The Chemistry of Organoborates. Part 8.[1] Unique Michael Reactions of Lithium Trialkylalkynylborates

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Lithium trialkylalkynylborates undergo unique Michael reactions involving migration of an alkyl group from boron to carbon. Oxidation or hydrolysis of the vinylboranes so produced yields compounds of synthetic potential. The generality and limitations of the Michael reactions are discussed.

WE have previously defined general equations to describe those ionic reactions of organoborates that involve 1,2-migration of organyl groups from boron to an adjacent atom.[2] These involve electrophilic attack β- to the boron atom to produce a dipolar intermediate (or transition state) which collapses to a neutral molecule by 1,2-migration.

In questioning whether such general equations fully define the ionic chemistry of organoborates we were led to test the effectiveness of alkynylborates as Michael donors (Scheme). If such reactions were successful migration of an organyl group from boron to carbon would be initiated not by *neutralisation* of charge, but by its *displacement* to an energetically more favourable position, and so a new field of boron chemistry would be opened up. In the event we have shown [3,4] that lithium trialkylalkynylborates (I) react with some Michael acceptors in true Michael reactions, but with a concomitant migration of an alkyl group that is unique both in the chemistry of the Michael reaction and of organoborates.

We now report our full results showing that compounds (I) react with a defined and wide range of Michael acceptors in a regio- but not stereo-specific fashion. The proportions of E- and Z-isomers (defined from the hydrolysis products) are similar to those given by the simple alkylation of (I),[5] though it is not certain that, in fact, the reaction proceeds in the same fashion. Hydrolysis of the intermediates yields the corresponding alkenes, whilst careful choice of oxidant produces ketones with the original functional groups intact.

RESULTS AND DISCUSSION

Lithium trialkylalkynylborates (I) (see Scheme) readily react (see Experimental section for conditions) with α,β-unsaturated nitro-compounds (IIa), alkylidenemalonates (IIb) and alkylideneacetoacetates (IIc) to give the corresponding intermediates (IIIa—c). The reactions of the three series proceed at a similar rate. *Uncatalysed* † reactions were not observed with acyclic and cyclic α,β-unsaturated ketones and acyclic α,β-unsaturated esters. Reaction occurs smoothly with compounds RCH:CXY in which CH_2XY has pK_A not higher than 11, the pK_A

† Following our initial report A. Suzuki (*Chem. Lett.*, 1980, 221) has noted a Lewis acid-catalysed reaction of alkynylborates with methyl vinyl ketone which, in our hands, gave 21% yield of 1,5-diketone.

being taken as a rough guide to the combined electron-withdrawing power of groups X and Y. Thus with those groups X and Y for which the reaction is successful (IIa—c) the conjugate acids CH_2XY have pK_A 10 (X = H, Y = NO_2) and between 9 and 11 (X = COR, CO_2R, and Y = CO_2R). For those acceptors (IId—f) for which the reaction did not succeed the conjugate acids have pK_A 35 (X = H, Y = SOPh) and 20—25 (X = H, Y = COR and CO_2R). On this basis we would predict that the alkylidene compounds produced from malononitrile (X = Y = CN, pK_A 11), cyano-acetates (X = CN, Y = CO_2R, pK_A 9) and acetyl-acetone (X = Y = $COCH_3$, pK_A 9) would all react smoothly with alkynylborates. We emphasise that these considerations apply only to the uncatalysed reactions.

The reaction suffers from one of the usual restrictions of Michael reactions in that *geminal*-substitution of the acceptor β- to the electron-withdrawing groups inhibits reaction (see Tables, reactions 12 and 24). However neither α-substitution nor mono β-substitution have any effect and the alkynyl group may be substituted by a phenyl as well as an alkyl group. The reaction is successful with tri-sec-alkyl- as well as tri-primary-alkylalkynylborates though, at best, it is seventeen times slower. We think that this is a kinetic effect involving steric problems of approach of the acceptor to the bulky organoborate rather than a measure of the migratory aptitudes of the groups. Thus when lithium dicyclo-hexyl-n-hexylhexynylborate is allowed to react with di-ethyl ethylidenemalonate the products from secondary and primary alkyl group migration are produced in the ratio 41 : 59 giving the migratory aptitude of cyclohexyl : n-hexyl as 0.35. A similar experiment with lithium bis(2-methylcyclohexyl)-n-hexylhexynylborate gave the relative migratory aptitudes of 2-methylcyclohexyl to n-hexyl as 0.11. When the two secondary alkyl groups were incorporated into a 9-borabicyclo-nonane (9-BBN) unit (I; R^1_2 = 9-BBN, R^1 = Hex^n, R^2 = Hex^n) and reacted with alkylidene nitro-compounds (X = NO_2, Y = H or Me), only a small yield was obtained of the required compound in which migration of the primary-alkyl group had occurred. Migration of the bridgehead secondary alkyl groups was highly competitive.

