Reaction of conjugated enones with divinylcopperlithium tri-*n*-butylphosphine complex. A new preparation of γ,δ-unsaturated ketones

JOHN HOOZ AND ROBERT B. LAYTON[1]

Department of Chemistry, University of Alberta, Edmonton, Alberta

Received February 16, 1970

A new synthesis of γ,δ-unsaturated ketones is reported, based on the reaction of α,β-unsaturated ketones with a vinyl ate complex.

Canadian Journal of Chemistry, **48**, 1626 (1970)

The discovery of lithium dimethylcuprate, $(CH_3)_2CuLi$, by Gilman and coworkers (1) has sparked renewed interest in the properties and reactions of ate complexes (2). Reagents of the type R_2CuLi, or analogs in which an alkyl (or aryl) copper reagent is stabilized by complexation with phosphorus- or sulfur-containing ligands possess considerable synthetic value for the construction of new carbon–carbon bonds (3–6). Recently, several vinyl ate complexes have also been prepared and demonstrated to undergo a coupling reaction with organic halides (5, 7), as well as oxidative and thermally-induced dimerization to dienes (8).

We wish to report that vinyl ate complexes efficiently transfer a vinyl group to the β-carbon atom of conjugated enones to provide good yields of γ,δ-unsaturated ketones. The reagent, formulated (merely for convenience)[2] as $(CH_2{=}CH)_2CuLiP(n\text{-}C_4H_9)_3$, is easily and rapidly prepared by the addition of two equivalents of a solution of vinyllithium in tetrahydrofuran (THF) to one equivalent of tetrakis[iodo-(tri-*n*-butylphosphine)copper (I)] (9) dissolved in THF at −78° under nitrogen.[3] Addition of a conjugated enone to the resultant deeply colored mixture gives, after suitable processing, good yields (65–89%) of the conjugate addition product. The reaction is usually complete in ca. 30 min at −78°, although β,β-disubstituted enones react more slowly. Some typical transformations are depicted in eqs. [1]–[6]. In all instances the products were analyzed by gas–liquid partition chromatography (g.l.p.c.), isolated, and characterized by infrared (i.r.), nuclear magnetic resonance (n.m.r.), and mass spectroscopy, as well as satisfactory combustion analysis.

Of particular note is the high yield obtained in the case of isophorone (eq. [6]). Although we have not undertaken any detailed systematic comparisons between the efficiency toward conjugate addition of vinylic copper ate complexes vs. the Kharasch–Michael[4] procedure (copper-catalyzed Grignard reaction), we have observed a maximum of 8% yield of 1,4-addition product when isophorone was treated with vinylmagnesium chloride using cuprous iodide catalysis.[5] This striking difference not only illustrates that different intermediates are involved in each case, but also points to the possible synthetic advantages of employing pre-formed ate complexes in certain structural situations.

Although the mechanistic details of either process are not yet fully understood, recent work has discounted the intermediacy of free radicals, carbanions, or a pathway involving a cyclic

---

[1] Holder of a 1967 Science Scholarship.

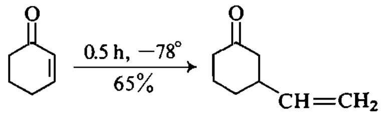
[2] We intend no structural implications by employing this designation; rather, this formulation is used for simplicity and by consideration of stoichiometry and analogy (2, 5).

[3] Alternatively, the phosphine-free species, $(CH_2{=}CH)_2CuLi$, may be prepared by treating vinyllithium (two equivalents) with cuprous iodide (one equivalent). The rate of formation of this reagent, and its rate of reaction with enones, however, is considerably slower than the phosphine-complexed species.

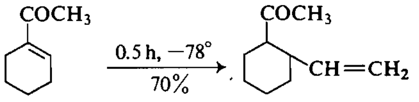
[4] We suggest this name combination as a succinct way of expressing "the copper-catalyzed 1,4-addition of Grignard Reagents to α,β-unsaturated carbonyl compounds", without any implications regarding mechanism.

[5] Also, mesityl oxide gives a maximum of 7% yield of conjugate addition product under similar conditions.

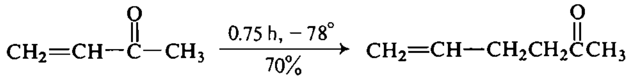
[1]



[2]

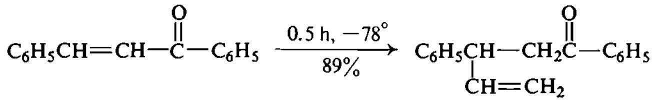


[3]



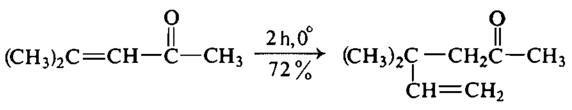
$$CH_2{=}CH{-}\overset{\overset{O}{\|}}{C}{-}CH_3 \xrightarrow[70\%]{0.75\ h,\ -78°} CH_2{=}CH{-}CH_2CH_2\overset{\overset{O}{\|}}{C}CH_3$$

