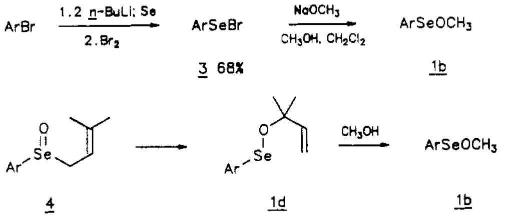
**Table I. Synthesis, Reactions, and $^{77}$Se Chemical Shifts of 1a and Related Compounds**

| no. | product ($\delta$ $^{77}$Se)[a] | starting material | reagents | yield,[b] % |
|---|---|---|---|---|
| **1a** | ArSeOH (1061[c]) | $ArSeOCH_3$ | $H_2O$ | 80 |
| | | $ArSeCH_2CH_2C_6H_5$ | *m*-CPBA | 60 |
| **1b** | $ArSeOCH_3$ (1269[d]) | ArSeBr | $CH_3ONa/CH_3OH$ | 78 |
| | | ArSeOH | $CH_3OH$ | 53 |
| | | $(ArSe)_2/ArSeO_2H$ | $CH_3OH$ | 43 |
| | | $ArSeCH_2CH{=}C(CH_3)_2$ | *m*-CPBA/$CH_3OH$ | 70 |
| **1c** | $ArSeOCH_2CH_3$ (1224[d]) | $NaH/CH_3CH_2OH$ | ArSeBr | 70 |
| **2a** | $ArSeO_2H$ (1217[d]) | ArSeOH | *m*-CPBA | >95 |
| **2b** | $ArSeO_2CH_2$ (1292[d]) | $ArSeOCH_3$ | *m*-CPBA | >95 |
| **2c** | $ArSeO_2CH_2CH_3$ (1282[d]) | $ArSeOCH_2CH_3$ | *m*-CPBA | >95 |
| **6** | $ArSeNHCH_2C_6H_5$ (680[d]) | $ArSeOCH_3$ | $C_6H_5CH_2NH_2$ | 95 |
| | | ArSeOH | $C_6H_5CH_2NH_2$ | >95 |
| **7** | $ArSeSCH_2C_6H_5$ (442[d]) | $ArSeOCH_3$ | $C_6H_5CH_2SH$ | >95 |
| | | ArSeOH | $C_6H_5CH_2SH$ | 91 |
| **9** | $ArSeCH_2CHO$ | $(ArSe_2)/ArSeO_2H$ | $CH_2{=}CHOCH_2CH_3$ | 28[e] |

[a] From $Me_2Se$. [b] NMR yields. [c] Acetone-$d_6$. [d] $CDCl_3$. [e] Isolated yields.

**Scheme I**



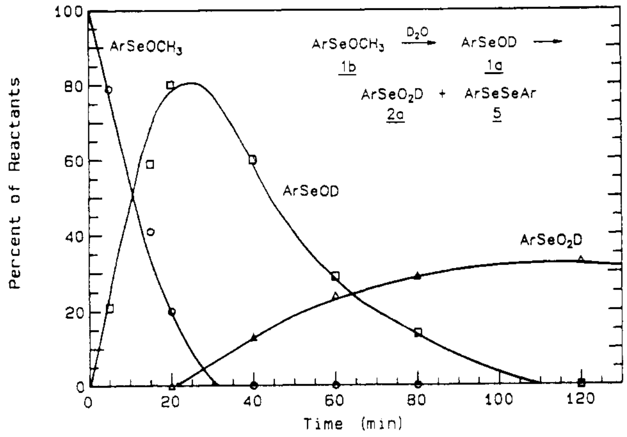


**Figure 1.** Hydrolysis of **1b** in 4% $D_2O/CD_3CN$ at 25 °C. The initial concentration of **1b** was 0.032 M. The diselenide **5** precipitated and was not measured.

Selenenic acid **1a** and its esters are the first to be characterized which lack coordination by an ortho substituent. Despite the size of the 2,4,6-tri-*tert*-butylbenzene substituent,[9] selenenic acid **1a** was far less stable than the *o*-nitro-, *o*-benzoyl-, and *o*-carbomethoxybenzeneselenenic acids previously observed.[1b,c,2c] The chemical reactivity of selenenic acid **1a** and acid **1b** was consistent with that expected for selenenic acids and esters. In particular, strong evidence for the comproportionation of diselenides with seleninic acids was obtained. Finally, we have for the first time demonstrated that only the acids but not the esters disproportionate and comproportionate.

