

allial series (see entry 5) could be interpreted as reflecting the opposing tendencies of axial alkylation and anti SN<sub>2</sub>' modes of attack.<sup>18</sup>

In any event this highly stereoselective process, conducted under extremely mild conditions, is likely to find application to various synthetic objectives.

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**Registry No.** 1a, 80127-55-5; 1b, 82740-79-2; 1c, 82740-80-5; 1d, 82740-81-6; 2a, 82740-82-7; 2b, 82740-83-8; 2c, 82740-84-9; 2d, 82740-85-0; 3, 82740-86-1; 4, 2873-29-2; 5, 52485-06-0; 6, 82740-87-2; 7, 82740-88-3; 8, 4098-06-0; 9, 82740-89-4; 10, 82795-64-0; ATMS, 762-72-1.

**Supplementary Material Available:** Representative experimental procedures for the synthesis of compounds 2a and 6 as well as spectral characterization of all new compounds (4 pages). Ordering information is given on any current masthead page.

(18) An alternative explanation for the glucal (4) and galactal (8) cases that cannot be rigorously excluded assumes that ionization of the allylic acetate occurs only when it is axially disposed. In that case, the principal products would be arising from an "equatorial" entry, presumably for reasons of steric hindrance. However, this formulation does not appear to embrace the finding in the allial (5) series.

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## Ultrasound in Organic Synthesis. 2.<sup>1</sup> Formation and Reaction of Organocopper Reagents

**Summary:** Organocopper reagents can be formed from alkyl and aryl halides under ultrasonic irradiation and reacted in situ with enones to give high yields of β-alkylated ketones.

**Sir:** Application of organocopper derivatives in synthetic organic chemistry has received considerable attention.<sup>3</sup> The useful SN<sub>2</sub> and SN<sub>2</sub>' reactions of these reagents have been extensively studied,<sup>3,4</sup> and their conjugate addition to α,β-unsaturated carbonyl compounds provides the most versatile methods of effecting reductive alkylations of these substrates.<sup>3,5</sup> The preparation of the copper reagents in

(1) Previous paper: Luche, J. L.; Damiano, J. C. *J. Am. Chem. Soc.* 1980, 102, 7926. For other recent examples of the use of ultrasound in organic chemistry, see the following: Han, B. H.; Boudjouk, P. *J. Org. Chem.* 1982, 47, 752. Suslick, K. S.; Schubert, P. R.; Goodale, J. W. *J. Am. Chem. Soc.* 1981, 103, 7342. Kitazume, T.; Ishikawa, N. *Chem. Lett.* 1981, 1679. Raucher, S.; Klein, P. *J. Org. Chem.* 1981, 46, 3558.











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(3) For an exhaustive literature survey, see: Posner, G. H. "An Introduction to Syntheses Using Organocopper Reagents"; Wiley: New York, 1980. Also see the following: Posner, G. H. *Org. React.* 1975, 22, 253. Casey, C. P.; Cesa, M. C. *J. Am. Chem. Soc.* 1979, 101, 4236. McDonald, T. L.; Reagan, D. R.; Brinkmeyer, R. S. *J. Org. Chem.* 1980, 45, 4740. Trost, B. M.; Klein, T. P. *Ibid.* 1980, 45, 4256. Normant, J. F.; Alexakis, A. *Synthesis* 1981, 841.

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(5) Posner, G. H. *Org. React.* 1972, 19, 1. House, H. O. *Acc. Chem. Res.* 1976, 9, 59.

Table I

enone	halide	method	isolated yield of the β-alkylated ketone	lit. % yield
	n-C <sub>4</sub> H <sub>9</sub> Br	A	89	82 <sup>a</sup>
		B	91	
		A	76	65 <sup>b</sup> -95 <sup>c</sup>
		B	88	
	t-C <sub>4</sub> H <sub>9</sub> Br	A	traces <sup>e</sup>	66 <sup>d</sup>
		B	71	
	n-C <sub>7</sub> H <sub>15</sub> Br	A	19 <sup>e</sup>	
		B	88	
	C <sub>6</sub> H <sub>5</sub> Br	A	64	
		B	67	
		A	36 <sup>e,f</sup>	91 <sup>d</sup>
		B	traces <sup>e</sup>	
		A	45 <sup>g</sup>	0 <sup>h</sup>
		B	traces	

