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STEREOSELECTIVE ADDITION OF READILY AVAILABLE ORGANOCOPPER REAGENTS TO DIMETHYL ACETYLENEDICARBOXYLATE

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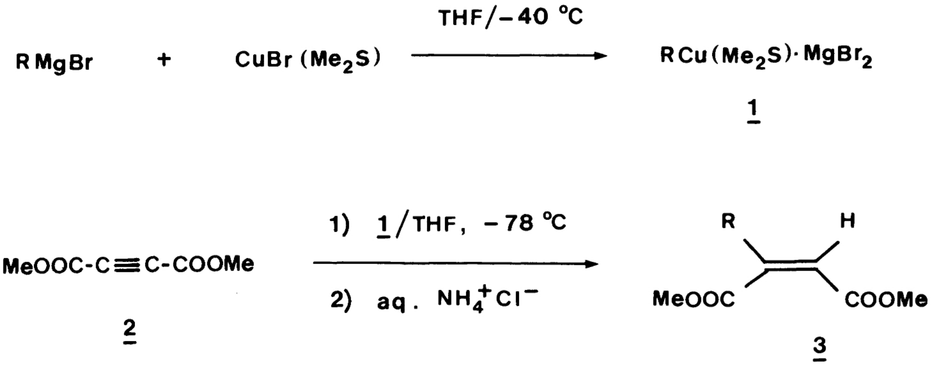
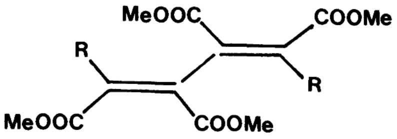
Organocopper reagents derived from cuprous bromide-dimethyl sulfide complex with Grignard reagents underwent stereoselective addition to dimethyl acetylenedicarboxylate to give 2-substituted maleates in good yields.

Stereocontrolled syn-addition of organocopper reagents to the triple bond of simple acetylenes or α,β-acetylenic carbonyl compounds was developed as a useful method in preparing naturally occurring trisubstituted olefins.[1] This technique can not be applied to the alkylation of acetylenes having electron withdrawing substituents, such as acetylenedicarboxylates, by means of common organocoppers or organocuprates,[1b] because the resulting copper intermediate was extremely unstable and induced rapid decomposition to corresponding dienes or polymeric materials.[2] In this context, Yamamoto and Maruyama recently succeeded in alkylation of dimethyl acetylenedicarboxylate by means of a particular organocopper reagents, $BuCu \cdot BR_3$.[3] In this communication, we report stereoselective alkylation of dimethyl acetylenedicarboxylate with more readily accessible organocopper reagents[1h] derived from cuprous bromide-dimethyl sulfide complex[4] and fairly wide range of Grignard reagents.



We attempted alkylation of dimethyl acetylenedicarboxylate by means of organocopper-dimethyl sulfide complexes 1 under the following condition. To a suspension of the organocopper-dimethyl sulfide complex (1.2 equiv. of 2) generated from cuprous bromide-dimethyl sulfide complex^4 with Grignard reagent in anhydrous tetrahydrofuran (1.2 mmol/8 ml), a solution of freshly distilled dimethyl acetylenedicarboxylate 2 in anhydrous tetrahydrofuran (1 mmol/2 ml) was added at -78 °C. After the mixture was stirred for 40 min., the reaction was quenched with aqueous ammonium chloride at -78 °C. The reactions with various alkyl and alkenyl Grignard reagents afforded stereoselectively syn-addition products, 2-substituted maleates, in good yields (Table 1).^{5} No anti-addition products, 2-substituted fumarates, were observed by means of NMR spectroscopy and liquid column chromatography monitored by RI. The reactions at the temperature above -40 °C gave mainly dienes 4.

Although organocopper-dimethyl sulfide complexes were found to add simple alkylacetylenes in the medium of excess dimethyl sulfide and ether, their efficient addition to acetylenes having electron withdrawing group is without precedent.^{1h} In the presence of dimethyl sulfide as a ligand, the vinyl carbon-copper bond might be configurationally stable and not in an equilibrium with the corresponding O-enolate 6. In spite of the absence of dimethyl sulfide as a ligand, trimethylsilylmethyl, phenyl, and benzyl copper reagents gave the corresponding maleates in high yields (Entry 8, 9, and 10).^{6} This was interpreted by stabilization of the vinyl carbon-copper bond through the σ,π-conjugation of the Si-C bond and the C-C double bond or the interaction of the phenyl ring and copper.