**Acknowledgment.** We thank the National Institutes of Health, NIADDK, for support of this research, and Dr. Carl A. Hoeger for exploratory studies on sterically hindered selenenic acids.[10]

**Registry No.** **1a**, 114031-53-7; **1b**, 114031-54-8; **1c**, 114031-55-9; **2a**, 114031-56-0; **2b**, 114031-57-1; **2c**, 114031-58-2; **3**, 114031-59-3; **5**, 20875-32-5; **6**, 114031-60-6; **7**, 114031-61-7; **8**, 114031-62-8; **9**, 114031-63-9; 2,4,6-$(t\text{-Bu})_3C_6H_2Br$, 3975-77-7; 2,4,6-$(t\text{-Bu})_3C_6H_2Se(CH_2)_2C_6H_5$, 114031-64-0; 2,4,6-$(t\text{-Bu})_3C_6H_2SeCH_2CH{=}C(CH_3)_2$, 114031-65-1.

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(10) Hoeger, C. A. Ph.D. Thesis, University of Wisconsin—Madison, 1983.

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(9) The size of the tri-*tert*-butylphenyl group is sufficient to stabilize ordinarily elusive functional groups such as C=S, P=As, P=Si, and P=Ge double bonds. Okazaki, R.; Ishii, A.; Fukuda, N.; Oyama, H.; Inamoto, N. *J. Chem. Soc., Chem. Commun.* **1982**, 1187. Cowley, A. H.; Lasch, J. G.; Norman, N. C.; Pakulski, M.; Whittlesey, B. R. *J. Chem. Soc., Chem. Commun.* **1983**, 881. Smit, C. N.; Lock, F. M.; Bickelhaupt, F. *Tetrahedron Lett.* **1984**, *25*, 3011. Escudie, J.; Couret, C.; Satge, J.; Andrianarison, M.; Andrianarison, J. D. *J. Am. Chem. Soc.* **1985**, *107*, 3378.

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## Synthesis and Reactivity toward Acyl Chlorides and Enones of the New Highly Functionalized Copper Reagents RCu(CN)ZnI

*Summary:* The new and highly functionalized copper reagents RCu(CN)ZnI obtained from readily available primary and secondary alkylzinc iodides by a transmetalation in THF with the soluble salt, CuCN·2LiX, react in good yields with acyl chlorides and enones, respectively, to afford ketones and 1,4-addition products.

*Sir:* Copper reagents have proven to be very useful in organic synthesis.[2] Their synthetic utility would still be enhanced if highly functionalized copper compounds could be prepared. Since lithium and magnesium organometallics are generally used for their synthesis, only a few functional groups are tolerated and only a direct synthesis using primary alkyl bromides and highly activated copper[3] allows the synthesis of some functionalized copper reagents. The easy generation of functionalized zinc deriva-

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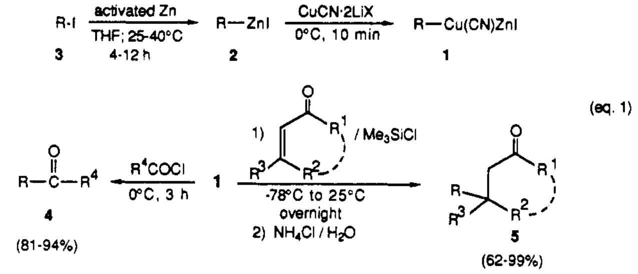
(1) Undergraduate research.

(2) For some reviews, see: (a) Posner, G. H. *Org. React. (N.Y.)* **1972**, *19*, 1; **1975**, *22*, 253. (b) Normant, J. F. *Synthesis* **1972**, 63. (c) Taylor, R. J. K. *Synthesis* **1985**, 364. (d) Yamamoto, Y. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 947; *Angew. Chem.* **1986**, *98*, 945. (e) Lipshutz, B. H. *Synthesis* **1987**, 325.