[4]



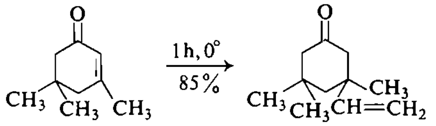
$$C_6H_5CH{=}CH{-}\overset{\overset{O}{\|}}{C}{-}C_6H_5 \xrightarrow[89\%]{0.5\ h,\ -78°} C_6H_5\underset{\underset{CH=CH_2}{|}}{C}H{-}CH_2\overset{\overset{O}{\|}}{C}{-}C_6H_5$$

[5]

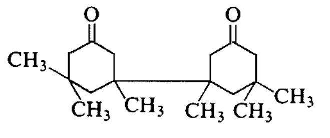


$$(CH_3)_2C{=}CH{-}\overset{\overset{O}{\|}}{C}{-}CH_3 \xrightarrow[72\%]{2\ h,\ 0°} (CH_3)_2\underset{\underset{CH=CH_2}{|}}{C}{-}CH_2\overset{\overset{O}{\|}}{C}{-}CH_3$$

[6]



six-centered transition state (3). The current hypothesis is that either partial or complete electron transfer from organometallic to enone occurs to give rise to, respectively, either a charge-transfer complex, or an ion radical (3). An observation we have made which lends some credence (but certainly offers no definitive proof) to the validity of this notion is the isolation, using the Kharasch–Michael reaction on isophorone, of ca. 7% of the dimer **1**.



1

The experimental procedure is illustrated for the preparation of 3-vinyl-3,5,5-trimethylcyclohexanone. A solution of vinyllithium[6] (90 mmole) in THF was slowly added to a cooled (−78°), stirred, THF solution of 45 mmole tetrakis[iodo-(tri-*n*-butylphosphine)copper(I)] (9) to yield a blue–black mixture. A solution of isophorone (22 mmole) in THF was added (20 min), the resultant solution was allowed to warm to 0°, then maintained at 0° for 1 h. The mixture was poured into a saturated ammonium chloride solution, and extracted with ether (3 × 50 ml). After removal of solvent from the combined, dried (Na_2SO_4) extracts, g.l.p.c. analysis indicated an 85% yield of product. Chromatography of the crude mixture on silicic acid (elution with chloroform), and subsequent distillation of the carbonyl-containing fraction afforded 1.56 g (60%) of 3-vinyl-3,5,5-trimethylcyclohexanone, b.p. 132–135°(34 mm); n_D^{25} 1.4655; i.r. (liquid film) 1710 (C=O), 910, 1635, 3080 cm^{-1} (—CH=CH_2); n.m.r. ($CDCl_3$) 4.2(—C*H*=CH_2, 1,m), 5.1(—CH=CH_2,2,m), 7.62(—COCH_2C(CH_3)-CH=CH_2, 2, q), 7.85(—COCH_2C$(CH_3)_2$, 2,s), 8.31 ($(CH_3)_2$C—CH_2C(CH_3)CH=CH_2, 2, s), 8.92 (—CH_3—CCH=CH_2, 3,s), 8.99 ((CH_3)$_2$C, 3,s),

---

[6] Obtained from Alfa Inorganics, Inc.

9.02 τ ((CH_3)$_2$C, 3,s); mass spectrum (70 eV) M^+ 166.

We wish to thank the National Research Council of Canada for financial support of this work.

1. H. Gilman, R. D. Jones, and L. A. Woods. J. Org. Chem. **17**, 1630 (1952); H. Gilman and G. M. Straley. Rec. Trav. Chim. **55**, 821 (1936).
2. W. Tochtermann. Angew. Chem. Int. Ed. Engl. **5**, 351 (1966); G. Wittig. Quart. Rev. (London), **20**, 191 (1966). Recent reviews of ate complexes.
3. H. O. House, W. L. Respess, and G. M. Whitesides. J. Org. Chem. **31**, 3128 (1966); H. O. House and W. J. Fischer, Jr. J. Org. Chem. **33**, 949 (1968).
4. E. J. Corey and G. H. Posner. J. Amer. Chem. Soc. **89**, 3911 (1967); **90**, 5615 (1968).
5. G. M. Whitesides, W. F. Fischer, Jr., J. San Filippo, Jr., R. W. Baske, and H. O. House. J. Amer. Chem. Soc. **91**, 4871 (1969).
6. E. J. Corey and J. A. Katzenellenbogen. J. Amer. Chem. Soc. **91**, 1851 (1969).
7. G. Büchi and J. A. Carlson. J. Amer. Chem. Soc. **90**, 5336 (1968).
8. G. M. Whitesides, J. San Filippo, Jr., C. P. Casey, and E. J. Panek. J. Amer. Chem. Soc. **89**, 5302 (1967); G. M. Whitesides and C. P. Casey. J. Amer. Chem. Soc. **88**, 4541 (1966).
9. G. B. Kauffman and L. A. Teter. Inorg. Syn. **7**, 9 (1963).