

Synthesis of α -Allenic Alcohols from Propargylic Cyclic Carbonates and Sulfites

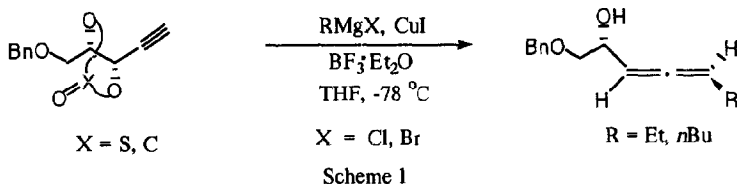
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Abstract: Reaction of cyclic carbonates or sulfites of acyclic alkynyl diols with organocopper reagents proceeded in S_N2' fashion and afforded α -allenic alcohols of high enantiomeric purity. The stereochemistry of this transformation was shown to be highly *anti*-diastereoselective.

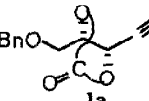
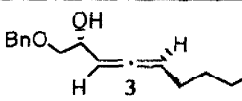
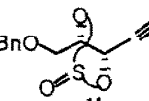
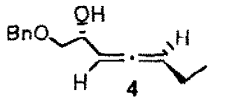
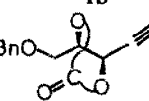
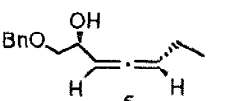
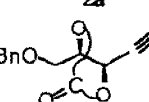
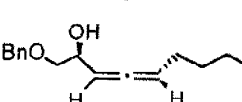
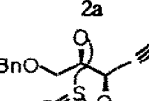
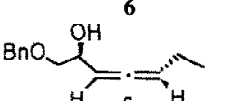
Optically active allenes have become versatile chiral synthons in organic synthesis.¹ It is known that allenes are readily synthesized² from propargylic derivatives such as acetates, carbamates, sulfonates, sulfonates, halides, and ethers with organocopper reagents. It is generally recognized that these kinds of S_N2' reactions proceed with *anti* 1,3-displacement.³ The enantiomeric purity of allenes formed by this method varies according to substrates, organometallic reagents,⁴ and leaving groups⁵ employed. Olsson and Claesson⁵ found that higher optical yields were obtained with better leaving groups, i.e., acetates and mesylates. Stereochemical studies are complicated by the fact that organocuprates have been shown to racemize the product allenes under normal conditions.⁶ Highest enantiomeric excesses were obtained when the reaction time was kept to a minimum (< 15 min).⁵ Herein we report a highly enantio-selective synthesis of α -allenic alcohols by addition of organocopper(I) reagents to carbonates and sulfites of alkynyl diols (Scheme 1).



The results of the reaction of the carbonates or sulfites with organocopper(I) reagents are summarized in Table 1. The carbonate **1a** with $nBuMgCl$ (1.2 eq.) and CuI (10 mol %) in the presence of $BF_3 \cdot Et_2O$ (1.0 eq.) in dry THF at $-78^\circ C$ for 10 min gave the diastereomerically pure allene **3'** as the sole product (entry 1). The *anti* diastereoselection of **3** was found to be nearly perfect (>99%) as judged by GLC and 1H -NMR (300 MHz, C_6D_6 solvent) analyses of the acetate of **3**. For the cyclic sulfite **1b**, $EtMgBr$ (1.2 eq.) and CuI (10 mol %) in the presence of $BF_3 \cdot Et_2O$ (1.0 eq.) afforded **4'** with high diastereoselectivity (97:3) (entry 2). The carbonate **2a** with $EtMgBr$ (2.5 eq.), $BF_3 \cdot Et_2O$ (1 eq.), and CuI (20 mol %) gave the allene **5** with lower diastereoselectivity (89:11) (entry 3). Presumably, the excess Grignard reagent caused epimerisation of the allene, probably *via* electron transfer. The diastereomeric allenes **5** could be differentiated by GLC analysis or 300 MHz 1H -NMR of the corresponding acetoxy derivatives. The carbonate **2a** with $Bu_2CuLi \cdot Me_2S$ (from 2.5 eq. of $nBuLi$ and 1.1 eq. of CuI) or the sulfite **2b** with $EtMgBr$ (1.2 eq.), $BF_3 \cdot Et_2O$ (1 eq.), and CuI (10 mol %) afforded the corresponding allenes **6** and **5**, respectively, with excellent diastereoselectivities (entry 4 and 5).

