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COPPER(I) ACETYLIDE INDUCED SUBSTITUTION IN ALLYLIC ETHERS OF BENZOTHIAZOLE. REGIO- AND STEREOSELECTIVE SYNTHESIS OF 1,4-ENYNES.

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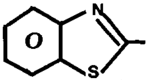
Allylic ethers of benzothiazole react with copper(I) acetylides to afford 1,4-enynes under complete regio- and stereoselective control.

The preparation of 1,4-enynes[1,4] which are the precursors of 1,4-dienes, has been accomplished by several synthetic methods, none of which is quite satisfactory. For example, the reaction of primary allylic halides with sodium 1-alkyn-1-ides in liquid ammonia yields in addition to the allylic rearrangement products, isomerization products (conjugated enynes) and diallylation products. Moreover, the coupling[5] of allylic halides with terminal alkynes under Cadiot-Chodkiewicz conditions, or the reaction[6] of allylic halides with cuprous acetylides in aprotic dipolar solvents, also proceeds with partial allylic rearrangement. In addition, the few stereoselective syntheses[7] of 1,4-enynes require allylic substrates with the proper geometry of the double bond, which are not easily available. In an effort to devise efficient and convenient regio- and stereoselective syntheses of insect pheromones, we showed[8] recently that heterocuprates react very readily with secondary allylic ethers of 2-hydroxybenzothiazole under complete regio- and stereoselective control. Now we report that these ethers react cleanly and under mild conditions with poorly reactive copper(I) acetylides in THF or DMF leading to 1,4-enynes in a regio- and stereospecific manner.

$$CH_2{=}CH{-}CHR{-}O{-}Btz + Cu{-}C{\equiv}C{-}R' \longrightarrow R'{-}C{\equiv}C{-}CH_2{-}\underset{(E)}{CH{=}CH}{-}R + Btz{-}O^-$$

R=Alkyl; R'=Alkyl, Phenyl; Btz=



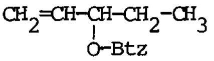
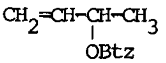
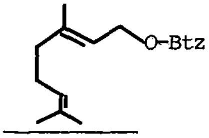
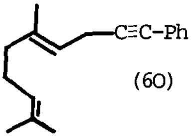
The following procedure for the synthesis of (E)1-phenyl-4-hepten-1-yne is typical. To a stirred suspension of 0.5 g of copper(I) phenyl acetylide (1 mol equiv.) in 5 ml of THF was added under nitrogen and stirring 0.66 g of 1-penten-3-(2'-benzothiazolyl) ether (1 mol equiv.) in5 ml of THF. The resulting suspension was stirred at 40° until the disappearance (TLC, 4h) of the ether. After filtration and solvent evaporation to dryness, the residue was extracted with hexane. The hexane extract was washed with 5% aq. NaOH to remove 2-hydroxybenzothiazole, with water and finally dried; after evaporation the 1,4-enyne is obtained in almost pure form. Chromatography (silica gel, hexane) yields 0.35 g (68%) of the desired product. H^1NMR(CCl_4) δ(ppm) 5.50(cm), 2H, olefinic; 3.01(dd), 2H, $C{\equiv}C{-}CH_2{-}C{=}C$. IR($CCl_4$) 2240, 1670, 960 cm^{-1}.

We believe that the enhanced reactivity and the high stereospecificity of the copper(I) acetylides can be ascribed to coordination of the organometallic species by the nitrogen of the heterocycle linked to the allylic moiety. Consequently, this method, which affords pure (E)-1,4-enynes has the following practical advantages:

i) The ready availability[9] of secondary allylic ethers with terminal double bonds avoids the use of allylic derivatives with prefixed double bond geometry.

ii) The C-C coupling can be accomplished even in wet solvents since the copper(I) acetylides are stable in acqueous media. The extention of this method to the synthesis of 1,4-dienols with both (Z,E)- and (E,Z)-configuration is under investigation. The results are summarized in the following Table.

TABLE

Substrate	Acetylide(Solvent)		Product[a,b] (Yield %)	Time (h)	Temp. (° C)
 $CH_2=CH-\underset{\text{O-Btz}}{CH}-CH_2-CH_3$	CuC≡C-Ph	(THF)	Ph-C≡C-CH_2-CH=CH-CH_2-CH_3 (E) (68)	(4)	(40)
..	CuC≡C-$(CH_2)_4CH_3$	(DMF)	$CH_3(CH_2)_4$-C≡C-CH_2-CH=CH-CH_2-CH_3(E) (40)	(2)	(40)
 $CH_2=CH-\underset{\text{OBtz}}{CH}-CH_3$	CuC≡C-Ph	(THF)	Ph-C≡C-CH_2-CH=CH-CH_3 (E) (70)	(2)	(65)
	CuC≡C-Ph	(THF)	 (60)	(3)	(40)

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a) Yield of isolated product from chromatography.

b) Satisfactory ^{1}HNMR and IR spectra were obtained for all compounds.

REFERENCES AND NOTES

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9) The benzothiazolyl ethers were synthesized by reaction of the potassium salts of the commercial allylic alcohols with 2-chlorobenzothiazole in ethyl ether at room temp.

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