	CF_3CH_2OH[c]	12.4	0–0.0375	6.9×10^8	–	CH_3CN
2[e]	$CF_3CHOHCF_3$[c]	9.30	0–0.009	2.9×10^9	–	CH_3CN
4[g]	CH_3OH	15.54	0.002–0.034	–	7×10^9	n-C_5H_{12}
9[h]	CH_3OH	15.54	–	–	2.5×10^6	n-C_5H_{12}
11[i]	CH_3OH	15.54	–	–	$\sim 10^{10}$	n-C_5H_{12}

[a] The pyridine concentration was 0.0031 M. [b] Linear plots were observed in this concentration range. [c] The alcohol and pyridine may be in appreciable equilibrium with the pyridinium ion and alkoxide ions under these conditions. [d] The precision in this region was quite poor. [e] This work. [f] [Pyridine] = 0.00464 M. [g] Reference 3. [h] Reference 10. [i] Phenylmethoxycarbene, ref 15. [j] Reference 17.

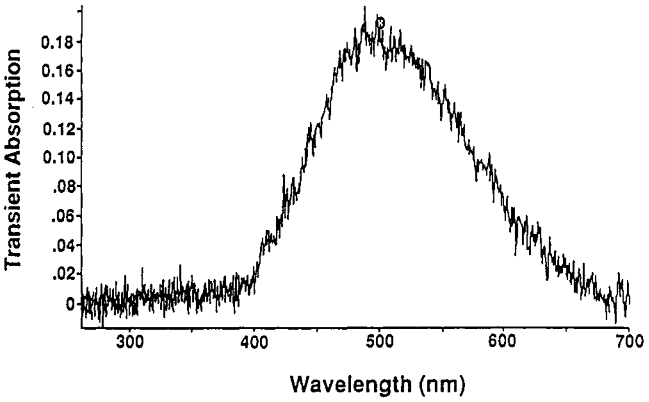

Figure 1. The transient spectrum produced by LFP of **1** in 3:1 acetonitrile–pyridine recorded 400 ns after the laser pulse, during a 1000-ns window.

351 nm, 17 ns, ~80 mJ/pulse) of a dilute solution (A_{351} = 0.182) of the diazirine **1** in acetonitrile does not produce a transient absorption spectrum that is useful for kinetic analysis. This is in contrast to methylmethoxycarbene (**4**), the syn and anti forms of which are known to absorb near 375 and 390 nm, respectively.[3] However, LFP of diazirine **1** in the presence of pyridine produces the intense transient absorption depicted in Figure 1, which is very similar to the spectra of pyridinium ylides[4,5] derived from dialkyl- and alkylhalocarbenes and is attributed to ylide **5**. As predicted from this assignment the rate of formation of **5** is described by a simple exponential function that can be analyzed to yield an observed rate constant k_{obs}. The values of k_{obs} is dependent upon the concentration of pyridine (PYR) as shown in eq 1.[2,6] A plot of k_{obs} versus

$$H_3C-\ddot{C}-OCH_3$$

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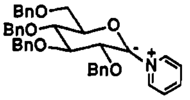

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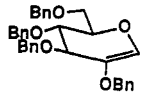

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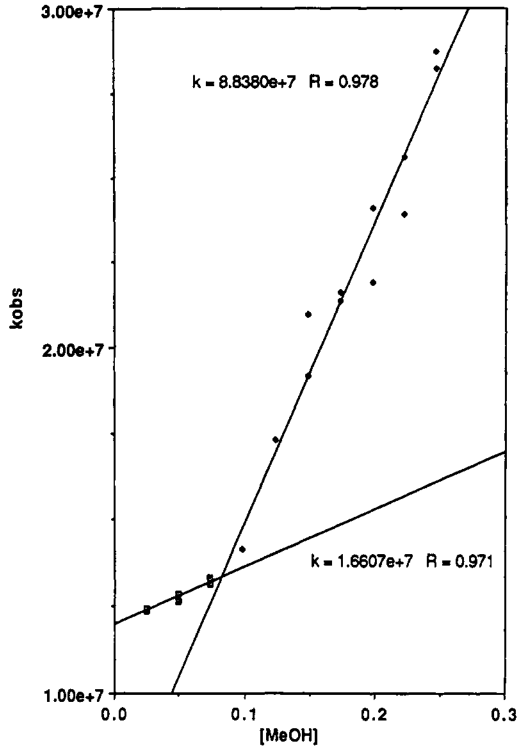

