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THE REACTION OF LITHIUM TRIALKYLALKYNYLBORATES WITH PROPARGYL BROMIDE AND IODOACETONITRILE. A CONVENIENT SYNTHESIS OF FUNCTIONALLY SUBSTITUTED KETONES AND OLEFINS OF DEFINED CONFIGURATION.

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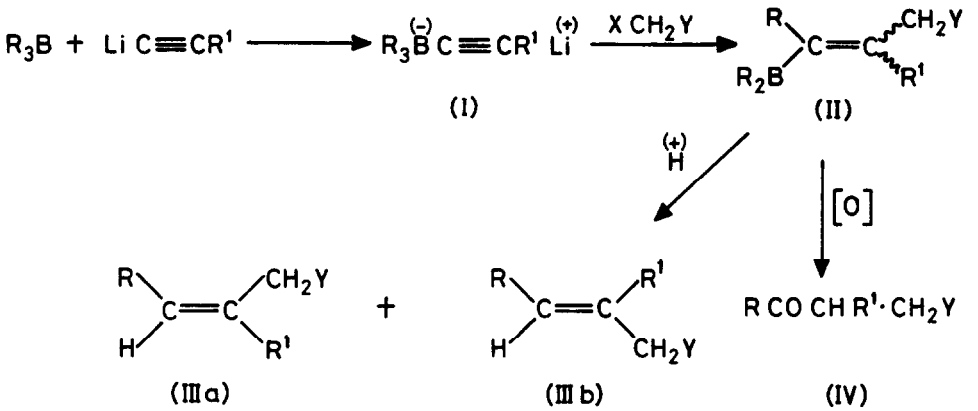
A wide variety of ketones and olefins may now be synthesised by the protonation and alkylation of trialkylalkynylborate salts (I).[1-5] The particular attraction of these syntheses is their flexibility since the various component parts of the products are derived from simple chemical building blocks which may be varied independently. Moreover, although the simple alkylation of the salts (I) shows little stereoselectivity, we have recently shown[6] that the alkylation of thexyldialkylalkynylborate salts proceeds stereoselectively to give ca. 9:1 ratio of olefins (IIIa) and (IIIb) (Y = R or H), compared with a ratio of ca. 65:35 for the simple salts (I).

The versatility of the alkylation reaction was demonstrated by the use of α-halocarbonyl compounds[2] as alkylating agents. This proved to be a stereospecific reaction



X = Br, Y = C≡CH, CO CH$_3$, CO$_2$Et.
X = I, Y = C≡N.

Scheme 1.

which gave 1,4-dicarbonyl compounds and βγ-unsaturated carbonyl compounds in good yield. However the stereochemistry assigned was in contrast with our later unequivocal assignments for simple alkylations in which the major products are always those in which the migrated group and the alkylating group finish up cis to each other as in (IIIa). We now report that alkynyl and cyano groups may be incorporated into the products in a stereospecific fashion to yield (IIIa) (Y = C≡CH, CN) and that a reversal of our previous assignments for the βγ-unsaturated carbonyl products must be made. A satisfyingly consistent picture of the stereospecific production of the Z-isomers (IIIa) emerges. Of course, in every case oxidation of the intermediates (II) gives the ketones (IV) with no possibility of ambiguity.

Propargyl bromide and iodoacetonitrile both reacted readily with salts (I) in mild conditions (see Table) inducing migration of one alkyl group. The intermediates (II) were not isolated but oxidised or hydrolysed as required. Oxidation (Table) gave γ-keto-alkynes or γ-ketonitriles (IV) whilst treatment with degassed isobutyric acid at 25°/3 h followed by appropriate work-up gave the trisubstituted olefins (IIIa) (R = C≡CH, CN) in good yield.