<sup>a</sup> See ref 11. <sup>b</sup> See ref 12. <sup>c</sup> See ref 8. <sup>d</sup> VPC estimation, see ref 11. <sup>e</sup> Enolate polymerization occurs extensively. <sup>f</sup> 22% allylic alcohol isolated. <sup>g</sup> 30% allylic alcohol isolated. <sup>h</sup> See ref 13.

most cases requires a separate preparation of the intermediate lithio or magnesio derivatives. Recently, in the course of our effort to develop applications of ultrasonic waves, we discovered<sup>1</sup> that the Barbier reaction<sup>6</sup> can be greatly improved through the physical effects of ultrasonic irradiation. Thus, a variety of organolithium compounds can readily be prepared, and in the presence of ketones and aldehydes, high yields of the desired alcohols are obtained. The efficiency of this method, by comparison with the usual two-step procedure,<sup>1</sup> prompted us to investigate the possibility of forming organocopper species under these conditions and to react them with α-enones. The feasibility of this one-step transformation is demonstrated by the preliminary results reported in this communication.

Initially, a Barbier-type reaction resulted on irradiation of a mixture of n-butyl bromide, lithium, and 2-cyclohexenone in the presence of copper iodide, yielding mostly 1-n-butyl-2-cyclohexen-1-ol. Ultrasonic irradiation was performed with a low-intensity generator (80 kHz, 30 W) without temperature control in dry THF. As the reaction of the intermediate RLi species is apparently much faster with the keto group than with the insoluble copper iodide, we attempted to overcome this difficulty through the acceleration of the reaction of RLi with the Cu<sup>I</sup> reagent, i.e., through the use of more energetic sonication conditions and/or the use of a soluble copper derivative. Two procedures resulted from these investigations. In the first procedure (method A) an organic halide, lithium sand,<sup>7</sup> CuI, or pentynylcopper-hexamethylphosphorous triamide C<sub>5</sub>H<sub>7</sub>-Cu-2HMP<sup>8</sup> (generally 1.5 mmol each) and an α-enone (1 mmol) at 0 °C in diethyl ether-THF (1:1) under an argon atmosphere are sonicated in a modified ultrasound laboratory cleaner.<sup>9a</sup> Generally, the metallic lithium is rapidly consumed (3-5 min), after which the resultant

(6) Blomberg, C.; Hartog, F. A. *Synthesis* 1977, 18.

(7) Obtained as a 50% suspension in mineral oil from Alfa.

(8) Corey, E. J.; Beames, D. J. *J. Am. Chem. Soc.* 1972, 94, 7210.

(9) (a) The generator provides a 50-kHz, 96-W acoustic wave. For a better temperature control, the electronic system of the generator was separated from the sonication bath. (b) 50 kHz, 130 W.

black mixture is poured into saturated aqueous  $\text{NH}_4\text{Cl}$ . Ether is added and the organic layer is washed (dilute  $\text{HCl}$ , then saturated  $\text{NH}_4\text{Cl}$ ) and dried. Evaporation of the solvent and purification of the crude mixture by silica gel chromatography affords the pure product identified by the usual spectral techniques and through comparison with authentic samples.

Table I gives some examples of the observed results. Usually no 1,2 adduct, i.e., the allylic alcohol, can be detected. However, this simple and easily performed reaction suffers from the formation in several cases of polar by-products having complex structures (IR and NMR), resulting from further reactions of the intermediate enolate.

Minimization of these undesired condensations was attempted by sonication at lower temperatures in less polar solvents (hexane-THF mixtures). It was observed that the reaction of the organolithio intermediate with the  $\text{Cu}^1$  derivative was dramatically slowed down at  $-30^\circ\text{C}$  and a large amount of allylic alcohol was formed at this temperature. Thus, a narrow balance exists between the requirements of rapid formation of the organocopper reagent and a decreased reactivity of the enolate. Although satisfactory yields can often be obtained with this procedure, we investigated a second method (method B) in which the organocopper reagent is generated in a first step and then treated with the enone. Thus, a mixture of 1.5 mmol (195 mg) of  $\text{C}_6\text{H}_7\text{Cu}$ , 3 mmol (480 mg) of HMP 1.5 mmol of an alkyl halide, and 45 mg (3 equiv) of lithium sand in 6 mL of dry THF-diethyl ether (1:1) is sonicated<sup>9b</sup> at  $-40^\circ\text{C}$  (ethanol-liquid nitrogen) for 10-30 min under an argon atmosphere. After consumption of the lithium, 1 mmol of the enone in 1 mL of dry THF is added dropwise with a syringe and sonication is continued for an additional 10 min. The mixture is then worked up as described above, and the reaction products are isolated by silica gel chromatography. Results are given in Table I. In most cases, the crude  $\beta$ -alkylated ketone is obtained in high purity as shown by analytical methods (IR, TLC) and almost no contamination (<5%) by the allylic alcohol is observed. This procedure also reduces considerably the amount of polar byproducts. In contrast, an experiment run with *n*-butyl bromide at  $0^\circ\text{C}$  rapidly gave a black mixture that left 2-cyclohexenone unchanged, probably due to the well-documented decomposition at this temperature of the organocopper derivatives.