Figure 2. A plot of k_{obs} versus [CH_3OH] at constant [pyridine], in benzene, see text.

$$k_{obs} = k_o + k_{PYR}[\text{pyridine}] \qquad (1)$$

[PYR] is linear, with a slope of 7.89×10^8 M^{-1} s^{-1}, which is the absolute rate constant for the reaction of carbene **2** with pyridine, and is very similar to rate constants reported for closely related carbenes with this substrate.[6] The intercept of the pyridine quenching plot is 1.3×10^6 s^{-1}, which is the sum of all first-order and pseudo-first-order decay processes of carbene **2** in acetonitrile in the absence of pyridine. Under our conditions, the lifetime of **2** in acetonitrile in the absence of pyridine is 772 ns, consistent with Moss' study of methylmethoxycarbene **4** where τ is 500–2000 ns.[3] Product studies reveal that photolysis of **2** in acetonitrile in the absence of alcohol and pyridine leads to a complex mixture of products, among which **6**,[7] the product of a 1,2 hydrogen shift, is a major

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(2) For recent reviews see Moss, R. A.; Turro, N. J. *Kinetics and Spectroscopy of Carbenes and Biradicals*, Platz, M. S., Ed.; Plenum: New York, 1990; p 213. Platz, M. S.; Maloney, V. M. *Ibid.* p 239.

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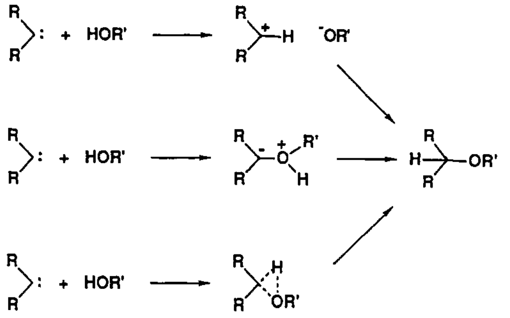
(6) The kinetic probe method described herein is based on the models developed by Scaiano for the study of radicals. (a) Small, R. D., Jr.; Scaiano, J. C. *J. Phys. Chem.* **1977**, *81*, 828. (b) Small, R. D., Jr.; Scaiano, J. C. *Chem. Phys. Lett.* **1977**, *50*, 431. (c) *Ibid.* **1978**, *59*, 246.

(7) Betz, R.; Ph.D. Thesis, University of Konstanz, 1984.

Scheme I



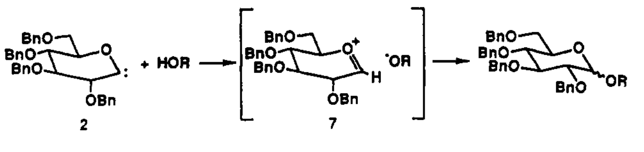
component. Further details will be published separately. The reaction of 2 with pyridine is rather insensitive to solvent: the absolute rate constant for ylide formation in benzene is 8.9×10^8 M^{-1} s^{-1}.

