

ADDITION OF ORGANOCUPRATES TO  $\alpha$ -IODOALKYL TRIMETHYLSILYL  
ETHERS FORMED FROM ALDEHYDES AND TRIMETHYLSILYL IODIDE

Michael E. Jung<sup>\*1</sup> and Pamela K. Lewis<sup>2</sup>

Department of Chemistry, University of California,  
Los Angeles, California 90024

Abstract

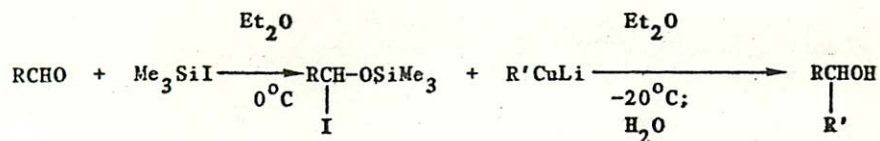
Reaction of organocuprates with the  $\alpha$ -iodoalkyl trimethylsilyl ethers formed by the addition of trimethylsilyl iodide to aldehydes affords good yields of the secondary alcohols after aqueous work-up.

Additions of organometallic reagents to carbonyl groups and their derivatives comprise one of the major methods for carbon-carbon bond formation available to synthetic chemists today. For many years now, a large amount of research has dealt with this area and has produced scores of methods to carry out this transformation in which the nucleophilic organometallic reagent and/or the electrophilic carbonyl component was varied.<sup>3</sup> New advances in this area

should be concerned with approaches and reagents that offer the possibility for selectivity and/or milder reaction conditions. We now report a simple method for the addition of organocuprates to the trimethylsilyl iodide adducts of aldehydes in good yield.

Recently, we reported<sup>4</sup> the facile formation of  $\alpha$ -iodoalkyl trimethylsilyl ethers 3 from the reaction of aldehydes 1 with the electrophilic reagent trimethylsilyl iodide 2<sup>5</sup> at room temperature or below. We have now begun an investigation of the reactivity of these aldehyde-trimethylsilyl iodide adducts toward nucleophiles. Several nucleophiles (e.g., water, alcohols, etc.) attacked the electrophilic silicon atom to regenerate the aldehyde functionality. But on the basis of hard-soft acid-base theory,<sup>6</sup> we expected that 'soft' nucleophiles such as organocuprates should react well with the  $\alpha$ -iodo ethers which would be expected to be soft electrophiles. This proved to be the case.

Addition of trimethylsilyl iodide 2 via syringe to the aldehydes 1abc in anhydrous diethyl ether at 0°C under an atmosphere of nitrogen produced a solution of the desired  $\alpha$ -iodoalkyl trimethylsilyl ethers 3abc. This solution was then added via syringe to an ethereal solution of the cuprates 4ab at -20°C and the resulting mixture allowed to stir at 0°C for 1h and then 25°C for a day. Aqueous workup afforded the desired alcohols 5abc in fair to good yields. The yields of the low molecular weight alcohols were somewhat lower due to their increased water solubility and volatility (Scheme). It is interesting to note that trimethylsilyl iodide 2



<u>1a</u> R=Et	<u>2</u>	<u>3a</u> R=Et	<u>4a</u> R'=Bu 48%	<u>5a</u> R=Et R'=Bu
<u>1b</u> R=Hx		<u>3b</u> R=Hx	<u>4b</u> R'=Me (good) 77%	<u>5b</u> R=Et R'=Me
			<u>5c</u> R=Hx R'=Bu 73%	<u>5d</u> R=Hx R'=Me

Scheme

reacts exclusively with the aldehyde 1 rather than the diethyl ether which is present in great excess as the solvent. The addition reaction is kinetically much faster than the dealkylation process for ethyl ethers.<sup>7</sup>

The mechanism of the reaction probably involves the direct substitution of the alkyl group of the organocuprate for the iodide in the  $\alpha$ -iodoalkyl silyl ethers presumably via a Cu(III) species as has been proposed for other reactions of organocuprates with organic iodides.<sup>8</sup> However, we cannot rule out the possibility that the reaction may proceed by the direct addition of the organocuprate to the aldehyde<sup>9</sup> which may be present as a very minor component in equilibrium with the  $\alpha$ -iodoether. The fact that <sup>1</sup>H NMR measurements show no evidence for the presence of the aldehyde in the reaction mixture does not rule out this latter possibility although it does make it less likely.

Although this method described above offers little advantage over the direct addition of organolithium reagents to aldehydes for the simple cases, it should be of value in polyfunctional molecules.

Experimental Section

General. Trimethylsilyl iodide 2 was prepared by our earlier methods.<sup>5</sup> Cuprous iodide was purified by dissolving 13.15g CuI in a solution of 100 ml water containing 130g KI. After addition of 1g of decolorizing charcoal to remove the yellow color, the solution was filtered and diluted with water to precipitate the CuI. The crystals were collected and dried by continuous extraction with tetrahydrofuran in the dark for four days under a nitrogen atmosphere. The CuI was then dried in vacuo and stored under nitrogen in the dark.

General Experimental Procedure. Copper iodide (0.4017g, 2.109 mmol) was placed in a 250 ml 3-neck round-bottom flask equipped with a reflux condenser, nitrogen inlet, septum, and magnetic stir bar and 50 ml of anhydrous diethyl ether added. The solution was stirred and cooled to  $-20^\circ\text{C}$  under a nitrogen atmosphere. The alkyllithium 4 (4.218 mmol) was then added via dried syringe to the stirring solution. After about 20 min, the solution gave a negative Gilman test,<sup>10</sup> implying complete formation of the cuprate. The aldehyde 1 (2.109 mmol) in 25 ml of diethyl ether was added to a 50 ml 3-neck round-bottom flask equipped with reflux condenser, nitrogen inlet, septum and stirbar, and the solution cooled to  $0^\circ\text{C}$ . The trimethyl-

silyl iodide 2 (0.300 ml, 2.109 mmol) was then added via dried syringe to the stirring solution. After allowing the solution to stir for approximately 10 min, the resulting iodohydrin trimethylsilyl ether 3 was added slowly via syringe to the previously prepared cuprate. The reaction mixture was warmed to 0°C and allowed to stir for 1h. After this time, the mixture was warmed to room temperature, allowed to stir for approximately 24h, and quenched by the addition of water. The alcohol 5 was extracted with dichloromethane with the final extraction being performed after the aqueous layer had been saturated with sodium chloride. The resulting organic layers were dried over sodium sulfate and the dichloromethane and diethyl ether evaporated in vacuo to give the nearly pure alcohols 5 in the yields indicated.

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#### References and Notes

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- (9) Posner, G. H.; Whitten, C. E.; McFarland, P. E. J. Am. Chem. Soc. **1972**, 94, 5160, footnote 15. We have also observed that organocuprates add to aldehydes at low temperatures in good yields.
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