

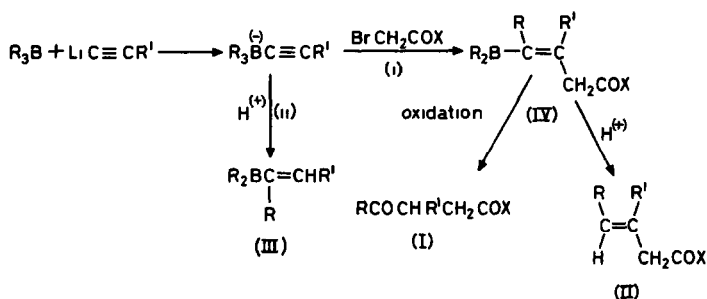
A NOVEL SYNTHETIC ROUTE TO 1,4-DICARBONYL COMPOUNDS,  
 $\beta\gamma$ -UNSATURATED KETONES AND ESTERS USING  
 TRIALKYLALKYNYLBORATES

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The production of 1,4-diketones (I, X = R) has long been of importance as they are intermediates in synthesis of furans<sup>1</sup>, pyrroles<sup>2</sup> and cyclopentenones.<sup>3</sup> The latter compounds are prostaglandin precursors<sup>4</sup> as indeed are the cyclopentan-1,3-diones<sup>5</sup> derived from  $\gamma$ -keto-esters (I, X = OEt) and hence there is a need for new versatile syntheses of (I).<sup>6</sup> This report describes a completely new method for the production of (I) and (II) using organoboranes, the first such direct synthesis.

We have already shown that alkylation of trialkylalkynylborates leads to intermediates which may be converted to either ketones or trisubstituted olefins in excellent yields.<sup>7</sup> It was therefore of interest to see whether  $\alpha$ -halocarbonyl compounds could be induced to react to yield intermediates (IV) which might be oxidised or hydrolysed to (I) or (II) respectively (Figure).



Figure

The process (i) proved to be slower than our previous alkylations and protonations and therefore traces of mineral acid had to be rigorously excluded from the starting halo-carbonyl compound. Even so process (ii) did compete with (i) to give some intermediate (III) which usually accounted for 5-10% of product. However the desired reaction (i) predominated, the transformation proceeding in mild conditions to yield (IV) which on oxidation gave (I). Some representative results are shown in Table 1 from which several points of interest emerge. Migration from the boron can involve a secondary as well

Table 1

R	R'	X	Time/°C	% Yield of RCOCHR'CH <sub>2</sub> COX <sup>a</sup>
n-Hexyl	n-Hexyl	Phenyl	12 h/25°	74 (8) <sup>b</sup>
"	"	Methyl	6 h/25°	75 (8)
Cyclopentyl	n-Butyl	"	5 h/40°	74 (9)
"	"	Ethoxy	6 h/55°	74 (<5)
n-Hexyl	n-Hexyl	"	4 h/40°	78 (<5)

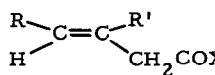
(a) All yields are of purified (column chromatography) characterised product

(b) The figure in parentheses is for the simple product derived from (IV).

as a primary group and phenacyl bromides react well so that whole series of substituted aryl derivatives can be made. Furthermore  $\gamma$ -keto-esters are produced as readily as 1,4-diketones. Clearly as R, R' and X may be varied independently a new flexible, high yield synthesis of substituted 1,4-diketones and  $\gamma$ -keto-esters is to hand. The substitution pattern may be varied as required for the corresponding cyclopentenones and cyclopentan-1,3-diones. In view of the gentle nature of the reaction it is likely that complex side chains will be tolerated as in the cyanoborate process.<sup>8</sup>

Hydrolysis of vinylborane intermediates (IV) was clean and was carried out with acetic acid at 25° or refluxing ethanol, so making substituted  $\beta\gamma$ -olefinic carbonyl compounds readily available (Table 2). Of the greatest interest is that the migration in this case proceeds stereospecifically so that the migrating group is trans to the alkylating agent, a result quite different from the simple alkylations which gave mixtures of stereoisomers. The reason for the difference is not known, though orbital interaction between the attacking  $\alpha$ -bromocarbonyl compound and the boron atom in the development of (IV) may be conjectured. The result however is a new stereospecific synthesis of trisubstituted olefins which contain a functional group in at least one side chain.

Table 2<sup>a</sup>

R	R'	X	% Yield <sup>b</sup> of	
n-Hexyl	n-Hexyl	Phenyl	74	
"	"	p-Chlorophenyl	77	
"	"	Methyl	75	
Cyclopentyl	n-Butyl	"	70	
"	"	Ethoxy	67	
n-Hexyl	n-Hexyl	"	69	

(a) Time and conditions of each reaction as in Table 1

(b) Yield given is of pure, characterised product.

This reaction joins the rapidly growing group of syntheses involving acetylenic groups attached to boron<sup>7,9,10</sup> and in particular complements the very recent reaction of trialkylalkynylborates with epoxides.<sup>10b</sup> A typical procedure is as follows.

A solution of Hex<sub>3</sub><sup>n</sup>B (5 mmole) in diglyme (4 ml) was prepared, under nitrogen, in a dropping funnel connected to a three-necked flask. In the flask a solution of oct-1-yne (5 mmole) in hexane was treated at 0° with LiBu (5 mmole) in hexane, introduced through a septum cap. The acetylide suspension was allowed to warm to 25° for 10 m., recooled to 0° and the borane added dropwise followed by a diglyme (1 ml) washing. The volatile solvents were removed at the pump, the clear solution allowed to stand for 45 m. at 25°, cooled to -78° and ethyl bromoacetate (5.25 mmole) and more diglyme (5 ml) introduced. Migration was completed by warming for 4 h. at 40° after which 4M NaOAc (10 ml) and 50% H<sub>2</sub>O<sub>2</sub> (3 ml) were added and the mixture stirred overnight at 25°. The neutral product was applied to a silica gel column from which the required product (1.16 g, 78%) (characterised by i. r., mass spectrum and g. l. c.) was eluted with dichloromethane.

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