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THE HYDROBORATION OF 3-BUTENYL DERIVATIVES WITH 9-BORABICYCLO[3.3.1]NONANE *

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Summary

The hydroboration of 3-butenyl derivatives, $CH_2{=}CHCH_2CH_2X$ where X represents OH, OMe, OAc, Cl, as well as the related carboxylic ester, $CH_2{=}CHCH_2COOEt$, and the nitrile $CH_2{=}CHCH_2CN$, with 9-borabicyclo[3.3.1]nonane (9-BBN) proceeds with remarkably high regio-selectivity. The boron is placed essentially on the terminal carbon (⩾98%), yielding stable organoboranes which can be readily oxidized to alcohols or subjected to other reactions. The yields of alcohols in the hydroboration—oxidation procedure are satisfactory, in the range of 82—99%. The hydroxy group liberates hydrogen rapidly and quantitatively but no further reaction is observed and hydroboration of the carbon—carbon double bond then proceeds normally. The chloro and methoxy groups are not affected by 9-BBN, whereas, the ester and nitrile groups are slightly (1.5—4.0%) reduced by the reagent at 25°C. Even this small amount of reduction can be circumvented or minimized by carrying out the hydroboration at 0°C. Although this procedure requires somewhat longer reaction times, the products are cleaner and the yields are higher.

Introduction

Exploration of the hydroboration reaction has made available a number of partially alkylated borane derivatives [1—3]. Among them, 9-borabicyclo[3.3.1]-nonane (9-BBN), a bicyclic dialkylborane, exhibits certain remarkable physical and chemical characteristics quite distinct from those of borane and other mono- and di-alkylboranes. It is a white, crystalline solid, m.p. 154—155°C, exceptionally stable thermally, relatively insensitive to air, and soluble in a variety of organic solvents. Its solution can be prepared and stored under inert atmosphere for an indefinite period of time. It hydroborates acyclic olefins with remarkable regio-

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* Dedicated to Professor Herbert C. Brown on the occasion of his 66th birthday.

selectivity, far greater than those observed with borane and many other dialkylboranes [4—7].

$$H_2\underset{\uparrow}{C}{=}\underset{\uparrow}{C}HCH_2CH_2CH_2CH_3$$

BH_3	94	6	
Sia_2BH	99	1	(Sia = siamyl)
9-BBN	99.9	0.1	

Diborane hydroborates carbon—carbon multiple bonds faster than it reduces a number of functional groups [8—16]. Although the competitive reduction of functional groups and the formation of minor hydroboration products could be minimized by using disiamylborane instead of diborane, the instability of disiamylborane [17] represents a serious limiting factor in its general application. It appeared that the use of 9-BBN for such hydroborations might circumvent the difficulties encountered in utilizing disiamylborane. 9-BBN reduces many functional groups relatively slowly [18], but still is a potential reagent for the hydroboration of carbon—carbon double bonds. Accordingly, as a part of the systematic exploration of the hydroboration reaction, a study of the hydroboration of representative 3-butenyl and related derivatives with 9-BBN was undertaken in order to establish whether the predicted predominant formation of the terminal-borane derivatives would actually occur in the presence of these functional groups.

Results and discussion

The hydroboration rate and products study

The following representative 3-butenyl derivatives were selected for study: 3-buten-1-ol, 4-methoxy-1-butene, 4-acetoxy-1-butene, 3-butenyl chloride, ethyl 3-butenoate, and 3-butenonitrile. A simple hydroboration utilized 1.00 "hydride"/mol of olefin. However, competitive reduction of the functional group may utilize some of the hydride and decrease the yield of the desired hydroboration product. Accordingly, a 1/1 ratio of hydride to olefin was used in all the experiments, except in the case of 3-buten-1-ol. In this case, the reaction of 9-BBN with the hydroxyl group is rapid. Consequently, the amount of hydride was increased to two hydrides per olefin to compensate for "hydride" utilized for hydrogen evolution in the initial stage. The reaction mixtures were maintained at 25°C. At appropriate intervals of time, 5 ml aliquots were removed and analyzed. From the amount of hydrogen evolved in the analysis, it was possible to determine residual hydride. When all of the active hydride had been consumed, the organoborane was oxidized by adding sodium hydroxide, followed by hydrogen peroxide. In the case of the ester and nitrile derivatives, oxidation was carried out by the simultaneous, dropwise addition of a 3 *M* solution of sodium acetate and hydrogen peroxide at 0°C, in order to avoid possible hydrolysis of these groups under more alkaline conditions. The results are summarized in Table 1.