Useful organic products (IV) and (V) are obtained from the intermediate vinylboranes (IIIa—c) either by oxidation or hydrolysis. Hydrolysis is normally accom-

$$\begin{array}{c} \text{Li}^+ \quad R^1{}_3\bar{B}C{\equiv}CR^2 \\ \text{(I)} \\ + \\ R^3R^4C{=}CXY \\ \text{(II)} \end{array} \longrightarrow R^1{}_2B{-}\overset{R^1}{\underset{}{C}}{=}C(R^2){\cdot}\overset{R^3}{\underset{R^4}{C}}{\cdot}\bar{C}XY$$

(III)

$$\text{[O]} \downarrow \qquad \qquad \downarrow \text{H}^+$$

R¹COCHR²·CR³R⁴·CHXY   R¹CH=C(R²)CR³R⁴·CHXY

(IV)   (V)

(a) X = NO₂, Y = H or Me
(b) X = Y = CO₂Et
(c) X = COCH₃, Y = CO₂Et

(d) X = SOPh, Y = H
(e) X = COR, Y = H
(f) X = CO₂Et, Y = H

SCHEME

plished by use of dry, degassed isobutyric acid at room temperature for 20 h. However considerably stronger conditions are required when secondary alkyl groups are attached to boron (Table 2, experiment 22). We were

m-chloroperbenzoic acid normally gives the desired 1,5-keto-esters without hydrolysis of the ester groupings (Table 1). When R¹ = cyclopentyl (Table 1, experiment 11), the vinylborane was not broken down by the

TABLE 1

Yields [a] of products from Michael addition-oxidation of (I) *

Compound and Experiment No.	R¹	R²	R³	R⁴	X	Y	Yield (%) of (4)
(1)	Hexⁿ	Hexⁿ	H	H	NO₂	H	80 [b,f]
(2)	Hexⁿ	Hexⁿ	Me	H [e]	NO₂	H	93 [b]
(3)	Hexⁿ	Hexⁿ	H	H	NO₂	Me	57 [b](5) [h]
(4)	c-Pent	Hexⁿ	Me	H [e]	NO₂	H	75 [b]
(5)	Pentⁿ	Hexⁿ	Me	H [e]	NO₂	H	75 [b]
(6)	Hexⁿ	Buⁿ	Me	H	CO₂Et	CO₂Et	91 [c]
(7)	Hexⁿ	Buⁿ	Ph	H	CO₂Et	CO₂Et	83 [c]
(8)	Hexⁿ	Buⁿ	H	H	CO₂Et	CO₂Et	67 [c]
(9)	Hexⁿ	Buⁿ	Me	H [e]	COCH₃	CO₂Et	74 [c]
(10)	Hexⁿ	Buⁿ	Ph	H [e]	COCH₃	CO₂Et	79 [c]
(11)	c-Pent	Buⁿ	Me	H	CO₂Et	CO₂Et	67 [d]
(12)	Hexⁿ	Hexⁿ	Me	Me	NO₂	H	0 [b]
(13)	Hexⁿ	Hexⁿ	H	H	SOPh	H	10 [b,g]

* Hexⁿ = n-hexyl, c-Pent = cyclopentyl, Pentⁿ = n-pentyl, Buⁿ = n-butyl.

[a] Yields of isolated, characterised products with satisfactory spectral properties; see Experimental section for characterisation. [b] Oxidation with NaOAc–H₂O₂. [c] Oxidation with m-chloroperbenzoic acid. [d] Oxidation with NaOAc–H₂O₂ for 75 h at 25 °C, gas chromatographic yield of 84%. [e] cis–trans Mixture of alkene used. [f] Alkene introduced as vapour in a stream of dry nitrogen. [g] Estimated by u.v. spectroscopy. [h] Hydrolysis product.

