Communications to the Editor

Direct Formation of Functionalized and Allylic Organocopper Reagents Derived from a Cuprous Cyanide–Lithium Bromide Complex

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In previous work, we have shown that functionalized organocopper reagents can be produced directly from a highly reactive form of zerovalent copper made via the reduction of CuI·PR$_3$ complexes by a solution of lithium naphthalenide in THF and under argon.[1] While active copper produced by this method was shown to oxidatively add to alkyl, aryl, and vinyl halides at low temperatures, the presence of phosphines complicated product isolation. We now report that active copper made from the reduction of a CuCN·2LiBr complex[2] produces functionalized organocopper reagents which cross-couple with acid chlorides and cleanly undergo 1,4-conjugate addition reactions. Significantly, this active copper was also found to oxidatively add to allyl chlorides and acetates at low temperature to allow the direct formation of allylic organocopper reagents without Wurtz-like homocoupling. Moreover, product isolation has been greatly simplified by using this new phosphine-free reagent.

The CuCN·2LiBr complex was reduced between the temperatures of −100 and −110 °C[3] to produce an active copper solution that reacted with organic iodides, bromides, and to some extent chlorides, to produce the organocopper species in high yields. Furthermore, very little homocoupling of the organic halide was seen (<1% as observed by GC).[4] Thus formation of functionalized organocopper reagents containing chloride, nitrile, and ester functionalities were produced from a readily available Cu(I) complex.

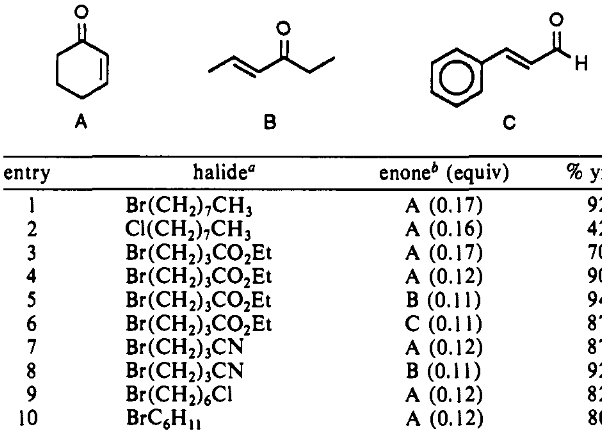
The cross-coupling of these functionalized organocopper species with benzoyl chloride proceeded smoothly at −35 °C in 30 min to produce the functionalized ketones shown in good to excellent yields (Table I). The products were easily isolated via flash silica gel chromatography. An excess of acid chloride must be used (generally 2–3 equiv based on organocopper reagent) since unreacted active copper will react with acid chlorides.[5]

Table I. Cross-Coupling of Benzoyl Chloride with Organocopper Reagents Derived from CuCN·2LiBr-Based Active Copper[a]

entry	halide (equiv)[b]	product[c]	% yield[d]
1	Br(CH$_2$)$_7$CH$_3$ (0.25)	PhCO(CH$_2$)$_7$CH$_3$	82
2	Br(CH$_2$)$_6$Cl (0.25)	PhCO(CH$_2$)$_6$Cl	80
3	Br(CH$_2$)$_3$CO$_2$Et (0.25)	PhCO(CH$_2$)$_3$CO$_2$Et	81
4	Br(CH$_2$)$_2$CO$_2$Et (0.25)	PhCO(CH$_2$)$_2$CO$_2$Et	43
5	Br(CH$_2$)$_3$CN (0.25)	PhCO(CH$_2$)$_3$CN	86
6	bromobenzene (0.20)	PhCOPh	87
7	*p*-BrC$_6$H$_4$CN (0.20)	*p*-NCC$_6$H$_4$COPh	60
8	*o*-BrC$_6$H$_4$CN (0.20)	*o*-NCC$_6$H$_4$COPh	74
9	*o*-BrC$_6$H$_4$CO$_2$Et (0.20)	EtO$_2$CC$_6$H$_4$COPh	51
10	*p*-BrC$_6$H$_4$Cl (0.20)	*p*-ClC$_6$H$_4$COPh	83