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Table 1. S_N2' Addition of Organocuprates to Propargylic Cyclic Carbonates and Sulfites

Entry	Substrate	Reagents ^a (mol eq)	Reaction Time (min)	Product	Isolated Yield(%) ^b	Anti/Syn ^c	$[\alpha]_D^{25}$ in $CHCl_3$
1		$nBuMgCl$ (1.2) CuI (10 mol %) $BF_3 \cdot Et_2O$ (1)	10		79	>99:1	+19.7 (c 0.33)
2		$EtMgBr$ (1.2) CuI (10 mol %) $BF_3 \cdot Et_2O$ (1)	10		31	97:3	+21.3 (c 0.54)
3		$EtMgBr$ (2.5) CuI (20 mol %) $BF_3 \cdot Et_2O$ (1)	10		75	89:11	-22.8 (c 0.35)
4		$Bu_2CuLi \cdot$ $(CH_3)_2S$ (1.1)	10		57	99:1	-17.4 (c 0.51)
5		$EtMgBr$ (1.2) CuI (10 mol %) $BF_3 \cdot Et_2O$ (1)	30		32	99:1	-20.2 (c 0.04)

^aThe typical procedure is as follows. To a stirred solution of CuI (8 mg, 10 mol %) in dry THF (2 ml) at $-78^\circ C$ under N_2 was added $nBuMgCl$ (0.2 ml, 0.48 mmol, 2 M in ether) followed by $BF_3 \cdot Et_2O$ (0.05 ml, 0.40 mmol) in dry THF (2 ml) and then **1a** (100 mg, 0.40 mmol) in dry THF (1 ml). After stirring for 10 min at $-78^\circ C$, the reaction was quenched with saturated NH_4Cl solution (2 ml). THF was evaporated and the residue was extracted with ether (30 ml). The ether layer was dried over anhydrous magnesium sulfate and evaporated *in vacuo*. The crude product was separated by SiO_2 column chromatography (EtOAc/hexanes 2:1, $R_f = 0.47$) afforded **3** (78.1 mg, 79 %). ^bYields are not optimized. ^cThe ratio was determined by GLC analysis of the acetates of the products using Hewlett Packard 5880 GC system (column: Hewlett-Packard SE-54, 0.2 mm x 16m, oven temp: $150 \rightarrow 300^\circ C$, carrier gas: N_2 , 1.0 ml/min, injection temperature: $280^\circ C$).

References and Notes

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- The spectral data of all the compounds described are in agreement with assigned structure. Selected data are as follows. **3**: 1H -NMR ($CDCl_3$, 300 MHz) δ 0.89 (t, 3H, $J = 6$ Hz), 1.34 (m, 4H), 2.01 (m, 2H), 3.45 (dd, 1H, $J = 11, 7$ Hz), 3.55 (dd, 1H, $J = 11, 4$ Hz), 4.36 (m, 1H), 4.58 (s, 2H), 5.25 (m, 1H), 5.30 (m, 1H), 7.32 (m, 5H). IR (neat) 3350, 1980 cm^{-1} . MS(m/e) 229 (M-OAc). **4**: 1H -NMR ($CDCl_3$, 300 MHz) δ 1.01 (m, 3H), 2.03 (m, 2H), 3.45 (dd, 1H, $J = 11, 4$ Hz), 3.55 (dd, 1H, $J = 11, 7$ Hz), 4.36 (m, 1H), 4.58 (s, 2H), 5.25 (m, 1H), 5.45 (m, 1H), 7.32 (m, 5H). IR (neat) 3350, 1980 cm^{-1} . MS(m/e) 201 (M-OAc).