Alkylation and Protonation of Alkynyltrialkylborate Salts - a New General Method for the Preparation of Ketones

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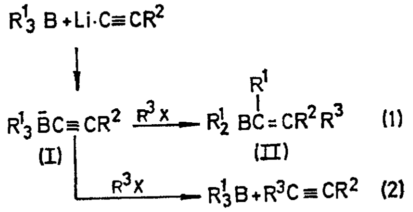
Summary Terminal alkynes ($R^2C{\equiv}CH$) may be converted into ketones ($R^2R^3CHCOR^1$) by the alkylation or protonation of lithium alkynyltrialkylborate salts followed by oxidation, this being a general route to specifically substituted ketones and a major extension of alkyne chemistry.

Following from our interest in the chemistry of systems of the type $R_2\bar{B}X{-}Y{\equiv}Z$ of which the Brown carbonylation processes[1] ($Y{\equiv}Z = \overset{+}{C}{\equiv}O$) and our cyanoborate reactions ($Y{\equiv}Z = C{\equiv}N$) are examples[2] we examined the effects of electrophilic attack upon alkynyltrialkylborates (I) ($Y{\equiv}Z = C{\equiv}CR^2$).

Previous observations by Binger and his colleague[3] had shown competitive reactions between β-attack with the desired migration [equation (1)] and α-attack with displacement of the trialkylborane [equation (2)]. It was noted that hydrolysis of the intermediate (II) could yield olefins, which were, however, mixtures of *cis*- and *trans*-isomers and this apparently discouraged further studies. In no case was a yield of olefin given or the conditions defined.

It occurred to us that oxidation of the intermediates (II) might provide a valuable new route to ketones (III) ($R^1{\cdot}CO{-}CHR^2R^3$) free of the complications associated with the production of the *cis,trans*-mixture. Indeed this proved to be the case and accordingly a detailed study was undertaken to maximise the yield of the ketone (III) produced *via* the oxidation of (II).



We have found that to obtain the yields quoted in the Table for the alkylation reaction it is necessary to use diglyme as solvent. The use of tetrahydrofuran led to yields of between 8 and 15% less but may be more convenient and less costly. The salts (I) were prepared by addition of the trialkylborane in diglyme to the appropriate acetylide under hexane at 0°. After removal of the volatile solvent the alkylating agent was added at −78°

TABLE

Ketone synthesis via *electrophilic attack on* $[R^1_3BC{\equiv}CR^2]^-Li^+$

Electrophilic reagent R^3X	Ketone $R^1COCHR^2R^3$			
	R^1	R^2	R^3	Yield (%)[a]
Me_2SO_4	n-Octyl	Bu^n	Me	85
”	n-Hexyl	n-Hexyl	”	84
”	Cyclopentyl	”	”	81
MeOTs	n-Hexyl	”	”	93
”	Cyclopentyl	”	”	88
$Et_3O^+BF_4^-$	n-Octyl	Bu^n	Et	88
”	n-Hexyl	n-Hexyl	”	90
”	Cyclohexyl	Bu^n	”	80
$CH_2{:}CH{\cdot}CH_2Br$	n-Octyl	”	Allyl	80
”	n-Hexyl	n-Hexyl	”	88
”	Cyclopentyl	Bu^n	”	86
$PhCH_2Br$	n-Octyl	”	Benzyl	79
”	n-Hexyl	n-Hexyl	”	78
”	Cyclopentyl	Bu^n	”	81
$MeSO_3H$	n-Octyl	n-Hexyl	H	78
”	n-Hexyl	Ph	”	79
”	Cyclopentyl	Bu^n	”	76
”	Cyclohexyl	”	”	86

[a] Yield of isolated, purified product after correction for traces of impurity shown by g.l.c.

and the cooling bath removed. Reaction with triethyloxonium borofluoride was instantaneous, whereas dimethyl sulphate required 5—10 min for complete reaction. Allyl bromide, benzyl bromide, and methyl toluene-*p*-sulphonate required warming at 40° for 2 h or were left at 25° for 5 h. The use of the latter reagent is of particular importance as it indicates that alcohols may be incorporated *via* the toluene-*p*-sulphonate into the final ketone in excellent yield. Oxidation with alkaline hydrogen peroxide[4] then gave the ketone (71—93% yield) sometimes accompanied by a little olefin (3—5%). For protonation, methanesulphonic acid was used and gave migrated product (II; $R^3 = H$) instantaneously. The oxidation procedure was the same as for the alkylation process. It is interesting that if a magnesium alkynyltrialkylborate salt is used, this being insoluble in diglyme, no migration product is isolated.[5]

It is clear that a major new synthetic route to ketones ($R^1COCHR^2R^3$) is to hand. The alkylation procedure is a novel solution to the problem of the specific mono-alkylation of ketones giving the product *via* non ketonic intermediates. It is of particular importance that the various portions of the final ketones are provided by simple building blocks that may be independently varied at will, *i.e.* R^1 from R^1_3B; R^2 from $R^2C{\equiv}CH$ and R^3 from R^3X. Migration of secondary groups as well as primary may be readily accomplished and the mild reaction conditions make it likely that many functional groups can be accommodated. The fact that the terminal alkynyl carbon atom is both alkylated and converted into a carbonyl group with the neighbouring carbon atom being either protonated or alkylated is an important extension of alkyne chemistry.

Hydrolysis of intermediates (II) with acetic acid gave olefins in excellent yields (73—96%) but unfortunately these were mixtures (*ca.* 70:30) of the two geometric isomers.

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