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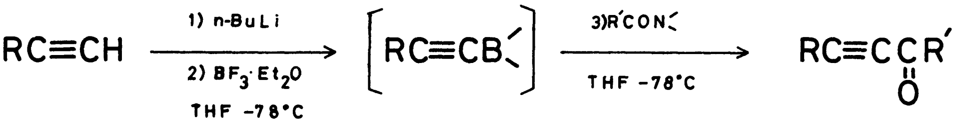
A NOVEL METHOD FOR THE SYNTHESIS OF ALKYNYL KETONES —— A REACTION OF ALKYNYL BORANES WITH AMIDES

Masahiko YAMAGUCHI,* Toshie WASEDA, and Ichiro HIRAO
Department of Industrial Chemistry, Kyushu Institute of Technology,
Sensui-cho, Tobata Kitakyushu 804

Alkynyl ketones are synthesized in high yields by the reaction of alkynyl boranes and amides under a mild reaction condition.

Alkynyl ketones are very useful precursors and intermediates in synthetic organic chemistry. The acetylene unit provides a convenient handle which may be transformed into a variety of functionalities. One of the most convenient methods for the preparation of alkynyl ketones is the acylation of metal acetylides. Thus, acid chlorides or acid anhydrides are reacted with various types of the acetylides.1) Other carboxylic acid derivatives such as amides,2) esters3) or acyl cyanides4) have been employed with less effectiveness. We have recently reported an efficient method for the synthesis of β-hydroxyacetylenes by the oxirane ring opening with alkynyl boranes.5) As a further synthetic study based on the reactive organoboranes, we now wish to report a new method for the synthesis of the alkynyl ketones by a novel coupling reaction of the alkynyl boranes 6) and amides.

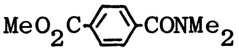
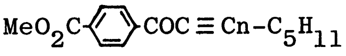
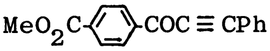
Alkynyl boranes prepared in situ from lithium acetylides and boron trifluoride etherate at -78°C in tetrahydrofuran (THF) are allowed to react with various tertiary amides at -78°C and alkynyl ketones are obtained in high yields (Scheme I). The results are summarized in Table, and in every case no tertiary alcohol generated by the addition of the acetylide to the alkynyl ketone is detected.



Scheme I

The examination of the reaction conditions revealed several characteristic features of the process. As for the solvent, the use of THF is essential, and no alkynyl ketone is detected when ether is employed. Tertiary amides react effectively with the alkynyl boranes, though a secondary amide such as acetanilide is recovered unchanged under the present reaction conditions. Also observed is an extraordinary high reactivity of the amide moiety against the organoboranes. Thus, as shown in Table, dimethylaminocarbonyl group is far more reactive than methoxycarbonyl group, and is comparable to ketone moiety in the reactiveness (Scheme II).

Table. A Synthesis of Alkynyl Ketones.

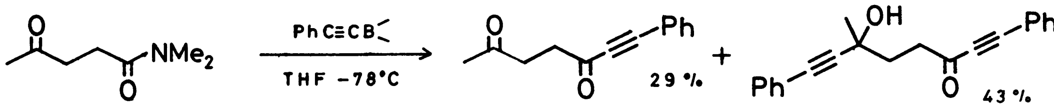
Amides	Acetylenes[c)]	Products	Yields(%)[a)]
$PhCONMe_2$	$n\text{-}C_5H_{11}C\equiv CH$	$n\text{-}C_5H_{11}C\equiv CCOPh$	88
	$PhC\equiv CH$	$PhC\equiv CCOPh$	83 (49)[b)]
	$THPOCH_2C\equiv CH$	$THPOCH_2C\equiv CCOPh$	77
$n\text{-}C_9H_{19}CONMe_2$	$n\text{-}C_5H_{11}C\equiv CH$	$n\text{-}C_5H_{11}C\equiv CCOn\text{-}C_9H_{19}$	94
	$PhC\equiv CH$	$PhC\equiv CCOn\text{-}C_9H_{19}$	89
PhCONMePh	$n\text{-}C_5H_{11}C\equiv CH$	$n\text{-}C_5H_{11}C\equiv CCOPh$	84
	$PhC\equiv CH$	$PhC\equiv CCOPh$	90 (68)[b)]
	$n\text{-}C_5H_{11}C\equiv CH$		97
	$PhC\equiv CH$		97

a) All the products gave satisfactory spectral data (^{1}H-NMR, IR, MS).

b) The molar ratio of amide:acetylene was 1:2.

c) The molar ratio of amide:acetylene was 1:3.

A typical procedure is described for the reaction of N,N-dimethylbenzamide and 1-heptyne: Under a nitrogen atmosphere, to a THF solution (3 ml) of 1-heptyne (336 mg, 3.0 mmol) was added a butyllithium-hexane solution (1.86 ml, 3.0 mmol) at -78°C, and the mixture was stirred for 10 min. Then, boron trifluoride etherate (0.4 ml, 3.2 mmol) was added to stir for further 10 min. Finally, a THF solution (2 ml) of N,N-dimethylbenzamide (149 mg, 1.0 mmol) was added. After 30 min at -78°C, the reaction was quenched with aqueous ammonium chloride, and an usual work up gave 1-phenyl-2-octyn-1-one (175 mg, 88 %).
NMR ($CDCl_3$) δ 0.7-1.1 (3H, m), 1.1-1.8 (6H, m), 2.45 (2H, t, J=6.5 Hz), 7.2-7.6 (3H, m), 8.0-8.2 (2H, m). IR (neat) 2240, 2200, 1640 cm^{-1}. Found m/e 200.1185. Calcd for $C_{14}H_{16}O$, 200.1202.



Scheme II

It should be noted that the present synthetic method for the alkynyl ketones is unique on the point that amides are effectively employed as the acylating reagent, which are quite stable molecules and easily prepared or isolated.

References

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