Sonication has an essential role in the process. As shown above, replacement of low-intensity sonication by more energetic irradiation has a pronounced effect on the reaction. In addition, the use of magnetic stirring in lieu of ultrasonic waves results in a much slower reaction with a different product distribution (increased 1,2 addition and lower conversion).

The cavitation effects<sup>10</sup> of acoustic waves are known to promote the erosion of metallic surfaces and are undoubtedly responsible for the rapid consumption of lithium. In summary, diverse organocopper reagents can be rapidly and efficiently prepared from the corresponding halides and used effectively in conjugate addition reactions with enones.<sup>14</sup> Extensions of this work is presently under investigation.

**Acknowledgment.** We thank Dr. A. E. Greene for many useful comments. Financial support from the CNRS (LA 332) is gratefully acknowledged.

**Registry No.** 2-Cyclohexenone, 930-68-7; 2-cyclopentenone, 930-30-3; 3-methylenebicyclo[2.2.1]heptan-2-one, 5597-27-3; 3,5,5-trimethyl-2-cyclohexen-1-one, 78-59-1; butyl bromide, 109-65-9; bromoethene, 593-60-2; *tert*-butyl bromide, 507-19-7; heptyl bromide, 629-04-9; bromobenzene, 108-86-1; 3-butylcyclohexanone, 39178-69-3; 3-ethenylcyclohexanone, 1740-63-2; 3-*tert*-butylcyclopentanone, 5581-94-2; 3-heptylcyclopentanone, 82741-92-2; 3-benzylbicyclo[2.2.1]heptan-2-one, 82741-93-3; 3-(2-propenyl)cyclohexanone, 20498-05-9; 3-(2-propenyl)-3,5,5-trimethylcyclohexanone, 62394-27-8; lithium, 7439-93-2; copper iodide, 7681-65-4; 3-bromo-1-propene, 106-95-6;  $\text{C}_6\text{H}_7\text{Cu}$ -2HMPT, 67840-54-4.

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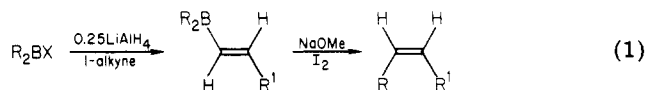
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### A General and Stereospecific Synthesis of Cis Alkenes via Stepwise Hydroboration: A Simple Synthesis of Muscalure, the Sex Pheromone of the Housefly (*Musca domestica*)

**Summary:** Base-induced iodination of the vinylborane intermediates, conveniently obtained via the hydroboration of 1-alkynes with alkylbromoboranes ( $\text{RBHBr}\cdot\text{SME}_2$ ), provides *cis*-disubstituted alkenes in good yields. Muscalure, the insect pheromone of the housefly (*Musca domestica*), has been prepared in 59% yield.

**Sir:** Recent developments<sup>1</sup> in the synthesis and application of insect pheromones have stimulated a search for simple methods to achieve the stereospecific synthesis of *Z* and *E* alkenes, structural features possessed by many insect pheromones. The application of organoboranes to carbon-carbon bond formation has been well-documented and a wide variety of synthetic methods for carbon skeletal assemblage via organoboranes are becoming available.<sup>2</sup> We recently reported<sup>3</sup> a general synthesis of *cis*-disubstituted alkenes via the iodine-induced transfer of dialkylvinylboranes, produced by the hydridation of dialkylhaloboranes in the presence of 1-alkynes, thus generalizing the elegant Zweifel<sup>4</sup> *cis*-alkene synthesis (eq 1).



This procedure suffers from two significant disadvantages. (1) Monohydroboration of 1-alkynes with dialkylboranes, particularly when the alkyl group is primary, is often complicated by competing dihydroboration. This can be suppressed by using a large excess of 1-alkyne. But such use of a large excess of 1-alkyne is not practical for

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