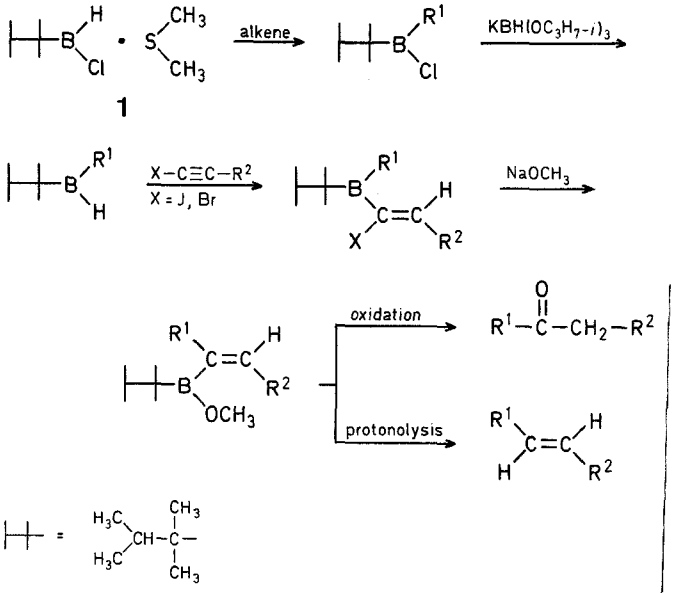
A Simple Synthesis of Alkynyl Ketones via Thexylchloroborane

Herbert C. BROWN*, N. G. BHAT, D. BASAVAIAH

Richard B. Wetherill Laboratory, Purdue University, West Lafayette, Indiana 47907, U.S.A.

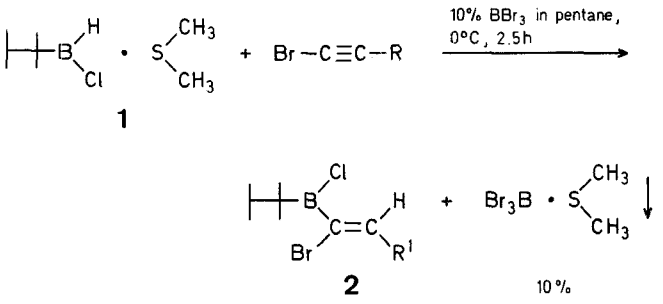
Synthetic applications[1-5] of thexylchloroborane, a new versatile hydroborating agent, have been well documented in the past 2-3 years. We have recently reported a simple convenient stereospecific synthesis of (*E*)-disubstituted alkenes[2] and a regiospecific synthesis of ketones[3] utilizing thexylchloroborane (Scheme **A**).



Scheme **A**

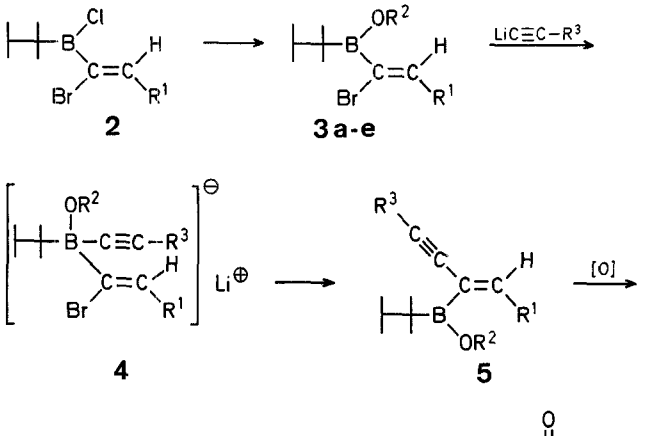
In a continuation of our studies[1,2,3] on the applications of thexylchloroborane for organic transformations, we herein report a simple synthesis of alkynyl ketones via the hydroboration of 1-bromo-1-alkynes with this versatile hydroborating agent.

Monohydroboration[4] of 1-alkynes and selective hydroboration of alkenes of various structural types[1] with thexylchloroborane have been well established. We now directed our studies toward the hydroboration of 1-bromo-1-alkynes with this reagent. Unfortunately, we encountered considerable difficulty. Hydroboration of 1-bromo-1-alkynes is inconveniently slow, requiring 10 h at room temperature for 70% reaction. However, this problem was surmounted by using 10% boron tribromide as catalyst[6], thus providing the vinylborane (**2**) cleanly (Scheme **B**).



Scheme **B**

The low migratory aptitude of the thexyl group[1-5] led us to explore the possibilities of employing **2** for the synthesis of alkynyl ketones (Scheme **C**). The formation of methyl thexyl-(*cis*-1-bromo-1-alkenyl)-borinate (**3a**) was not clean when methanol or sodium methoxide in methanol was used to replace the chlorine substituent. However, the use of solid sodium methoxide in tetrahydrofuran provided the desired methyl borinate esters (**3a**). Subsequent treatment with alkynyllithium affords the corresponding ate complex (**4a**) which results in the intramolecular migration of the alkynyl group from boron to the adjacent carbon, displacing the bromine, to produce the corresponding *cis*-vinylborane (**5**). Migration of the alkynyl group is slow, requiring 6 h at room temperature. Oxidation of **5** provides the desired alkynyl ketones (**6**) in 60% yield (G.L.C.). Use of zinc(II) chloride to induce alkynyl group migration did not result in any increase in the yield of alkynyl ketones. Best results were realized when isopropyl borinate esters (**3b**) were employed, improving the yield of alkynyl ketones to 72% (G.L.C.). Attempts to further improve the yield of alkynyl ketones by utilizing more hindered *t*-butyl or 3-ethyl-3-pentyl borinate esters (**3c** or **3d**) or utilizing cyclohexyl borinate esters (**3e**) of intermediate steric requirement resulted in lower yields of the alkynyl ketones. Representative alkynyl ketones (**6a-f**) were prepared in reasonably good yields using isopropyl borinate esters (**3b**) (Table).