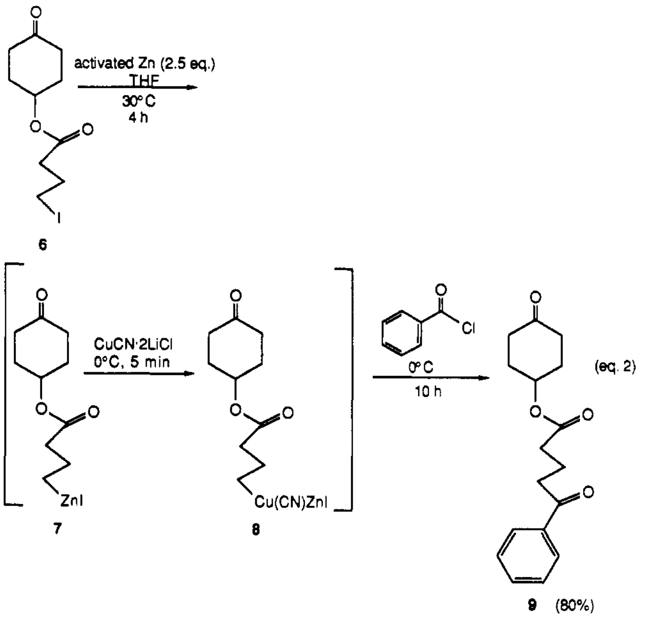
(3) (a) Ebert, G. W.; Rieke, R. D. *J. Org. Chem.* **1984**, *49*, 5280. (b) Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1987**, *52*, 5056. (c) Wu, T.-C.; Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1987**, *52*, 5057.

tives[4,5] and some preliminary results[6] have led us to examine the transmetalation of organozinc compounds into the corresponding organocopper compounds by using copper cyanide.[6,7]

We now wish to report a general preparation of a new class of organocopper reagents $RCu(CN)ZnI$ 1 by the reaction of a soluble copper salt $CuCN\cdot 2LiX$ (X = Cl, Br) with various zinc organometallics 2 (eq 1). Furthermore, we developed a mild and high yield (85–95%) synthesis of polyfunctional zinc organometallics 2 by treating various functionalized iodides 3 with activated zinc in THF.[9] Thus, primary iodides react with zinc at 30 to 40 °C, provided that the metal has been first activated with 4 mol % of 1,2-dibromoethane[9] and then with 3 mol % of chlorotrimethylsilane (see the typical procedure).[10] Under these conditions, secondary iodides react even at 25 °C and no side reactions like homocoupling could be detected. The new copper reagents 1 react rapidly with acyl chlorides (0 °C, 2–3 h) and furnish the ketones 4 in high yields (81–94%; see eq 1 and Table I). Very similar yields are obtained when a catalytic amount of $CuCN\cdot LiX$ (10 mol %) was used. However, without CuCN, the reaction became very sluggish, and the opening of THF by the acyl chloride was an important side reaction. The low cost of CuCN and the short reaction times, as well as the high yields obtained, make this reaction a possible alternative to the corresponding palladium(0)-catalyzed coupling reaction.[12] Furthermore, we found after much experimentation that the copper reagents 1 react in the presence of chlorotrimethylsilane[13] with enones to afford the 1,4-addition products[14] of type 5 in acceptable yields (62–99%; see eq 1 and Table II).



The mild conditions used to generate the zinc organometallic 2 have allowed us to use as a substrate an iodide containing an unprotected ketone group.[15] Thus, the slow addition of a THF solution of the iodide[16] 6 to an excess of activated zinc (2.5 equiv) at 30 °C led to the fast formation (4 h) of the corresponding zinc derivative 7 in 87% GC yield.[8] The transmetalation with $CuCN\cdot 2LiCl$ (0.86 equiv, 0 °C, 5 min) yielded the corresponding copper derivative 8, which was treated with benzoyl chloride (0.86 equiv, 0 °C, 10 h) to afford the diketo ester 9 in 80% isolated yield (eq 2). This behavior was general, and it was possible to generate isopropylzinc iodide and cyclohexylzinc iodide from the corresponding iodides in the presence of cyclohexanone[17] (1 equiv). After a transmetalation with $CuCN\cdot 2LiCl$ and the reaction with benzoyl chloride under standard conditions, the desired ketones were isolated in 86% and 92% yield, respectively, whereas cyclohexanone was recovered in 80% GC yield.



