

Preliminary communication

**DIFFERENCES IN THE REACTION OF ELECTRON DEFICIENT OLEFINS
WITH ORGANOCOPPER(I)-LEWIS ACID REAGENTS AND EVIDENCE
FOR A DIANIONIC EQUIVALENT**

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Summary

Treatment of diethyl fumarate and triethoxycarbonylethylene with $\text{Bu}_2\text{CuLi} \cdot \text{AlCl}_3$ led to 1,4-addition to give butylated products in high yields. In sharp contrast, diethyl maleate and tetraethoxycarbonylethylene predominantly gave the respective reduction products. The first evidence for a presumed dianionic intermediate by trapping with some electrophiles was also presented.

Since advent of organocopper(I)-boron trifluoride complexes [1a], much current interest is centered around the development of an effective method using Lewis acid-mediated organocopper(I) reagents because of several drawbacks of the ordinary organocopper(I) reagents [1]. Although reactions between electron deficient olefins and some ordinary organocopper(I) reagents have been described in a few papers [2,3], systematic studies on the reaction of Lewis acid-mediated organocopper(I) reagents with electron deficient olefins remain to be done. In the present investigation, disclosure of the following points has been attempted using $\text{R}_2\text{CuLi} \cdot \text{AlCl}_3$, $\text{R}_2\text{CuLi} \cdot \text{BF}_3$, and some Lewis acid-mediated organocopper(I) reagents: (i) which would be the orientation of addition to asymmetrically substituted olefin? (ii) does conjugate addition to the double bond or does reduction of the double bond take place? (iii) could any differences in the above respect be seen between geometrical isomers? Typical examples of the present investigation are given in Table 1 and Scheme 1.

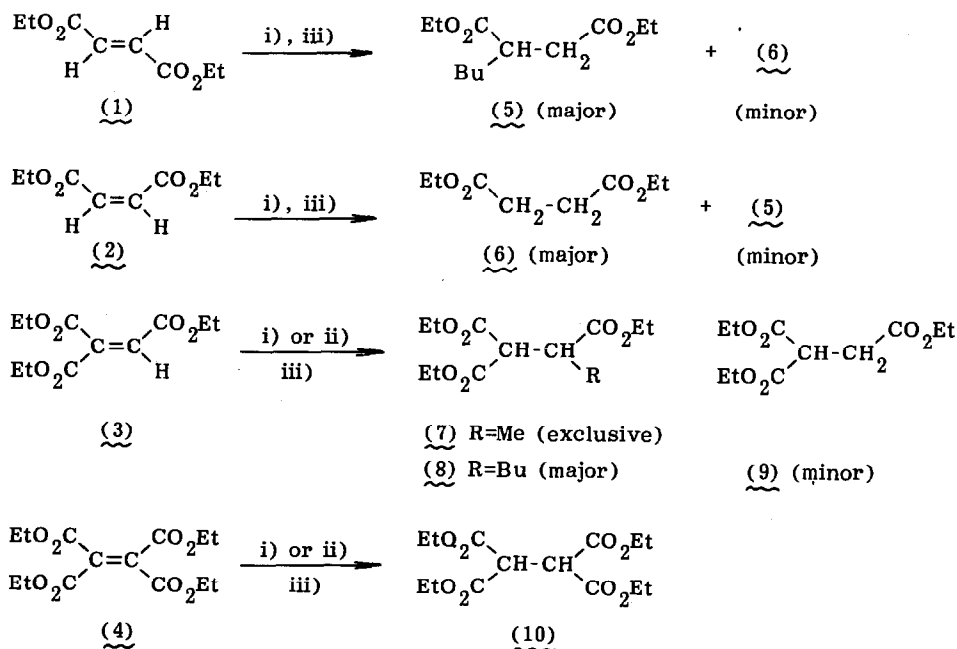
The reaction of diethyl fumarate (1) with $\text{Bu}_2\text{CuLi} \cdot \text{AlCl}_3$ in ether, after the

usual aqueous work-up, gave a conjugate adduct, diethyl butylsuccinate (5) (94%), and a trace amount of a reduction product, diethyl succinate (6) (Expt. 1). In sharp contrast, diethyl maleate (2) gave the reduction product (6) (92%) under the same reaction conditions, and a small amount of the conjugate adduct (5) (1.8%) (Expt. 2). Explanation for the different reactivity