TABLE 2

Yields [a] of products from Michael addition-hydrolysis of (I) *

Compound No.	R¹	R²	R³	R⁴	X	Y	Yield (%) of (5)	Ratio of isomers [b]
(14)	Hexⁿ	Hexⁿ	Me	H [e]	NO₂	H	82	64 : 36
(15)	Hexⁿ	Buⁿ	Me	H	CO₂Et	CO₂Et	80	64 : 34
(16)	Octⁿ	Buⁿ	Me	H	CO₂Et	CO₂Et	93	67 : 33
(17)	Hexⁿ	Hexⁿ	Me	H	CO₂Et	CO₂Et	88	68 : 32
(18)	Hexⁿ	Buⁿ	Ph	H	CO₂Et	CO₂Et	82	75 : 25
(19)	Hexⁿ	Buⁿ	H	H	CO₂Et	CO₂Et	84	73 : 27
(20)	Hexⁿ	Buⁿ	Me	H [e]	COCH₃	CO₂Et	75	78 : 22
(21)	Hexⁿ	Buⁿ	Ph	H [e]	COCH₃	CO₂Et	80	67 : 33
(22)	c-Pent	Buⁿ	Me	H	CO₂Et	CO₂Et	72	64 : 36 [d]
(23)	Ph	Buⁿ	Me	H	CO₂Et	CO₂Et	0	
(24)	Hexⁿ	Buⁿ	Me	Me	CO₂Et	CO₂Et	0	

* Hexⁿ = n-hexyl, Octⁿ = n-octyl, c-Pent = cyclopentyl, Buⁿ = n-butyl.

[a] Yields of isolated, characterised products with satisfactory spectral properties; see Experimental section for characterisation. [b] Isomer with C-5 at lower field in the ¹³C n.m.r. spectrum given first. [e] cis–trans Mixture of alkene used. [d] Refluxed in THF with isobutyric acid for 44 h.

unable to obtain a hydrolysis product from triphenylhexynylborate (Table 2, experiment 23) despite resorting to isobutyric acid in refluxing diglyme.

Oxidation of products (IIIa) with buffered alkaline hydrogen peroxide is successful but, in general, this method fails for the esters (IIIb and c). However use of

peracid but, somewhat surprisingly, extended oxidation with buffered peroxide was successful in this case.

The lack of success of the reaction with monofunctional unsaturated ketones and esters is of little significance as the products of the alkylidene-malonate and -acetoacetate reactions can be saponified and decarboxylated

in good yields. Thus we have hydrolysed and decarboxylated ethyl 4-butyl-2-ethoxycarbonylundec-4-enoate (19) to the corresponding monocarboxylic acid in 78% (isolated) yield.

The large range of Michael acceptors and alkynylborates for which the reaction is successful shows that this unique class of Michael reaction has broad synthetic potential. We will report separately on the (successful) Michael reactions of trialkylalkenylborates.

EXPERIMENTAL

Ether solvents were distilled under nitrogen from calcium hydride or lithium aluminium hydride. Other solvents and liquid reagents were purified by standard procedures and distilled over calcium hydride. Diborane was kept as a BF_3-free solution in tetrahydrofuran (THF) and was standardised before use. I.r. spectra were recorded on a Perkin-Elmer 257, [1]H n.m.r. spectra on a Varian HA-100, [13]C n.m.r. spectra on an XL-100 FT and mass spectra using an A.E.I. MS9 spectrometer. A Perkin-Elmer F11 instrument with 5% SE30 adsorbed on Chromosorb G (60—80 mesh) column was used for gas chromatography. Most of the compounds were analysed using a programmed run of 50—280 °C followed by 20 min at 280 °C and gave single peaks. Commercially available n-butyl-lithium in hexane was standardised and used directly.

All manipulations prior to work-up were carried out in dry glassware under nitrogen and dry syringes were used to transfer liquids.[6] Hydroborations were accomplished according to published procedures.[6]

The reaction vessel used was a 100-ml three-necked flask fitted with a magnetic stirrer. One neck was connected via a three-way tap to a source of oxygen-free nitrogen (with pressure release bubbler) and also to a high vacuum pump. Another was sealed with a tap, capped with a silicone rubber septum used for direct introduction of reagents. The centre neck was fitted with a pressure-equalised dropping funnel and sealed with a serum cap which was used for the preparation and addition of trialkylboranes. The apparatus was assembled hot, evacuated, flushed with nitrogen several times, and allowed to cool.