3	R^2
a	CH_3
b	i-C_3H_7
c	t-C_4H_9
d	$ClC_2H_5)_3$
e	

6	R^1	R^3	6	R^1	R^3
a	n-C_4H_9	n-C_4H_9	d	n-C_6H_{13}	n-C_5H_{11}
b	n-C_4H_9	n-C_6H_{13}	e	n-C_6H_{13}	n-C_6H_{13}
c	n-C_4H_9	t-C_4H_9	f	n-C_6H_{13}	

Scheme **C**

Table. The Synthesis of Alkynyl Ketones from Alkynes and 1-Bromo-1-alkynes via Thexylchloroborane[a]

1-Bromo-1-alkyne	1-Alkyne	Product[b,c]	R^1	R^3	Yield[d] [%]	b.p. [°C]/torr	n_D^{20}
1-bromo-1-hexyne	1-hexyne	**6a**	n-C_4H_9	n-C_4H_9	62	90–92°/0.6 [Lit.[19], 107–108°/4]	1.4529 [Lit.[19], 1.4521]
1-bromo-1-hexyne	1-octyne	**6b**	n-C_4H_9	n-C_6H_{13}	62 (72)[e]	84–86°/0.01	1.4541
1-bromo-1-hexyne	t-butylacetylene	**6c**	n-C_4H_9	t-C_4H_9	63	88–90°/3.6	1.4416
1-bromo-1-octyne	1-heptyne	**6d**	n-C_6H_{13}	n-C_5H_{11}	61	92–94°/0.01	1.4553
1-bromo-1-octyne	1-octyne	**6e**	n-C_6H_{13}	n-C_6H_{13}	62	100–102°/0.01	1.4557
1-bromo-1-octyne	cyclohexylethyne	**6f**	n-C_6H_{13}	c-C_6H_{11}	63	96–97°/0.01	1.4751

[a] All reactions were carried out in 20-mmol scale.
[b] Chemical purities of all products are >98% by G.L.C.
[c] All products gave satisfactory spectral data.
[d] Yields of pure distilled products.
[e] G.L.C. yield.

It should be mentioned that very recently Yamaguchi and coworkers reported a facile synthesis of alkynyl ketones by the action of alkynyldifluoroborane with tertiary amides in high yields[7]. Our present studies on thexylchloroborane also provide an alternate convenient synthesis of alkynyl ketones which are useful precursors and important intermediates in organic synthesis[8,9]. Also, this procedure offers considerable advantages over earlier conventional methods[10–14].

We have also successfully utilized the intermediate **3** for the stereospecific synthesis of (*E*)-enynes[15]. We are currently exploring the utility of these methods for the synthesis of insect pheromones.

Boiling points are uncorrected. The G.L.C. analyses were carried out either on a Varian 1400 gas chromatograph (column 12 ft × 1/8 in packed with 10% SE-30 on Chromosorb W AW DMCS) or on a Hewlett Packard 5750 research chromatograph (column 6 ft × 1/4 in packed with 10% SE-30 on Chromosorb W AW DMCS). I.R. spectra were recorded on a Perkin-Elmer 137 Spectrophotometer. ^{1}H-N.M.R. and ^{13}C-N.M.R. spectra were recorded on Varian T-60 and FT-80A spectrometers, respectively. The alkynes (from Farchan Acetylenes) were converted into 1-bromo-1-alkynes by the action of bromine on the corresponding alkynyllithium[16].

Dodec-7-yn-6-one (6a); Typical Procedure:

To thexylchloroborane/dimethyl sulfide[17] (**1**; 3.88 g, 20 mmol) are added *n*-pentane (20 ml) and 1-bromo-1-hexyne (3.22 g, 20 mmol) at 0°C, followed by the slow addition of boron tribromide (501 mg, 2 mmol) under nitrogen[18]. The reaction is allowed to proceed for 2.5 h at 0°C. Isopropyl alcohol (22 mmol, 1.7 ml) is then added at −10°C and the mixture is stirred for 0.5 h at −10°C. Solvents are removed under reduced pressure and the resulting borinate ester is dissolved in tetrahydrofuran (10 ml). To this solution at −78°C is added hexynyllithium [20 mmol; prepared from 1-hexyne (20 mmol, 2.3 ml) and *n*-butyllithium solution (20 mmol, 7.8 ml, 2.56 molar)] and the mixture is maintained for 0.5 h at −78°C. The mixture is allowed to warm to room temperature. After 6 h, the resulting *cis*-alkenylborane is oxidized in the usual way[3] to afford, after distillation, **6a**; yield: 2.23 g (62%); b.p. 90–92°C/0.6 torr; n_D^{20}: 1.4529 [Lit.[19], b.p. 107–108°/4 torr, n_D^{20}: 1.4521).

I.R. (film): ν = 2200 (C≡C), 1675 cm^{-1} (C=O).

^{1}H-N.M.R. ($CDCl_3$/TMS): δ = 0.75–1.89 (m, 16H); 2.20–2.69 ppm (m, 4H).

^{13}C-N.M.R. ($CDCl_3$/TMS): δ = 12.93; 13.34; 18.00; 21.60; 22.15; 23.43; 29.72; 30.91; 45.04 (alkyl C); 80.64; 92.11 (C≡C); 185.61 ppm (C=O).

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* Address for correspondence.

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