Under our standard conditions, the copper species 1 do not react with epoxides. However, they react readily with allylic halides and afford with high regioselectivity the $S_N2'$ substitution products. Thus, the reaction of (3-cyanopropyl)zinc iodide with cinnamyl bromide and 3-chloro-

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(4) In these cases, the organozinc compound was generated in the presence of the electrophile. (a) Tamaru, Y.; Ochiai, H.; Yamada, Y.; Yoshida, Z. *Tetrahedron Lett.* **1983**, *24*, 3869. (b) Knochel, P.; Normant, J. F. *Tetrahedron Lett.* **1984**, *25*, 1475. (c) Petrier, C.; Dupuy, C.; Luche, J. L. *Tetrahedron Lett.* **1986**, *27*, 3149. (d) Ochiai, H.; Tamaru, Y.; Tsubaki, K.; Yoshida, Z. *J. Org. Chem.* **1982**, *52*, 4420.

(5) (a) Tamaru, Y.; Ochiai, H.; Nakamura, T.; Tsubaki, K.; Yoshida, Z. *Tetrahedron Lett.* **1985**, *26*, 5559. (b) Tamaru, Y.; Ochiai, H.; Nakamura, T.; Yoshida, Z. *Tetrahedron Lett.* **1986**, *97*, 955. (c) Comins, D. L.; O'Connor, S. *Tetrahedron Lett.* **1987**, *28*, 1843. (d) Nakamura, T.; Kuwajima, I. *Tetrahedron Lett.* **1986**, *27*, 83. (e) El Alami, N.; Belaud, C.; Villieras, J. *J. Organomet. Chem.* **1987**, *319*, 303. (f) Nakamura, E.; Sekiya, K.; Kuwajima, I. *Tetrahedron Lett.* **1987**, *28*, 337.

(6) Knochel, P.; Normant, J. F. *Tetrahedron Lett.* **1986**, *27*, 4427, 4431.

(7) The complex copper bromide–dimethyl sulfide was reported to be able to transmetalate a zinc homoenolate into the corresponding copper species. However, the presence of HMPA as a cosolvent was required to promote the initial transmetalation: (a) Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1984**, *106*, 3368. (b) See ref 5f.

(8) The formation of the zinc organometallic was monitored by GC using an internal standard (undecane or tridecane). The yield can be approximately determined by weighing the residual zinc.

(9) Gaudemar, M. *Bull. Soc. Chim. Fr.* **1962**, 974.

(10) Erdik, E. *Tetrahedron* **1987**, *43*, 2203.

(11) Trimethylchlorosilane has been used for the preparation of zinc enolates: (a) Gawronsky, J. K. *Tetrahedron Lett.* **1984**, *25*, 2605. (b) Picotin, G.; Miginiac, P. *J. Org. Chem.* **1987**, *52*, 4796. (c) Picotin, G.; Miginiac, P. *Tetrahedron Lett.* **1987**, *28*, 4551. We found that this activation can be extended for the formation of various organozinc compounds. Thus, without trimethylchlorosilane (only 1,2-dibromoethane activation), a temperature of 55 to 60 °C was required to form butylzinc iodide.[9] However, with the trimethylchlorosilane activation, the reaction proceeds at 40 to 45 °C (90% yield).

(12) (a) Negishi, E.; Bagheri, V.; Chatterjee, S.; Luo, F.-T. *Tetrahedron Lett.* **1983**, *24*, 5181. (b) Grey, R. A. *J. Org. Chem.* **1984**, *49*, 2288.

(13) (a) Chuit, C.; Foulon, J. P.; Normant, J. F. *Tetrahedron Lett.* **1981**, *37*, 1385; **1980**, *36*, 2305. (b) Bourgain-Commercon, M.; Foulon, J. P.; Normant, J. F. *J. Organomet. Chem.* **1982**, *228*, 321. (c) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1985**, *26*, 6015, 6019. (d) Alexakis, A.; Berlan, J.; Besace, Y. *Tetrahedron Lett.* **1986**, *27*, 1047. (e) Horiguchi, Y.; Matsuzawa, S.; Nakamura, E.; Kuwajima, I. *Tetrahedron Lett.* **1986**, *27*, 4025. (f) Nakamura, E.; Matsuzawa, S.; Horiguchi, Y.; Kuwajima, I. *Tetrahedron Lett.* **1986**, *27*, 4029.

(14) The intermediate silyl enol ethers were not isolated and directly hydrolyzed with an aqueous $NH_4Cl$ solution to compounds 5.

(15) Very recently the generation of similar zinc organometallics in benzene/HMPA (8:1) was reported: Tamaru, Y.; Ochiai, H.; Nakamura, T.; Yoshida, Z. *Angew. Chem.* **1987**, *99*, 1193.