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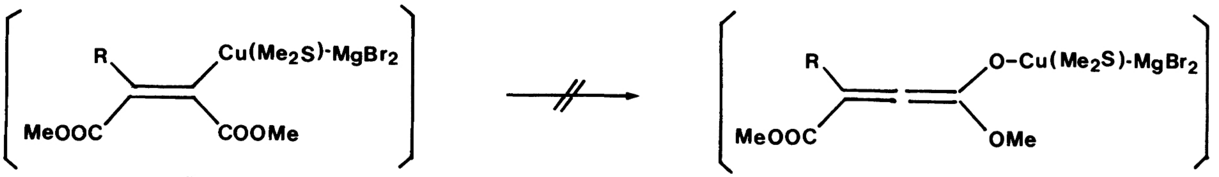

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Butylcopper phosphine complex was also effective in providing the maleate with dimethyl acetylenedicarboxylate (Entry 11), however, the separation of the product from tributylphosphine was less easy than from volatile dimethyl sulfide.

Thus, we have found a stereoselective addition of the organocopper-dimethyl sulfide complexes and several free organocopper reagents to dimethyl acetylenedicarboxylate as a versatile and considerably general method for the preparation of the 2-substituted maleates.

Table 1

Addition of Organocopper Complexes to Dimethyl Acetylenedicarboxylate

Entry	Organocopper Complex[a]		3 Yield(%)[b]	B.p.(°C/mmHg)[c]
	$RCu(Me_2S)\cdot MgBr_2$			
1	R=	C_2H_5	83	85-90/20
2		$n\text{-}C_4H_9$	90	90-95/21
3		$n\text{-}C_6H_{13}$	86	100-105/20
4		$n\text{-}C_8H_{17}$	82	110-115/19
5		$(CH_3)_2CH{=}CHCH_2CH_2$	71	95-100/20
6		$CH_2{=}CH$	71	90-95/20
7		$CH_3CH{=}CH$	66	120-125/29
	$RCu\cdot MgX_2$[d]			
8		$(CH_3)_3SiCH_2$	97	100-110/20
9		C_6H_5	85	120-125/3
10		$C_6H_5CH_2$	84	120-125/3
11	$n\text{-}C_4H_9Cu[P(n\text{-}C_4H_9)_3]\cdot MgBrI$[d]		78	-
12	$n\text{-}C_4H_9Cu[P(OCH_3)_3]\cdot MgBr_2$[d]		49	-

a. All organocopper complexes (1.2 mmol, 1.2 equiv. of 2) were prepared from a stoichiometric amount of copper complexes and Grignard reagents in THF (8 ml) at -40 °C for 40 min. All reactions were performed at -78 °C for 40 min and quenched with aqueous ammonium chloride at -78 °C. The products were extracted with ether. b. Isolated by silica gel column chromatography (ether-hexane as eluent). Satisfactory spectroscopic data (NMR, IR, mass spectrum) and elemental analyses were obtained for these compounds.
c. Kugel Rohr. d. Prepared from C_6H_5MgBr and CuI, $C_6H_5CH_2MgCl$ and CuI, $(CH_3)_3SiCH_2MgCl$ and CuI, C_4H_9MgBr and $CuI\cdot P(n\text{-}C_4H_9)_3$[7a], C_4H_9MgBr and $CuBr\cdot P(OCH_3)_3$[7b], respectively.

References and Notes

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5. Treatments of dimethyl acetylenedicarboxylate at -78 °C with n-butyl and vinyl copper reagents obtained from Grignard reagents and cuprous iodide (1:1) gave the corresponding maleates in low yields (n-C_4H_9, 15%; CH_2=CH, 40%).
6. Trimethylsilylmethyl, phenyl, and benzyl copper-dimethyl sulfide complexes did not undergo the addition reaction to dimethyl acetylenedicarboxylate under similar conditions.
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