[a] To the organocopper species (see ref 3) was added benzoyl chloride (3 equiv based on organocopper) neat via syringe at −35 °C. The solution was stirred for 30 min, quenched with NH$_4$Cl(satd) (5 mL), and worked up with standard flash silica gel chromatographic techniques. [b] Based on 1 equiv of CuCN, alkyl halides were allowed to react for 10 min at −35 °C. Aryl halides were added at 0 °C and allowed to react for 1 h. [c] All products gave consistent ^{1}H and ^{13}C NMR spectra. [d] Isolated yields.

Table II. Conjugate Additions with Organocopper Reagents Derived from CuCN·2LiBr-Based Active Copper



entry	halide[a]	enone[b] (equiv)	% yield[c]
1	Br(CH$_2$)$_7$CH$_3$	A (0.17)	92
2	Cl(CH$_2$)$_7$CH$_3$	A (0.16)	42
3	Br(CH$_2$)$_3$CO$_2$Et	A (0.17)	70
4	Br(CH$_2$)$_3$CO$_2$Et	A (0.12)	90
5	Br(CH$_2$)$_3$CO$_2$Et	B (0.11)	94
6	Br(CH$_2$)$_3$CO$_2$Et	C (0.11)	87
7	Br(CH$_2$)$_3$CN	A (0.12)	87
8	Br(CH$_2$)$_3$CN	B (0.11)	92
9	Br(CH$_2$)$_6$Cl	A (0.12)	82
10	BrC$_6$H$_{11}$	A (0.12)	80
11	BrC$_6$H$_5$	A (0.11)	45
12	ClCH$_2$CH=C(CH$_3$)$_2$	A (0.10)	81[d]

[a] The halide, 0.25–0.30 equiv based on 1 equiv of CuCN, was transferred to the active copper solution at −35 °C. After 15 min, the flask was cooled to −78 °C. A 2–3-fold excess of TMSCl, in respect to the equivalents of 1,4-adduct, was injected neat into the flask (a 6-fold excess of TMSCl was used for entry 6). The 1,4-adduct was dissolved in THF (10 mL) in a separate vial and delivered dropwise to the organocopper solution. After 1.5 h at −78 °C, the flask was gradually warmed to room temperature. [b] Enone: A = 2-cyclohexen-1-one, B = 4-hexen-3-one, C = *trans*-cinnamaldehyde. [c] Isolated yield of 1,4-conjugate addition product (not shown). All products gave consistent IR, HRMS, and ^{1}H and ^{13}C NMR spectra. [d] The enone was injected neat at −90 °C. 3-(3-Methyl-2-butenyl)cyclohexanone was the sole product isolated.

The addition of TMSCl[6] to the organocopper reagents made from CuCN·2LiBr-based active copper allowed for 1,4-conjugate additions to occur readily at −78 °C in good to excellent yields (Table II). Both cyclic and acyclic enones can be used with the ideal organocopper to enone ratio being approximately 2.5:1, respectively. These functionalized organocopper reagents also add to α,β-unsaturated aldehydes in the presence of TMSCl to afford highly functionalized aldehydes (entry 6). The competitive 1,2-

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(3) A representative procedure for the formation of a functionalized organocopper reagent: Li (8.46 mmol) and naphthalene (10.1 mmol) in anhydrous THF (15 mL) were stirred under argon until the Li was consumed (approximately 2 h). The flask was then cooled to −100 °C. CuCN (8.00 mmol) and LiBr (17.27 mmol) in THF (5 mL) were stirred under argon until the Cu(I) salt was solubilized. The CuCN·2LiBr solution was cooled to −40 °C and transferred into the LiNap with a cannula. The solution was stirred for 5 min. The active copper solution was warmed to −35 °C and charged with ethyl 4-bromobutyrate (1.95 mmol). (For aryl halides, the solution was warmed to 0 °C, immediately charged with the aryl halide, and allowed to mix for 1 h.) The solution was stirred for 10 min and was ready for use for acid chloride couplings or conjugate additions.

