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A CONVENIENT METHOD FOR THE STEREOSPECIFIC SYNTHESIS OF (E)-3-ALKEN-1-OLS UTILIZING THE RING-OPENING REACTION OF 2,3-DIHYDROFURAN WITH ORGANOCUPRATES

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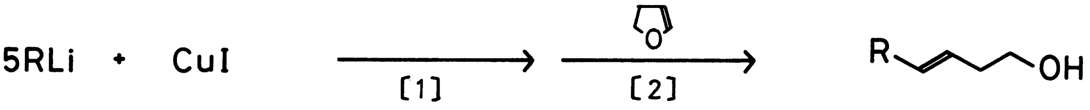
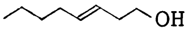
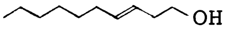
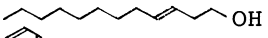
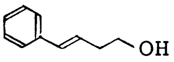
(*E*)-3-Alken-1-ols were stereospecifically synthesized in good yields utilizing the regioselective nucleophilic ring-opening reaction of 2,3-dihydrofuran with several kinds of organocuprates under mild conditions.

Although reactions of enol ethers leading to the carbon-carbon bond formation using their nucleophilic character are well documented,$^{1)}$ the reaction with organometallics as nucleophiles is not appreciably reported. Giving a few examples, a cyclic enol ether, 2,3-dihydropyran reacts with Grignard reagents to give 4-alken-1-ol or 1-alkanal,$^{2a)}$ in which the regioselectivity depends on the substituents of the Grignard reagents. Recently, nickel compounds have been found to catalyze effectively the reaction of enol ethers with methyl and phenyl Grignard reagents to afford coupled olefin.$^{2b)}$ 2,3-Dihydropyran also reacts with butyllithium to give (*E*)-4-nonen-1-ol.$^{2c)}$ On the other hand, lithium dialkylcuprates or trialkylaluminum reacts with reactive enol esters such as enol phosphate$^{3)}$ or sulfonate$^{4)}$ to give the substitution products. We wish to report here the regio- and stereospecific reaction of 2,3-dihydrofuran with organocuprates leading to a convenient synthesis of (*E*)-3-alken-1-ols.

The reaction of 2,3-dihydrofuran with butyllithium under the same conditions as the case of 2,3-dihydropyran$^{2c)}$ or with lithium dibutylcuprate gave the desired 3-octen-1-ol in 7% or 15% yield, respectively. It is known that dilithium trialkylcuprate is more reactive than lithium dialkylcuprate in some cases.$^{5)}$ An attempt to use dilithium tributylcuprate resulted in raising the yield up to 70%. Among solvents examined such as diethyl ether, dimethoxyethane, THF, and dioxane, the best solvent was found to be diethyl ether and the addition of dimethyl sulfide as a co-solvent increased further the yield of 3-octen-1-ol up to 75%. By the continuing examination of the reactivity using various ratios of butyllithium and copper(I) iodide, it was found that the more excess use of butyllithium showed the tendency increasing the yield of the desired product. Thus, the species$^{6)}$ prepared from six equivalents of butyllithium and one equivalent of copper(I) iodide gave 3-octen-1-ol quantitatively. However, from the point of view of synthetic utility, the best conditions for the synthesis of 3-alken-1-ols were determined as the use of the spicies$^{6)}$ prepared from five equivalents of alkyllithium and one equivalent of copper(I) iodide for two and a half equivalents of 2,3-dihydrofuran, which gave 3-octen-1-ol in 83% yield. As shown in the Table, the reaction of 2,3-dihydrofuran with *n*-alkylcuprates gave the corresponding 3-alken-1-ols in high yields, which were determined to be exclusive E isomers by glpc analysis. (*E*)-3-Hexen-1-ol from

Table. Reaction of 2,3-Dihydrofuran with Several Organocuprates[a]



R	Reaction Conditions		Product[b]	Yield(%)[c]
	[1]	[2]		
C_2H_5	0 °C, 30 min	0 °C, 5 h		59 (74)[d]
C_4H_9	0 °C, 30 min	0 °C, 3 h		83 (91)[d]
C_6H_{13}	-10 °C, 30 min	0 °C, 5 h		83
C_8H_{17}	-10 °C, 30 min	0 °C, 5 h		62 (74)[d]
C_6H_5	0 °C, 30 min	0 °C, 3 h		30

[a] All reactions were performed by the same procedure described in the text. The molar ratio of RLi, CuI and 2,3-dihydrofuran is 5:1:2.5 unless otherwise noted. [b] All products were identified by IR and NMR spectra. [c] The yields were based on 2,3-dihydrofuran. [d] The yields by the reaction of the molar ratio of RLi, CuI and 2,3-dihydrofuran of 5:1:1 were shown in the parentheses.

ethylcuprate is known as an attractant of *Bombyx mori*, 7a) and (*E*)-3-dodecen-1-ol from octylcuprate is reported as a sex pheromone of *Scrobipalpa ocellatella boyd* as its acetate form.7b) Although phenylcuprate gave 4-phenyl-(*E*)-3-buten-1-ol in a yield of 30%, none of alkenol was obtained from *s*- and *t*-alkylcuprates.

A typical procedure is as follows; To a solution of copper(I) iodide (190 mg, 1.00 mmol) in dry Et_2O (4 ml)-Me_2S (1 ml) was added butyllithium (4 ml of 1.25M *n*-hexane solution, 5.00 mmol) at 0 °C, and stirred at the same temperature for 30 min. A solution of 2,3-dihydrofuran (215 mg, 2.50 mmol) in dry Et_2O (2 ml) was then added. After stirring for 3 h at 0 °C, the reaction was quenched with a saturated aqueous NH_4Cl solution, and usual work-up afforded (*E*)-3-octen-1-ol in 83% yield.

The conventional process for the preparation of 3-alkenol consists of multi steps, *e.g.* 3-hexenol from tetrahydrofuran in three steps8) and four steps synthesis of (*E*)-3-alkenol.9) Accordingly the following advantages make the present ring-opening reaction of 2,3-dihydrofuran with organocuprates attractive: 1) the easy availability of 2,3-dihydrofuran, 2) the simplicity of the experimental procedure, and 3) high regio- and stereospecifity.

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