(16) The iodide 6 was prepared in three steps from 1,4-cyclohexanediol: (i) $ClCH_2CH_2CH_2COCl$ [1 equiv, 2 h, 20 °C, pyridine (1 equiv), 65%]. (ii) PCC (3 equiv, 20 °C, 3 h, 73%). (iii) NaI (1.5 equiv, 80 °C, 14 h in 2-butanone, 72%).

(17) In a calibration experiment, a THF solution of butylzinc iodide, cyclohexanone (1 equiv), and an internal standard was stirred at 28 °C. Aliquots were taken at various times and quenched with an excess of iodine. GC analysis shows that 100%, 95%, and 45% of the butylzinc iodide was present after 2, 7, and 21 h, respectively. See also: Hansen, M. M.; Bartlett, P. A.; Heathcock, C. H. *Organometallics* **1987**, *6*, 2069.

(18) Satisfactory spectral data (IR, $^1H$ and $^{13}C$ NMR, mass spectra) and elemental analyses were obtained for all new compounds.

**Table I. Reaction of Acyl Chlorides with Organocopper Reagents 1[18]**

| RCu(CN)ZnI | $R^4COCl$ | $R^4COR$ | yield,[a] % |
|---|---|---|---|
| BuCu(CN)ZnI | Ph(CO)Cl | Ph(CO)Bu | 85 |
| BuCu(CN)ZnI | $C_5H_{11}(CO)Cl$ | $C_5H_{11}(CO)Bu$ | 85 |
| BuCu(CN)ZnI | c-$C_6H_{11}(CO)Cl$ | c-$C_6H_{11}(CO)Bu$ | 81 |
| *i*-PrCu(CN)ZnI | Ph(CO)Cl | Ph(CO)-*i*-Pr | 88 |
| *i*-PrCu(CN)ZnI | $ClCH_2CH_2CH_2(CO)Cl$ | Cl-$CH_2CH_2CH_2(CO)$-*i*-Pr | 90 |
| *i*-PrCu(CN)ZnI | Ph(OAc)CH(CO)Cl | Ph(OAc)CH(CO)-*i*-Pr | 82 |
| *sec*-BuCu(CN)ZnI | $ClCH_2CH_2CH_2(CO)Cl$ | Cl-$CH_2CH_2CH_2(CO)$-*sec*-Bu | 94 |
| c-$C_6H_{11}Cu(CN)ZnI$ | Ph(CO)Cl | Ph(CO)-c-$C_6H_{11}$ | 84 |
| $EtO_2CCH_2CH_2CH_2Cu(CN)ZnI$ | Ph(CO)Cl | $Ph(CO)CH_2CH_2CH_2CO_2Et$ | 87 |
| *t*-$BuOCOCH(CH_3)CH_2CH_2CH_2Cu(CN)ZnI$ | Ph(CO)Cl | $Ph(CO)CH_2CH_2CH_2CH(CH_3)OCO$-*t*-Bu | 93 |
| N≡C-$CH_2CH_2CH_2Cu(CN)ZnI$ | Ph(CO)Cl | $Ph(CO)CH_2CH_2CH_2CN$ | 93 |

[a] Isolated yield.

**Table II. Products of Type 5 Obtained by the Reaction of Enones with Organocopper Reagents 1[18]**

| | product of type 5 | | | | |
|---|---|---|---|---|---|
| RCu(CN)ZnI | $R^1$ | $R^2$ | $R^3$ | R | yield,[a] % |
| | Reaction with 2-Cyclohexen-1-one | | | | |
| BuCu(CN)ZnI | $(CH_2)_3$ | | H | Bu | 97 |
| *i*-PrCu(CN)ZnI | $(CH_2)_3$ | | H | *i*-Pr | 98 |
| c-$C_6H_{11}Cu(CN)ZnI$ | $(CH_2)_3$ | | H | c-$C_6H_{11}$ | 98 |
| $EtO(CO)CH_2CH_2CH_2Cu(CN)ZnI$ | $(CH_2)_3$ | | H | $CH_2CH_2CH_2(CO)OEt$ | 94 |
| *t*-$BuO(CO)CH(CH_3)CH_2CH_2CH_2Cu(CN)ZnI$ | $(CH_2)_3$ | | H | $CH_2CH_2CH_2(CH_3)CH(CO)O$-*t*-Bu | 94 |
| $N{\equiv}CCH_2CH_2CH_2Cu(CN)ZnI$ | $(CH_2)_3$ | | H | $CH_2CH_2CH_2CN$ | 97 |
| | Reaction with 2-Cyclopenten-1-one | | | | |
| $N{\equiv}CCH_2CH_2CH_2Cu(CN)ZnI$ | $(CH_2)_2$ | | H | $CH_2CH_2CH_2CN$ | 81 |
| | Reaction with *trans*-4-Phenyl-3-buten-2-one | | | | |
| $N{\equiv}CCH_2CH_2CH_2Cu(CN)ZnI$ | $CH_3$ | H | Ph | $CH_2CH_2CH_2CN$ | 99 |
| | Reaction with 3-Methyl-2-cyclohexen-1-one | | | | |
| BuCu(CN)ZnI | $(CH_2)_3$ | | Me | Bu | 62 |