Competitive hydroboration and reduction. Directive effects

In order to explore how serious might be the competitive reaction of 9-BBN

TABLE 1

RATE AND OXIDATION PRODUCTS FOR THE REACTION OF 9-BBN IN THF WITH VARIOUS 3-BUTENYL DERIVATIVES

Exp.	Reactants (mmol)	Reaction time (h)	mmol H^- utilized/ mmol olefin	Oxidation products (yield (%))
1	9-BBN (20)	0.5	1.55	1,4-Butadediol (89.4)
		1	1.75	
	3-Buten-1-ol (10)	2	1.89	1,3-Butanediol (1.8)
		4	1.95	
		6	1.99	
2	9-BBN (10)	0.5	0.90	4-Methoxy-1-butanol (99)
	4-Methoxy-1-butene (10)	1	0.97	4-Methoxy-2-butanol (0.2)
		2	1.00	
3	9-BBN (10)	0.5	0.89	4-Chloro-1-butanol (97)
	3-Butenyl chloride (10)	1.5	0.97	4-Chloro-2-butanol (1.3)
		2	1.00	
4	9-BBN (10)	0.5	0.87	Ethyl-4-hydroxybutanoate (82)
	Ethyl 3-butenoate (10)	1	0.94	1,4-Butanediol (4)
		2	1.00	Ethyl-3-hydroxybutanoate (1)
				Ethyl 3-butanoate (14)
5	9-BBN (20)	0.5	0.86	4-Acetoxy-1-butanol (86)
	4-Acetoxy-1-butene (20)	1	0.90	4-Acetoxy-2-butanol (1.5)
		2	0.96	1,4-Butanediol (3)
		3	1.00	4-Acetoxy-1-butene (6)
6	9-BBN (20)	0.5	0.82	4-Hydroxybutyronitrile (83)
	3-Butenonitrile (20)	1	0.88	3-Hydroxybutyronitrile (1.7)
		2	0.97	4-Aminobutanol (1.4)
		3	0.99	3-Butenonitrile (12)

with functional groups in the course of the hydroboration of a terminal double bond, a number of competitive reactions were examined. Equimolar mixtures of 1-hexene and n-butyl derivatives containing representative functional groups were treated with one equivalent of 9-BBN at 25°C and the reaction allowed to proceed to completion. Oxidation of the reaction product, as described above, yielded 1-hexanol. The yield of reduction product established the extent of the competitive side reaction of 9-BBN with the functional group. The results are summarized in Table 2. They reveal that only three to four percent reduction of the functional group competes with the hydroboration of the 1-hexene.

Similarly, attack of the functional groups examined in the 3-butenyl derivatives is only minor, so that excellent yields of the 9-BBN derivatives or the corresponding alcohols, after oxidation, are realized. Moreover, the directive effect of the 9-BBN reagent is so powerful, that the influence of the substituent in altering its preference for the terminal double bond is not significant. A comparison of the directive influence in the hydroboration of these 3-butenyl derivatives with diborane, disiamylborane [8], and 9-BBN, all in THF, is summarized in Table 3. It is evident from the data that the hydroboration of these 3-butenyl derivatives with 9-BBN at 25°C is as regioselective as, or even better than, that achieved with disiamylborane at 0°C.

TABLE 2

COMPETITION REACTIONS OF 1-HEXENE AND n-BUTYL DERIVATIVES TOWARD 9-BBN AT 25°C

Exp.	Reactants (mmol)	Reaction time (h)	H_2 evolved	Oxidation products (yield (%))
1	9-BBN (20) 1-Hexene (10) 1-Butanol (10)	2	1.0	1-Hexanol (96) 1-Butanol (99)
2	9-BBN (10) 1-Hexene (10) 1-Butanol (10)	2	0.85	1-Hexanol (14) 1-Hexene (80) 1-Butanol (98)
3	9-BBN (10) 1-Hexene (10) n-Butyl methyl ether (10)	2		1-Hexanol (93) 1-Hexene (1) n-Butyl methyl ether (89)
4	9-BBN (10) 1-Hexene (10) n-Butyl chloride (10)	2		1-Hexanol (95) 1-Hexene (2) n-Butyl chloride (93)
5	9-BBN (10) 1-Hexene (10) Ethyl butyrate (10)	2		1-Hexanol (82) 1-Hexene (14) 1-Butanol (4) Ethyl butyrate (90)
6	9-BBN (10) 1-Hexene (10) Butyl acetate (10)	2		1-Hexanol (87) 1-Hexene (10.5) Butyl acetate (94) 1-Butanol (3.6)
7	9-BBN (10) 1-Hexene (10) Butyronitrile (10)	2		1-Hexanol (83) 1-Hexene (13) Butyronitrile (93)