Upon LFP of diazirine 1 in the presence of alcohols the glycosylidene carbene can insert into an OH bond of the quencher in competition with the other processes previously described. Under these conditions, the observed rate constant for formation of ylide 5 is given by eq 2, which for the sake of simplicity *assumes no interaction* between pyridine and alcohol. Thus a plot of k_{obs} versus [ROH]

$$k_{obs} = k_o + k_{PYR}[PYR] + k_{ROH}[ROH] \qquad (2)$$

at constant [PYR] should be linear with a slope equal to the absolute rate constant of reaction of carbene 2 with [ROH]. Typically these plots are not linear (c.f. Figure 2), even in the absence of pyridine (for carbenes which can be directly detected), but show curvature due to oligomerization of the alcohol quencher.[8] Customarily the linear region of the plot obtained at low [ROH] (~0–0.2 M alcohol) is associated with quenching by monomeric alcohol, and the data obtained at large [ROH] (>0.3 M alcohol) is associated with quenching by oligomeric alcohol. The rate constants so obtained are given in Table I, and as a consequence of the curvature are rather imprecise for methanol and ethanol but still clearly demonstrate that the carbenic reactivity tracks the acidity of ROH. Linear plots are obtained with the fluorinated alcohols because they are sufficiently reactive to allow LFP studies at very low concentrations of alcohol, where the alcohol is uniformly monomeric.

A carbene can react with an OH bond by at least three mechanisms, proton transfer most likely to form an ion pair, ylide formation, or by a concerted insertion into the OH bond (Scheme I). The absolute kinetic data of Table I are most consistent with a proton-transfer mechanism leading to an intermediate ion pair as illustrated below, or perhaps with a highly polarized insertion process, because increasing acidity of the alcohol leads to an increase in its reactivity with the oxacarbene. Due to the acidity of the fluorinated alcohols there may be some quenching of the carbene by pyridinium ion. However, under our conditions most of the pyridine cannot be protonated, as it is still capable of trapping the carbene to form ylide 5. Thus we feel that eq 2 is not an unreasonable simplification. The mechanistic conclusion is not surprising considering the nucleophilicity of methylmethoxycarbene 4,[3] and the expected stability of the ion pair 7. Furthermore, protonation reactions of carbenes have been repeatedly postulated,[9] and in fact Kirmse and co-workers have recently directly detected the formation of benzhydryl cation from diphenylcarbene.[10] Similar mechanistic conclusions have been drawn for 9 and 10, two closely related carbenes,[11,12] and laser flash photolysis of adamantyldiazirine in acetonitrile containing *p*-nitrophenol produces *p*-nitrophenolate ion.[13] What is perhaps most surprising is that carbene 2 is 100 times less reactive toward methanol than is the parent methylmethoxycarbene 4, the rate constant for which was determined in pentane. We believe that the large difference in rate between carbenes 2 and 4 is not due simply to a solvent effect, as the rate constant for the reaction of 2 with methanol is very nearly the same in acetonitrile and benzene (note that 1 is insoluble in pentane).



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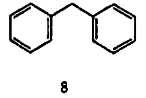

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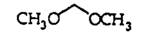

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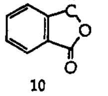

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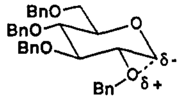
Unlike methylmethoxycarbene 4, glycosylidene carbene 2 does not react with acrylonitrile and methyl acrylate at a rate that is sufficiently rapid to be determined by LFP. This is consistent with the lower reactivity of 2 with methanol relative to carbene 4. The low reactivity of 2 may be a consequence of steric retardation provided by the flanking benzyloxy moiety, or perhaps to an interaction between the flanking oxygen and the carbene center.



Alternatively, the lower reactivity of carbene 2 toward methanol may be due to the σ-acceptor effect of the alkoxy substituents, as this effect is known to influence the reactivity of glycosyl donors by destabilization of cationic intermediate 7.[14]

Experimental Section

The synthesis of diazirine 1 has been described.[1] Acetonitrile was purified by distillation over K_2CO_3 followed by distillation over anhydrous P_2O_5. The alcohols used in this work were purified by distillation over sodium or in the case of $(CF_3)_2CHOH$ the alcohol was dried over molecular sieves and passed through activated basic alumina. The LFP system in use at The Ohio State

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University has been described previously.[16]

Acknowledgment. Support of this work by the NSF (CHE-8814950) and the Swiss National Science Foundation is gratefully acknowledged.