General Procedure.—A solution of trialkylborane (5 mmol) in THF was prepared under nitrogen in the dropping funnel. To a stirred solution of the alkyne (5 mmol) in light petroleum (b.p. 30—40 °C; 5 ml), in the ice-cooled round-bottomed flask, n-butyl-lithium (5 mmol) in hexane was added dropwise. The alkynyl–lithium precipitated as a white solid and butane was evolved. The ice-bath was removed and the mixture stirred for 30 min. The flask was re-cooled to 0 °C and the solution of trialkylborane was added dropwise. The dropping funnel was washed with THF (*ca.* 2 ml), the ice-bath removed, and the resulting clear solution stirred at room temperature for 15 min. All volatiles were removed on the pump to leave the syrupy

TABLE 3

Characterisation of products from Michael reactions of alkynylborates

Product No.	Name	$n_D^{25 \circ C}$	Found (%)			Acc. Mass	Formula	Required (%)			Acc. Mass
			C	H	N			C	H	N	
(1)	3-Hexyl-1-nitrodecan-4-one	1.4555	67.2	10.55	4.95	285.2294	$C_{16}H_{31}NO_3$	67.36	10.87	4.91	285.2303
(2)	3-Hexyl-2-methyl-1-nitrodecan-4-one	1.4550	68.0	11.1	4.6		$C_{17}H_{33}NO_3$	68.22	11.03	4.68	
(3)	3-Hexyl-1-methyl-1-nitrodecan-4-one	1.4520	68.25	11.2	4.6		$C_{17}H_{33}NO_3$	68.22	11.03	4.68	
(4)	Cyclopentyl 2-methyl-1-nitrononan-3-yl ketone	1.4710	67.75	10.4	4.85		$C_{16}H_{29}NO_3$	67.84	10.25	4.95	
(5)	3-Hexyl-2-methyl-1-nitrononan-4-one	1.4625	67.15	10.7	4.9		$C_{16}H_{31}NO_3$	67.39	10.88	4.91	
(6)	Ethyl 4-butyl-2-ethoxycarbonyl-3-methyl-5-oxoundecanoate	1.4500	67.7	10.05		370.2719	$C_{21}H_{38}O_5$	68.10	10.27		370.2719
(7)	Ethyl 4-butyl-2-ethoxycarbonyl-3-phenyl-5-oxoundecanoate	1.4880	71.7	9.65		432.2877	$C_{26}H_{40}O_5$	72.22	9.26		432.2876
(8)	Ethyl 4-butyl-2-ethoxycarbonyl-5-oxoundecanoate	1.4470	67.45	10.25			$C_{20}H_{36}O_5$	67.41	10.11		
(9)	Ethyl 2-acetyl-4-butyl-3-methyl-5-oxoundecanoate	1.4600	70.0	10.65			$C_{20}H_{36}O_4$	70.58	10.58		
(10)	Ethyl 2-acetyl-4-butyl-3-phenyl-5-oxoundecanoate	1.4915	74.6	9.5			$C_{25}H_{38}O_4$	74.62	9.45		
(11)	Diethyl 3-cyclopentylcarbonyl-heptan-2-ylmalonate	1.4580	67.8	9.75			$C_{20}H_{34}O_5$	67.79	9.60		
(14)	3-Hexyl-2-methyl-1-nitrodec-3-ene	1.4580	72.1	11.7	4.9		$C_{17}H_{33}NO_2$	72.08	11.66	4.95	
(15)	Ethyl 4-butyl-2-ethoxycarbonyl-3-methylundec-4-enoate	1.4500	71.0	10.95		354.2773	$C_{21}H_{38}O_4$	71.19	10.73		354.2769
(16)	Ethyl 4-butyl-2-ethoxycarbonyl-3-methyltridec-4-enoate	1.4510	72.25	10.95		382.3083	$C_{23}H_{42}O_4$	72.25	10.99		382.3083
(17)	Ethyl 2-ethoxycarbonyl-4-hexyl-3-methylundec-4-enoate	1.4529	72.9	11.3		382.3082	$C_{23}H_{42}O_4$	72.25	10.99		382.3083
(18)	Ethyl 4-butyl-2-ethoxycarbonyl-3-phenylundec-4-enoate	1.4875	74.75	9.51			$C_{26}H_{40}O_4$	75.00	9.61		
(19)	Ethyl 4-butyl-2-ethoxycarbonyl-undec-4-enoate	1.4505	70.55	10.35			$C_{20}H_{36}O_4$	70.58	10.58		
(20)	Ethyl 2-acetyl-4-butyl-3-methylundec-4-enoate	1.4545	74.3	11.45			$C_{20}H_{36}O_3$	74.07	11.11		
(21)	Ethyl 2-acetyl-4-butyl-3-phenylundec-4-enoate	1.4950	77.45	9.8			$C_{25}H_{38}O_3$	77.72	9.84		
(22)	Ethyl 4-butyl-5-cyclopentyl-2-ethoxycarbonyl-3-methylpent-4-enoate	1.4640	71.0	9.9			$C_{20}H_{34}O_4$	71.00	10.05		

