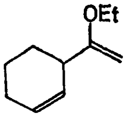
Copper 'ate' Complexes of α-Ethoxyvinyl-lithium: Reagents for Coupling and 1,4 Addition of a Masked Acyl Anion

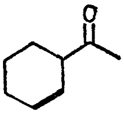
By Robert K. Boeckman Jr* and Kenneth J. Bruza
(*Department of Chemistry, Room* 277 *Chemistry Building, Wayne State University, Detroit, Michigan* 48202)
and J. E. Baldwin* and O. W. Lever, Jr.
(*Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts* 02139)

Summary Stoicheiometric and mixed organocuprate reagents have been prepared from α-ethoxyvinyl-lithium and undergo ready conjugate addition and coupling reactions.

The transfer of masked acyl anions *via* coupling and conjugate addition has received considerable attention recently.[1] The use of copper complexes of masked acyl anions has met with some difficulties. Complexes of dithian anions, perhaps the most readily accessible acyl anion equivalents, do not exhibit the desired reactivity.[2] An acyclic thioacetal has been used in an isolated case.[3] This reactivity problem has been circumvented by use of vinyl silyl copper reagents, but considerable manipulation is required to liberate the masked carbonyl.[4] Use of metallated vinyl ethers[5] eliminates the difficulties of hydrolysis, although reactivity is limited to additions to carbonyl derivatives and alkylation. We therefore examined the possibility that an organocopper reagent could be prepared, to extend the utility of metallated vinyl ethers in conjugate addition reactions.



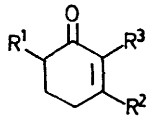
(1)

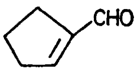


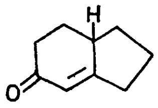
(2)

Rapid treatment of a suspension of purified[6] copper iodide (1 equiv.) in tetrahydrofuran (THF) at −78 °C with a THF solution of α-ethoxyvinyl-lithium (2 equiv.),[5] warmed slowly to and kept at −25 to −30 °C for 1 h affords a deep red solution of the cuprate reagent. The solution was cooled to −78 °C and the substrate (1 equiv.) in THF added. After warming slowly to 0° (*ca.* 2 h), the mixture was hydrolysed† and the products isolated. The yields (Table) ranged from 70—90% for the initial adducts. The reagent appears to be very sensitive to steric congestion in the substrate, so that we were unable to effect addition to $\beta\beta$-disubstituted enones in good yield. In this respect, the silicon reagents are apparently superior.

Hydrolysis of the adducts to the corresponding diketones was effected by dilute HCl in ether. The conditions for each case (*e.g.* time required) were adjusted to maximize the yield of diketone, some of which were apparently acid sensitive. In very sensitive cases, exposure to wet silica gel in benzene at room temperature for *ca.* 12 h will also effect the hydrolysis under very mild conditions.


(3)


(4)


(5)

TABLE

Substrate	Yield/%[a,b]	
	1,4 Adduct	1,4 Diketone
(3) $R^1 = R^2 = R^3 = H$	84	95
(3) $R^1 = Me$, $R^2 = R^3 = H$	90	90
(3) $R^1 = Pr^i$, $R^2 = R^3 = H$	78	57
(3) $R^1 = R^2 = H$, $R^3 = Me$	80	
(3) $R^1 = R^3 = H$, $R^2 = Me$	—[c]	
(4)	—[d]	
$Me_2C{=}CH{-}C(O)Me$	25[c]	
(5)	—[c]	

[a] Isolated yields. [b] New compounds characterized by i.r., n.m.r. and m.s. analysis (high and low resolution). [c] Unsaturated substrate recovered along with small amounts of 1,2 addition products. [d] Exclusive 1,2 addition occurred in this case.

We have extended the scope of reactivity to halide coupling. Treatment of 3-bromocyclohexene (1 equiv.) with cuprate reagent[7] (5 equiv.) afforded the adduct (**1**) (74%) and the $\beta\gamma$ enone (**2**) upon hydrolysis[8] (70%). Under the same conditions and also prolonged reaction at −20 °C (8 h), 1-bromo-octane failed to undergo coupling. Because simple alkylation can be accomplished without conversion into the copper complex, the use of the copper complex should allow selective coupling in the presence of simple halide and carbonyl functions. Attempts to use the cuprate to open oxirans were unsuccessful. Epoxycyclohexane failed to react under the usual conditions.

We have also demonstrated that a mixed cuprate complex[9] is formed without the aid of a solubilizing ligand, from a suspension of pent-1-ynylcopper[10] and α-ethoxyvinyllithium under the conditions described for the stoicheiometric reagent. Addition of the substrate to the yellow homogeneous solution at −78 °C following the above procedure affords the adduct from 2-cyclohexen-1-one in 83% yield. This allows the more efficient use of complex vinyl ethers.

We thank the National Science Foundation, the Petroleum Research Fund, administered by the American Chemical Society, and National Institutes of Health for support.

(*Received, 11th April* 1975; *Com.* 422.)

---

† Buffered NH_4Cl (pH = 8; NH_4OH) was used.

[1] G. Stork and J. Maldanado, *J. Amer. Chem. Soc.*, 1971, **93**, 5286; H. Yammamoto, K. Oshima, K. Shimoji, H. Takahashi, and H. Nozaki, *ibid.*, 1973, **95**, 2695; J. E. Richman, J. L. Herrmann, and R. H. Schlessinger, *Tetrahedron Letters*, 1973, 3267, 3273.

[2] D. Seebach, *Synthesis*, 1969, **1**, 17.

[3] T. Mukiayama, K. Narasaka, and M. Furusato, *J. Amer. Chem. Soc.*, 1972, **94**, 8641.

[4] R. K. Boeckman, Jr., and K. J. Bruza, *Tetrahedron Letters*, 1974, 3365.

[5] J. E. Baldwin, G. A. Höfle, and O. W. Lever, Jr., *J. Amer. Chem. Soc.*, 1974, **96**, 7125.

[6] G. B. Kauffman and L. A. Teter, *Inorg. Synthesis*, 1963, **7**, 8.

[7] E. E. van Tamelen and J. P. McCormick, *J. Amer. Chem. Soc.*, 1970, **92**, 737.

[8] D. Burn and V. Petrow, *J. Chem. Soc.*, 1962, 364.

[9] E. J. Corey and D. J. Beames, *J. Amer. Chem. Soc.*, 1972, **94**, 7210.

[10] C. E. Castro, E. J. Gaughan, and D. C. Owsley, *J. Org. Chem.*, 1966, **31**, 4071.