Hydroboration with 9-BBN at 0°C

The only drawback of using 9-BBN is the relatively small amount of reduction (1.5—4%) of ester and nitrile groups accompanying the hydroboration of these 3-butenyl derivatives. Fortunately, the reduction of such groups at 0°C is much slower, whereas, the hydroboration of terminal olefins, such as 1-hexene, proceeds at a reasonable rate under these conditions [19]. Consequently, the small amount of reduction products in the ester and nitrile functional deriva-

TABLE 3

DIRECTIVE EFFECTS IN THE HYDROBORATION OF 3-BUTENYL DERIVATIVES [a]

	Normalized primary vs. secondary isomer ratio		
	Diborane at 0°C	Disiamylborane at 0°C	9-BBN at 25°C
3-Buten-1-ol	86/14	98/2	98/2
4-Methoxy-1-butene	89/11	98/2	99.8/0.2
3-Butenyl chloride	82/18	99/1	98.7/1.3
Ethyl 3-butanoate	83/17	97.8/2.2	98.9/1.1
4-Acetoxy-1-butene	84/16	98.6/1.4	98.4/1.6
3-Butenonitrile	—	—	98/2

[a] Values for diborane and disiamylborane [8] are included for comparison.

TABLE 4

HYDROBORATION WITH 9-BBN AT 0°C

Reactants (mmol)	Reaction time (h)	mmol H^- utilized/ mmol olefin	Oxidation products (yield (%))
9-BBN (20)	24	0.91	Ethyl 4-hydroxybutanoate (90)
Ethyl 3-butenoate (20)	48	0.98	1,4-Butanediol (trace) Ethyl-3-hydroxybutanoate (trace) Ethyl 3-butenoate (8)
9-BBN (20)	24	0.87	4-Hydroxybutyronitrile (87)
3-Butenonitrile (20)	48	0.97	3-Hydroxybutyronitrile (not detected) 4-Aminobutanol (trace) 3-Butenonitrile (8.5)

tives could be circumvented or minimized by carrying out the hydroboration at 0°C for longer periods of time. This procedure provides even cleaner products. The results are summarized in Table 4.

Experimental

Materials

The n-alkanes (Phillips), employed as internal GLPC standards, were used as received. Tetrahydrofuran was freshly distilled from a small amount of lithium aluminum hydride [3]. 9-BBN was either synthesized from borane/tetrahydrofuran and 1,5-cyclooctadiene [3,6,20] or purchased from Aldrich * and recrystallized once from tetrahydrofuran before use. The physical constants and sources of the 3-butenyl derivatives are listed in Table 5. The compounds used were examined by GLPC and judged to be at least 98% pure.

Methods

A stock solution of 9-BBN in tetrahydrofuran was prepared and standardized by hydrolyzing 5-ml aliquot with 1/1 mixture of THF/MeOH at 40°C and measuring the hydrogen evolved. Hydrolysis is complete in 15—20 minutes. The same procedure was used for the analysis of residual active hydride in the reaction mixture. All glassware was dried at 140°C for at least 4 h, assembled hot, and allowed to cool under a purge of nitrogen, All reactions were carried out under a static pressure of nitrogen. The transfers of liquids were done with oven-dried, nitrogen-purged hypodermic syringes fitted with stainless steel needles **. All reactions were stirred magnetically using oven-dried, Teflon-coated stirring bars.

Procedure for competition reactions

The reaction of 9-BBN with 1-hexene and butyl acetate is representative. A

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* 9-BBN is now available commercially from the Aldrich Chemical Co., Milwaukee, WI.