TABLE 1
YIELDS OF PRODUCTS IN THE REACTION OF ELECTRON DEFICIENT OLEFINS WITH SOME ORGANOCOPPER(I) REAGENTS^a

Expt.	Substrate	Reagent	Reaction conditions	1,4-Adduct	Reduction product	Recovered
1	1	Bu ₂ CuLi·AlCl ₃ (4 eq.)	-65 to -40°C, 1 h	5 (94%)	6 trace	—
2	2	Bu ₂ CuLi·AlCl ₃ (4 eq.)	-65 to -40°C, 1 h	5 (1.8%)	6 (92%)	—
3	2	Bu ₂ CuLi·AlCl ₃ (4 eq.)	-65 to -40°C, 1 h	5 (9%)	6 (66%)	2 (25%)
4	1	Bu ₂ CuLi (4 eq.)	-65 to -40°C, 1 h	5 (23%)	6 (11%)	1 (65%)
5	2	Bu ₂ CuLi (4 eq.)	-65 to -40°C, 1 h	5 (1%)	6 (57%)	2 (37%)
6	2	Bu ₂ CuLi (8 eq.)	-70 to -40°C, 2 h	5 (<5%)	6 (<5%)	2 (90%)
7	3	Me ₂ CuLi·AlCl ₃ (4 eq.)	-70 to -40°C, 1 h	7 (97%)	—	—
8	3	Me ₂ CuLi·BF ₃ (4 eq.)	-70 to -40°C, 1 h	7 (97%)	—	—
9	3	Bu ₂ CuLi·AlCl ₃ (4 eq.)	-70 to -40°C, 1 h	8 (80%)	9 (7%)	—
10	3	Bu ₂ CuLi·BF ₃ (4 eq.)	-65 to -40°C, 1 h	8 (78%)	9 (8%)	—
11	4	BuCu·AlCl ₃ (4 eq.)	-65 to -30°C, 1 h	—	10 (91%)	—
12	4	BuCu·BF ₃ (4 eq.)	-65 to -30°C, 1 h	—	10 (95%)	—
13	4	MeCu·AlCl ₃ (4 eq.)	-65 to -15°C, 1.5 h	—	10 (94%)	—
14	4	MeCu·BF ₃ (4 eq.)	-65 to -0°C, 20 min	—	10 (94%)	—
15	4	Bu ₂ CuLi·AlCl ₃ (4 eq.)	-65 to -40°C, 1 h	—	10 (100%)	—
16	4	Bu ₂ CuLi·BF ₃ (4 eq.)	-65 to -40°C, 1 h	—	10 (99%)	—

^a Except for the Expt. 3 and 6, all reactions were carried out in dry Et₂O. Expt. 3: solvent, Et₂O/THF 3/2; Expt. 6: solvent, THF.



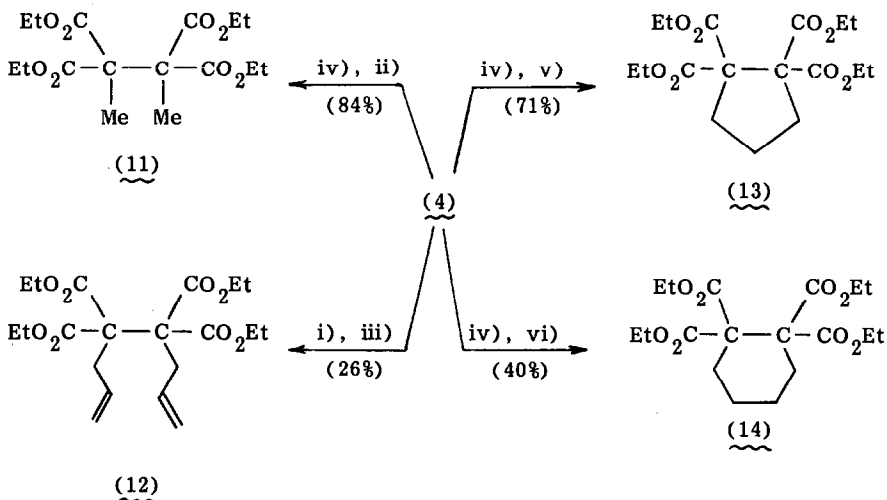
SCHEME 1. Reagents, (i) Bu₂CuLi·AlCl₃, (ii) Me₂CuLi·AlCl₃, (iii) H₃O⁺.

in the above reactions is rather difficult, since little structural information of the reagent is available. Nonetheless, it is of special interest to note that the direction of the reaction path is highly dependent upon the geometry of the substrate. Addition of AlCl_3 to Bu_2CuLi is essential for the completion of the above reactions (Expt. 4 and 5). Diethyl ether is the solvent of choice since reactions in a mixture of tetrahydrofuran (THF) and diethyl ether or in THF were too sluggish to be practicable (Expt. 3 and 6) [4].