borate salt. The apparatus was refilled with nitrogen and the residue dissolved in THF (8 ml). The reaction flask was cooled in ice and the Michael-acceptor (5 mmol) added dropwise through the septum cap. The ice-bath was then removed and the reaction mixture allowed to warm to room temperature. After 1 h (20 min in the case of α,β-unsaturated nitro-compounds) at room temperature, oxidation or hydrolysis was carried out.

Some of the Michael-acceptors have a tendency to polymerise on standing and therefore these compounds were distilled immediately before use.

Oxidative Work-up.—(a) *Buffered hydrogen peroxide.* Oxidation was achieved by addition at 0 °C of 5M-aqueous NaOAc (5 ml) followed by dropwise addition (care!) of 50% H_2O_2 (5 ml). After being stirred for at least 3 h at 20 °C the solution was acidified with 5M-aqueous HCl (6 ml) and the crude product extracted with diethyl ether. Chromatographic purification gave the ketone.

(b) m-*Chloroperbenzoic acid* (m-*CPBA*). Solid *m*-CPBA [20 mmol of commercial (85%), 4.4 g] was added slowly while the reaction mixture was cooled in ice. After being stirred at 20 °C overnight (*ca.* 20 h) the reaction mixture was extracted with diethyl ether and washed thoroughly with saturated sodium carbonate ($\times 4$) and then with water. The ether extract was dried (MgSO$_4$). Chromatography over silica gel (60—120 mesh) gave the pure ketone, generally eluted with dichloromethane.

Hydrolytic Work-up.—Hydrolysis was carried out by allowing the reaction mixture to stand with dry, degassed isobutyric acid (2 ml) for *ca.* 20 h, followed by neutralisation and oxidation (to destroy borinates and make product isolation easier) as before. For alkylidene-malonates and -acetoacetates no oxidation was carried out. The reaction mixture was extracted with diethyl ether and the ether extract thoroughly washed with saturated sodium carbonate and then with water. The ether extract was then dried (MgSO$_4$). The residue, after evaporation of the diethyl

ether, was purified by column chromatography on silica gel to give the olefin (dichloromethane–pentane 1 : 1).

The physical constants of the oxidation and hydrolysis products are recorded in Table 3.

Hydrolysis and Decarboxylation of Ethyl 4-Butyl-2-ethoxycarbonylundec-4-enoate (19).—Compound (19) (170 mg, 0.5 mmol) was heated under reflux with 20% ethanolic KOH (1 ml) for 3 h. The reaction mixture was allowed to cool to 23 °C, the ethanol removed under reduced pressure and the residue acidified with 3M-HCl. The mixture was extracted with diethyl ether (3 $\times$ 20 ml) and the combined diethyl ether extracts were washed with water, and dried (MgSO$_4$). The residue after filtration and removal of the diethyl ether was heated on an oil-bath at 180 °C for 1 h under N$_2$. The product was purified by passage through a short column of silica gel with diethyl ether (50 ml) as eluant, yield 94 mg (78%), $n_D^{25\,°C}$ 1.4589 (Found: C, 74.75; H, 11.75%; M^+, 240.2088. $C_{15}H_{28}O_2$ requires C, 75.00; H, 11.66%; M, 240.2089), δ_H 11.02br (1 H, exchanges with D$_2$O, CO$_2H$), 5.14 (1 H, t, RCH:CR^2).

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