** For a detailed review of techniques for the handling of air-sensitive substances see ref. 21.

TABLE 5

PHYSICAL CONSTANTS OF THE 3-BUTENYL DERIVATIVES

	Observed constant		Literature values		
	B.p. (°C/mmHg)	n_D^{20}	B.p. (°C/mmHg)	n_D (t, °C)	Ref.
3-Buten-1-ol [a]		1.4223	113.5(760)	1.4224	23
4-Methoxy-1-butene		1.3971	68—69	1.398(20)	24
4-Acetoxy-1-butene [b]	121—122/750	1.4118	122—125	1.4130(18)	25
3-Butenyl chloride [a]		1.4245	75(773)	1.4233(20)	23
Ethyl 3-butenoate	116—118/755	1.4100	119	1.4105(20)	23
3-Butenonitrile [c]	118/741	1.4070	119	1.4060(20)	23

[a] Chemical Samples Co. [b] Synthesized from 3-buten-1-ol and acetyl chloride in the presence of pyridine. [c] Eastman Kodak Co.

dry, nitrogen-flushed 100-ml flask equipped with a rubber syringe cap, a magnetic stirring bar, and a reflux condenser, was connected to a gas buret through a dry ice trap. The flask was immersed in a water bath (25 ± 0.5°C) and 19.6 ml (10 mmol, 0.51 M) solution of 9-BBN in THF was introduced into the flask, followed by 1.00 ml (5.6 mmol) of n-nonane to serve as the internal standard. Finally, 1.25 ml (0.84 g, 10 mmol) of 1-hexene and 1.32 ml (1.16 g, 10 mmol) of butyl acetate was injected simultaneously into the flask. No hydrogen evolution was observed. At the end of 2 h, the reaction mixture was cooled to 0°C, oxidized by simultaneous and dropwise addition of 3.3 ml of 3 M sodium acetate and 3.7 ml (10% excess) of 30% hydrogen peroxide. The flask was brought to room temperature and allowed to stir overnight. Anhydrous potassium carbonate was added to separate the water. The oxidation mixture was then analyzed by 14-ft column packed with 5% Carbowax 20M on Chromosorb W using a Varian (Series 1400) gas chromatograph.

Hydroboration of 3-buten-1-ol at 25°C

To 40.0 ml (20 mmol, 0.5 M) of a solution of 9-BBN in THF was added 1.00 ml (3.42 mmol) of n-hexadecane as the internal standard. Then, 1.72 ml (1.44 g, 10 mmol) of 3-buten-1-ol was added, the hydrogen evolved was collected and measured. At the end of 6 h, hydrolysis of an aliquot indicated that all of the hydride had been consumed, The mixture was cooled to 0°C and oxidized by 3 M NaOH and 30% H_2O_2 followed by stirring at room temperature overnight. Excess potassium carbonate was added to facilitate recovery of the diols [22]. The THF layer was separated and the aqueous layer was extracted with THF (3 × 10 ml). The combined extracts were dried over anhydrous magnesium sulfate, followed by crushed 3 Å molecular sieves. An aliquot of the dried extract, 0.2 ml, was treated with 0.3 ml of *N,O*-bis(trimethylsilyl)trifluoroacetamide with 1% trimethylchlorosilane (Pierce). This was heated for 3 h at 50°C. The resulting bis-TMS derivatives of the diols were analyzed by 12-ft column of 5% SE-30 on Chromosorb W.

Hydroboration of 3-butenyl chloride at 25°C

3-Butenyl chloride (10 mmol) was added to 10 mmol of 0.5 M solution of 9-BBN in THF. The reaction mixture was oxidized by 3 M NaOAc and 30%

H_2O_2 at 0°C and then stirred at room temperature overnight. After saturation with K_2CO_3, the THF layer was analyzed for alcohols by 6-ft column of 10% Carbowax 1540 on Fluoropak.

Hydroboration of other 3-butenyl derivatives at 25°C

Essentially the same procedures were followed for 4-methoxy-1-butene, 4-acetoxy-1-butene, ethyl 3-butenoate, and 3-butenonitrile. In the case of 4-acetoxy-1-butene and ethyl 3-butenoate, the diol by-products could be analyzed on the same columns. However, in the case of 3-butenonitrile, the reduction product, 4-aminobutanol, was analyzed on a 6-ft column of 28% Pennwalt 223 and 4% KOH on Gas-Chrom R.

Hydroboration of ethyl 3-butenoate at 0°C

Twenty mmol of a 0.5 *M* solution of 9-BBN/THF in a 100-ml flask was put in a 0°C constant temperature bath. The cloudy solution of 9-BBN was stirred vigorously and 20 mmol of ethyl 3-butenoate was added dropwise. At the end of 48 h, the reaction mixture was oxidized by 3 *M* NaOAc and 30% H_2O_2 at 0°C and then stirred at room temperature overnight. Alcohols were analyzed (GLC) by Carbowax 1540 column, diols were converted to bis-TMS derivatives and analyzed by SE-30 column.

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