(4) Eliminated byproducts such as alkene were seen for the alkyl halides in 5–10% yield.

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Table III. Reaction of Allyl Organocopper Reagents Derived from $CuCN{\cdot}2LiBr$ with Benzoyl Chloride

entry	allyl chloride[a]	PhCOR[b]	% yield[c]
1	$ClCH_2CH=CH_2$	$PhCOCH_2CH=CH_2$	65
2	$AcOCH_2CH=CH_2$	$PhCOCH_2CH=CH_2$	63
3	$ClCH_2C(CH_3)=CH_2$	$PhCOCH_2C(CH_3)=CH_2$	75
4	$CH_3CH(Cl)CH=CH_2$	$PhCOCH(CH_3)CH=CH_2$	72
5	$ClCH_2CH=C(CH_3)_2$	$PhCOC(CH_3)_2CH=CH_2$	74

[a] To a solution of active copper at −100 °C was added the allyl chloride (0.25 equiv) which was previously cooled to −78 °C in a vial admixed with THF (1 mL). The PhCOCl (3 equiv based on organocopper) was added neat via syringe at −100 °C and allowed to react for 15 min. [b] All products had consistent ^1H, ^{13}C, and ^{13}C DEPT NMR spectra. [c] Isolated yields.

addition was not seen by GC analysis.

The chemistry of allyl organocopper reagents has received renewed interest with Lipshutz's development of higher order (HO) allylic cyanocuprates,[7] which have been shown to be among the most reactive cuprates yet developed. A common route to allylic organocopper reagents is the transmetalation of allylic stannanes with an appropriate organocopper reagent, itself derived from a transmetalation of an organolithium or Grignard reagent. Significantly, the active copper reported in this paper reacts with allylic chlorides and acetates at −100 °C to produce the corresponding allylic organocopper species with less than 10% of the homocoupled diene byproduct.[8] The resulting organocopper reagents were trapped with benzoyl chloride to produce the ketones shown (Table III). Unsymmetrical allyl chlorides presumably yield the primary organocopper reagent upon reaction with active copper. Since the 1,4-conjugate addition of prenylcopper with cyclohexenone proceeded via α attack (Table II, entry 12), reaction of prenylcopper with benzoyl chloride must involve γ attack (Table III, entry 5). This is the first reported formation of an allyl organocopper reagent formed directly from an allyl chloride and acetate.

In summary, a new type of highly reactive zerovalent copper has been produced which reacts readily with functionalized organic halides at low temperature to form the corresponding functionalized organocopper reagents. These organocopper reagents cross-couple with acid chlorides and undergo conjugate addition in high yields to afford highly functionalized ketones. The isolation of these compounds has been greatly simplified since the use of phosphines has been circumvented. Significantly, this active copper allows the direct formation of allylic organocopper species from allyl chlorides and acetates. The nature of these organocopper reagents and additional cross-coupling reactions are currently under investigation.