Registry No. 1, 126709-14-6; 2, 134418-71-6; 5, 68536-67-4; 6, 4132-26-7; ethanol, 64-17-5; methanol, 67-56-1; 1,1,1,3,3,3-hexafluoro-2-propanol, 920-66-1; pyridine, 110-86-1; 2,2,2-trifluoroethanol, 75-89-8.

Supplementary Material Available: A plot of k_{obs} versus [pyridine] in CH_3CN and a plot of k_{obs} versus [CH_3OH] at constant [pyridine] (3 pages). Ordering information is given on any current masthead page.

Direct Formation and Subsequent Substitution of Remote Ketone-Functionalized Organocopper Reagents

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Remote ketone-functionalized aryl- and alkylcopper reagents have been synthesized by the use of a highly activated form of zero-valent copper. 5-Bromo-2-pentanone and 4-iodobenzophenenone undergo oxidative addition with activated copper to form 5-cuprio-2-pentanone and 4-cupriobenzophenone, respectively. These, in turn, can be cross-coupled with alkyl halides to produce the corresponding alkylated ketones and with acid chlorides to form the corresponding diketones. By use of this methodology, a two-step, one-pot synthesis of methyl (*E*)-9-oxo-2-decenoate and 8-nonen-2-one have been achieved. The former compound is the methyl ester of the "queen substance" of the honey bee, and the latter is part of an "attractant mixture" for cheese mites found in cheddar cheese. These syntheses were accomplished by converting commercially available 6-bromo-2-hexanone to 6-cuprio-2-hexanone followed by cross-coupling with commercially available methyl 4-bromocrotonate and allyl bromide, respectively.

Introduction

Organocopper compounds[2] are an exceptionally useful class of synthetic reagents primarily due to their ability to undergo substitution reactions[3] with alkyl halides and 1,4-conjugate addition reactions[4] with α,β-unsaturated carbonyl compounds. α-Cuprio ketones have been obtained by forming the enolate of the ketone followed by treatment with a suitable copper(I) salt.[5] This approach, obviously, cannot be used for reagents in which the carbonyl is remote from the desired copper site due to the incompatibility of ketones with the lithium or Grignard precursors used to form the organocopper reagents. Such reagents can be formed by traditional methods only if steps are taken to first mask or protect the ketone, adding time and cost to any synthesis and lowering overall yields.

Rieke and Ebert[6] have recently developed a highly reactive form of copper that permits the direct formation of organocopper compounds from organic halides without utilizing the traditional organolithium or Grignard precursors. This active copper is prepared by reducing an ethereal solution of $CuI{\cdot}PR_3$ with an ethereal solution of lithium naphthalenide or biphenylide under argon. The resulting copper is sufficiently reactive to allow direct oxidative addition to alkyl halides (eqs 1 and 2).

$$\underset{1}{Li^+nap.^{\bullet-}} + \underset{2}{CuI{\cdot}PR_3} \rightarrow \underset{3}{Cu^0} + nap. + PR_3 + LiI \qquad (1)$$

$$2\underset{3}{Cu^0} + RX \rightarrow CuR + CuX \qquad (2)$$

Table I. Stability of Ketones in the Presence of Active Copper

entry	ketone	temp, °C	% recovery, 30 min[a]
1	PhC(O)Ph	25	86
		−78	92
2	$(CH_3)_3CC(O)C(CH_3)_3$	25	82
		−78	87
3	$CH_3C(O)Ph$	25	26
		−78	75
4	$CH_3C(O)CH_2CH_2CH_3$	25	55
		−78	80
5	$CH_3C(O)CH_3$	25	22
		−78	71

[a] GC yields.

Using this highly reactive copper, Rieke and co-workers have further developed stable primary alkylcopper compounds containing ester, chloro, and nitrile functionalities. They have explored the reactions of these reagents with epoxides, acid chlorides, and α,β-unsaturated ketones.[7]

In our own laboratory, we have also continued to study and develop zero-valent copper and wish to report the

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