Table

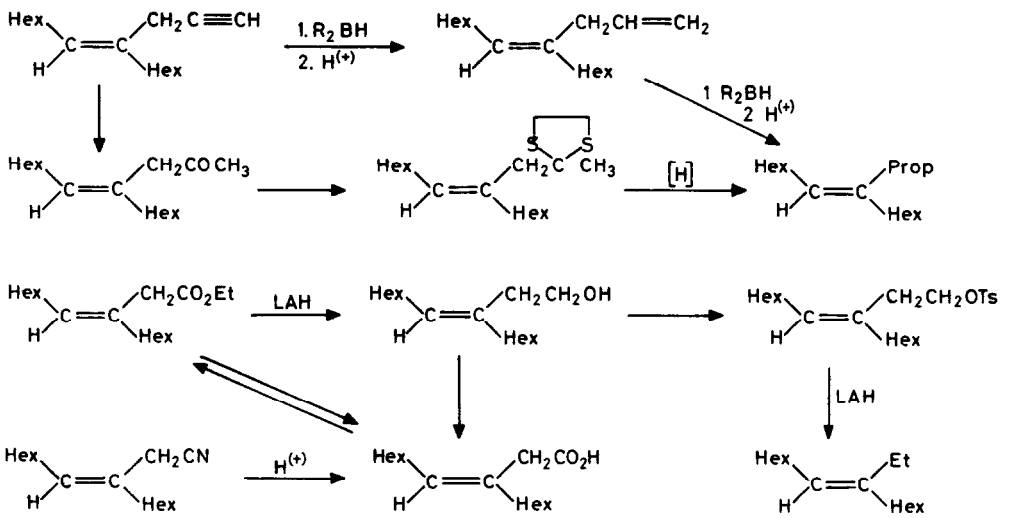
R	R'	Y	Time/°C	% Yield of $RCO.CHR'CH_2Y$[a]		% Yield of $RCH=CR'.CH_2Y$[a]
n-Hexyl	n-Hexyl	-C≡CH	6 h/25°	80[b]		74
n-Octyl	n-Butyl	-C≡CH	6 h/25°	76[b]		75
Cyclopentyl	n-Butyl	-C≡CH	3.5 h/40°	75[b]		77
n-Hexyl	n-Hexyl	-C≡N	1.5 h/25°	69[b]	71[c]	72
n-Octyl	n-Butyl	-C≡N	1.5 h/25°	66[b]	70[c]	68
Cyclopentyl	n-Hexyl	-C≡N	2.5 h/25°	51[b]	62[c]	64

(a) Yields of purified and characterised product.

(b) Oxidation with acetate buffered hydrogen peroxide for 15 h at 25°.

(c) Oxidation with four equivalents of anhydrous trimethylamine N-oxide at 50° for 4 h.[7]

In all cases g.l.c. examination and ^{1}H n.m.r. suggested that one olefin only had been formed by a stereospecific alkylation, as previously indicated for the α-halocarbonyl alkylations.[2] Representative examples (III) (R = R' = n-hexyl) were interconverted and/or converted into olefins whose stereochemistry we had previously established.[6] (Scheme 2). For those cases where Y = CN, C≡CH, $COCH_3$ only one product was always obtained (>98% by g.l.c.). Where Y = CO_2Et the reaction seemed rather more sensitive to reactive conditions, almost complete stereoselectivity being obtained by use of glyme as



Scheme 2

solvent. Total selectivity in this case was produced when thexyldialkylalkynylborate salts were used in place of (I).

A typical procedure is as follows. A solution of tri-n-hexylborane (5 mmole) in THF (5 ml) was prepared under nitrogen in a dropping funnel attached to a three-necked flask fitted with both nitrogen and septum inlets. In the flask a stirred solution of 1-octyne (5 mmole) in light petroleum was treated at 0° with n-butyllithium (5 mmole) in hexane. The suspension of the acetylide was allowed to warm to 25° for 10 min, recooled to 0° and the solution of tri-n-hexylborane added dropwise from the funnel. The reaction mixture was stirred for 45 min at 25° and the volatiles removed at the pump. The syrupy borate was dissolved in glyme (1,2-dimethoxyethane) (5 ml) and cooled to 0° when freshly distilled propargyl bromide (5.5 mmole) was added. The reaction mixture was stirred for 6 h at 25° to complete the migration process and then oxidised overnight at 25° by addition of saturated aqueous sodium acetate (10 ml) and hydrogen peroxide (50%, 3 ml). The neutral product was applied to a silica gel column when elution with dichloromethane yielded the required 4-hexyl-1-undecyn-5-one (IV, R, R' = n-Hex, Y = C≡CH)(1.01 g, 80%) which was characterised by spectroscopic data and elemental analysis.

The incorporation of nitrile and acetylene groups into ketones and olefins is an important extension to the scope of synthesis using trialkylalkynylborates. The oxidation reaction gives a convenient route to γ-ketoacetylenes and γ-ketonitriles which show promise as intermediates in heterocyclic synthesis.[8] The hydrolysis procedure results

in high yield, stereospecific formation of trisubstituted olefins bearing functional groups in one side chain.

It is of interest that the acetylene derivatives (IIIa, Y = C≡CH) may potentially be converted to new borate salts and further transformed with any of the extensive range of electrophiles now available.[1-5]

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