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Registry No. A, 930-68-7; B, 2497-21-4; C, 14371-10-9; CuCN, 544-92-3; LiBr, 7550-35-8; $Br(CH_2)_7CH_3$, 111-83-1; $Br(CH_2)_6Cl$, 6294-17-3; $Br(CH_2)_3CO_2Et$, 2969-81-5; $Br(CH_2)_2CO_2Et$, 539-74-2; $Br(CH_2)_3CN$, 5332-06-9; C_6H_5Br, 108-86-1; p-BrC_6H_4CN, 623-00-7; o-BrC_6H_4CN, 2042-37-7; o-$BrC_6H_4CO_2Et$, 6091-64-1; p-BrC_6H_4Cl, 106-39-8; $PhCO(CH_2)_7CH_3$, 6008-36-2; $PhCO(CH_2)_6Cl$, 17734-41-7; $PhCO(CH_2)_3CO_2Et$, 73172-56-2; $PhCO(CH_2)_2CO_2Et$, 6270-17-3; $PhCO(CH_2)_3CN$, 10413-00-0; PhCOPh, 119-61-9; p-NcC_6H_4COPh, 1503-49-7; o-NcC_6H_4COPh, 3717-78-0; o-$EtO_2CC_6H_4COPh$, 604-61-5; p-ClC_6H_4COPh, 134-85-0; $Cl(CH_2)_7CH_3$, 111-85-3; BrC_6H_{11}, 108-85-0; $ClCH_2CH=C(CH_3)_2$, 503-60-6; $ClCH_2CH=CH_2$, 107-05-1; $AcOCH_2CH=CH_2$, 591-87-7; $ClCH_2C(CH_3)=CH_2$, 563-47-3; $CH_3CH(Cl)CH=CH_2$, 563-52-0; $PhCOCH_2CH=CH_2$, 6249-80-5; $PhCOCH_2C(CH_3)=CH_2$, 52813-35-1; $PhCOCH(CH_3)CH=CH_2$, 50599-02-5; $PhCOC(CH_3)_2CH=CH_2$, 62894-04-6; PhCOCl, 98-88-4; naphthalene, 91-20-3; 3-octylcyclohexanone, 57242-85-0; ethyl 4-(cyclohexanon-3-yl)butyrate, 100315-21-7; ethyl 5-methyl-7-oxononanoate, 132514-88-6; ethyl 6-formyl-5-phenylhexanoate, 118744-16-4; 3-(3-cyanopropyl)cyclohexanone, 110718-80-4; 1-cyano-4-methyl-6-oxooctane, 132514-89-7; 3-(6-chlorohexyl)cyclohexanone, 110718-81-5; 3-(cyclohexyl)cyclohexanone, 7122-93-2; 3-phenylcyclohexanone, 20795-53-3; 3-(3-methyl-2-butenyl)cyclohexanone, 29843-83-2.

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(8) The amount of homocoupling was determined by GC using a known sample of 1,5-hexadiene.

Novel Imido– and Phosphorane–Imido–Nickel(II) Complexes. Crystal and Molecular Structure of $(\mu_3\text{-NH})(\mu_3\text{-NPMe}_3)(\text{NiClPMe}_3)_3$

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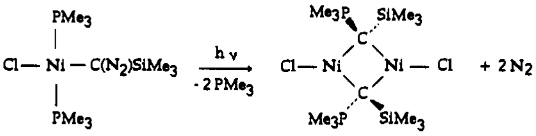
Up to now, the chemistry of nitrene or imido ligands coordinated to late transition metals (groups 8 to 10) has been little developed whereas numerous complexes of the early transition metals have been reported.[1-3]

We recently described the synthesis of the phosphine ylide bridged complex $[NiCl\{C(PMe_3)(SiMe_3)\}]_2$ by photoactivation of the diazomethyl precursor $(PMe_3)_2ClNi[C(N_2)(SiMe_3)]$[4]



(1)

Diazoalkanes and azido derivatives are isoelectronic, and both react with a wide range of organic substrates in the same way.[5] It was thus of interest to investigate the photoactivation of the isoelectronic azido $(PMe_3)_2ClNi(N_3)$ complex **1**. In contrast to diazo complexes, azido compounds are well-known and several nickel-azido species have been prepared.[6a] However, no description of their photochemical reactivity has been reported.

We observed that the photochemical activation of $(PMe_3)_2ClNi(N_3)$ resulted in the formation of new trimetallic and tetrametallic diamagnetic nickel clusters **2** and **3**, with phosphorane–imido and imido ligands in capping positions (eq 2). This result is interesting because only one trimetallic cluster with Ni–imido bonds, $[Ni_3Cp_3(\mu_3\text{-}NR)]$, exists in this class, but as a 49e paramagnetic cluster,[7] and because no phosphorane–imido

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