In the case of triethoxycarbonylethylene (3), the conjugate adduct (7) was isolated as the sole product by treatment with $\text{Me}_2\text{CuLi} \cdot \text{AlCl}_3$ or $\text{Me}_2\text{CuLi} \cdot \text{BF}_3$ (expt. 7 and 8). In these reactions, we did not detect any reduction products by gas chromatographic analysis. However, reaction of 3 with $\text{Bu}_2\text{CuLi} \cdot \text{AlCl}_3$ or $\text{Bu}_2\text{CuLi} \cdot \text{BF}_3$ gave the conjugate adduct (8) (78–80%) accompanied by a small amount (7–8%) of the reduction product (9) (Expt. 9 and 10). These results indicate that the asymmetrical substrate (3) was regio-specifically attacked by the reagents at the less substituted position. The exclusive or predominant formation of the conjugate adducts (7 and 8) should be contrasted with the complete reduction of tetraethoxycarbonylethylene (4) described below.

Tetraethoxycarbonylethylene (4), the most electron deficient olefin, gave the reduction product (10) (91–100%) exclusively by treatment with the Lewis acid-mediated organocopper(I) reagents (Expt. 11–16).

Considerable current effort has been directed toward the preparation and reaction of dianions having electron-withdrawing groups and these dianions are prepared exclusively from saturated diesters or their equivalents by treatment with strong bases such as lithium diisopropylamide [5,6]. In our present experiment (Expt. 2 and 11–16), the reduction intermediate (presumably dianions) from the unsaturated substrates (2 and 4) would be generated by two-electron transfers [2] from the organometallic reagents. The electron transfer (reduction) is particularly interesting since, in living organisms, cop-



SCHEME 2. Reagents, (i) Me_2CuLi ; (ii) MeI ; (iii) $\text{CH}_2=\text{CHCH}_2\text{Br}$; (iv) Bu_2CuLi ; (v) $\text{Br}(\text{CH}_2)_3\text{Br}$; (vi) $\text{Br}(\text{CH}_2)_4\text{Br}$.

per proteins are frequently involved in the electron transfer processes in membranes and mitochondria [7].

Because chemical evidence for dianionic species formed by electron transfer from organocopper(I) has no precedent in the literature, attempts to trap the reduction intermediate were made*. Thus, the presumed dianionic intermediate of tetraethoxycarbonylethylene (4) with the ordinary organocopper(I) reagents on treatment with electrophiles gave the dialkylated or annulated products (11–14) in moderate yields**,*** (Scheme 2).

The above trapping with electrophiles presents evidence that double bond reduction involves an intermediate dianion and the dialkylated products (11 and 12) and the annulated products (13 and 14) strongly indicate that copper hydride [8] was not involved in the reduction.

The possibility that this reduction-alkylation could serve as a method for synthetic chemistry is currently under investigation.

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*The presumed dianionic species formed by reaction with organocopper(I)-Lewis acid reagents are limited by their low solubility for the trapping with electrophiles. Bu₂CuLi and Me₂CuLi were used for the generation of the presumed dianionic intermediate since the most electron deficient olefin (4) was readily reduced by the ordinary organocopper(I) reagents [2].

**The following procedure for the trapping reaction is typical. To a stirred solution of Bu₂CuLi (4 equiv.) in dry THF/HMPPT (6/1, 7 ml) at -70°C was added a solution of the olefin (4, 158 mg) in 3 ml of dry THF at -70°C and the mixture was stirred for 30 min. 1,3-Dibromopropane was added (0.5 ml, 10 equiv.) to the mixture and the temperature gradually raised to room temperature. Stirring was continued for 18 h and after the usual work-up and silica gel column chromatographic separation, the annulated product (13) (122 mg, 71%) was obtained.

***Structures of by-products in the trapping experiments with electrophiles will be presented in a full paper.

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