[a] Isolated yield.

1-butene afford 5-phenyl-6-heptenenitrile (0 °C, 1 h, 88%) and 6-octenenitrile (0 °C, 1 h, 85% cis/trans mixture), respectively. In both cases, less than 4% of the $S_N2$ substitution products was detected.[19]

**Typical Procedure.** A suspension of 1.7 g (26 mmol) of zinc (99.99% purity) in 2 mL of THF containing 190 mg (1.0 mmol) of 1,2-dibromoethane was heated to 65 °C for a minute and cooled to 25 °C, and 0.1 mL (0.8 mmol) of chlorotrimethylsilane was added. After 15 min at 25 °C, a solution of the iodide (25 mmol) in 10 mL of THF was slowly added (at 25 °C in the case of a secondary iodide; at 30 °C in the case of a primary iodide). After the end of the addition, the reaction mixture was stirred 12 h at 25–30 °C (or at 35–40 °C in the case of a primary iodide). Usually less than 100 mg of zinc remains, indicating a yield of 90%. The clear, colorless solution was then cooled to −10 °C, and a solution of 1.98 g (22 mmol) of CuCN and 1.9 g (44 mmol) of LiCl (dried at 150 °C for 1 h) in 22 mL of THF was rapidly added. The resulting light green solution was stirred at 0 °C for 10 min and was then ready to use.

**(a) Reaction with Acyl Chlorides or Allylic Halides.** The acyl chloride or the allylic halide (18.7 mmol) was slowly added to the above prepared solution of the copper reagent 1 at −25 °C. The reaction mixture was then stirred for 3 h at 0 °C. After the usual workup, the residue obtained was purified by distillation or flash chromatography.[18]

**(b) Reaction with 2-Cyclohexen-1-one.** A solution of 1.73 g (18 mmol) of 2-cyclohexen-1-one and 5.5 mL (43 mmol) of chlorotrimethylsilane in 10 mL of ether was slowly added (0.5 h) to the above prepared solution of the copper reagent cooled at −78 °C. After 3 h of stirring at −78 °C, the reaction mixture was allowed to warm up to 25 °C overnight and then worked up.

The high tolerance of important functional groups like esters, nitriles, and ketones as well as the high stability of new copper reagents RCu(CN)ZnI should find broad applications in organic syntheses. Studies concerning the reactivity of these organometallics toward other electrophiles are currently under way in our laboratory.

**Acknowledgment.** We thank the Chemistry Department of The University of Michigan for support of this work and La Vieille Montagne Co. (France) for the gift of zinc.

**Supplementary Material Available:** Spectral data and elemental analyses for new compounds (8 pages). Ordering information is given on any current masthead page.

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*Received February 24, 1988*

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[19] $R_2Zn$ in the presence of $CuBr{\cdot}Me_2S$ has been reported to give very high $S_N2'/S_N2$ product ratios: Nakamura, E.; Aoki, S.; Sekiya, K.; Oshino, H.; Kuwajima, I. *J. Am. Chem. Soc.* **1987**, *109*, 8056. See also: Ochiai, H.; Tamaru, Y.; Tsubaki, K.; Yoshida, Z. *J. Org. Chem.* **1987**, *52*, 4418.

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## The Low-Temperature, Ionic Diels–Alder Addition of Vinyl Ortho Esters to 1,3-Dienes

*Summary:* 3,3,3-Triethoxypropene (triethyl orthoacrylate) was added to a series of 1,3-dienes in the presence of

0022-3263/88/1953-2392$01.50/0