A new facile approach to highly selective hydroboration of alkenes with sodium malonyloxyborohydride

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Received (in Montpellier, France) 4th January 2001, Accepted 21st March 2001
First published as an Advance Article on the web 14th May 2001

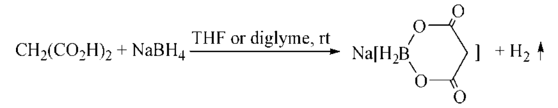
The preparation and properties of sodium malonyloxyborohydride (SMB) are described. As a white solid, SMB is very sensitive to moisture in air. It is also highly sensitive to the structure of alkenes. Thus SMB, prepared *in situ* from the reaction of malonic acid with equimolar $NaBH_4$ in dry THF, hydroborates alkenes showing that terminal aliphatic alkenes undergo facile hydroboration with 98% of the boron moiety placed on the terminal position and 2% at the 2 position. On the other hand, trisubstituted alkenes and cyclohexene show poor reactivity in the hydroboration as compared with terminal alkenes. These characteristics indicate that SMB is a highly regioselective monofunctional hydroborating reagent for terminal alkenes.

Introduction

Hydroborations based on borane have become a highly valuable tool and have extensive applications in organic synthesis.[1] To date, borane–tetrahydrofuran and borane–dimethyl sulfide (BMS) have been the two most widely used hydroborating reagents, however the development of new economical, safe, easily used and highly selective hydroborating reagents is still an important topic in hydroboration research.[2] Exotic borane hydroborating reagents are not readily available. Sodium acetoxyborohydride (SAB, $NaBH_3OAc$),[3] prepared *in situ* from acetic acid and sodium borohydride, could provide an alternative for the hydroboration of alkenes as perhaps one of the most convenient and efficient reagents.[4] More systematic studies indicated that the reaction of alkenes with SAB proceeds smoothly to dialkylboron species at 50 °C in THF; even in the presence of an excess of alkenes the reaction does not proceed further. However, it is difficult to halt the reaction at the monoalkylboron species stage; even in the case of a 1 : 1 molar ratio at room temperature, the reaction is relatively slow and gives an equivalent mixture of mono- and di-alkylboron species.[5] On the other hand, the preparation of sodium malonyloxyborohydride (SMB) as a weaker reducing agent was reported.[6] Monoalkylboron species have great synthetic potential in carbon–carbon bond forming reactions to prevent the loss of “R” groups.[7] We investigated the hydroboration behavior of alkenes by using SMB as a monofunctional hydroborating agent. In this paper, we report the preparation and properties of SMB and its selective hydroboration of alkenes in a one pot reaction.

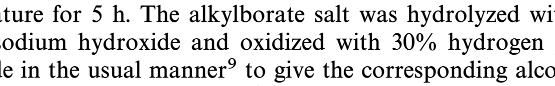
Results and discussion

The hydroborating reagent SMB was prepared from the interaction of sodium borohydride with equimolar malonic acid in THF or diglyme (2,5,8-trioxanonane) at room temperature in quantitative yield [eqn. (1)]. It is a white solid which does not melt and decomposes at over 350 °C. It is insoluble in THF, diglyme, chloroform and other non-protonic solvents and highly sensitive to the moisture in air, decomposing immediately to release hydrogen. It burns in air with a green–yellow flame which indicates it is an organoboron compound. The infrared spectrum of SMB did not show characteristic absorption peaks at 2222, 2291 and 2383 cm^{-1} due to $NaBH_4$,[8] whereas a clear absorption at 2470 cm^{-1}, perhaps due to the characteristic stretching vibration of the B–H bond, appeared. This absorption, however, was quite weak because the B–H bond in SMB is very sensitive to hydrolysis by traces of moisture in air. On the other hand, the absence of absorption at 1740 cm^{-1} due to the carbonyl group of malonic acid and a very strong absorption at 1688 cm^{-1} resulting from the C=O stretching vibration of SMB was observed.



(1)

The hydroboration of alkenes with SMB prepared *in situ* has been studied in THF at various temperatures. We used 1-heptene, 1-octene and 2-methyl-2-butene and cyclohexene as representative terminal and internal alkenes respectively. For example, the hydroboration of a terminal alkene with a 10% excess of SMB, prepared *in situ* from the reaction of $NaBH_4$ with equimolar malonic acid in THF at room temperature for 1 h, proceeds in THF using an oil bath which was first heated gradually to 60 °C and then was maintained at the same temperature for 5 h. The alkylborate salt was hydrolyzed with 3 M sodium hydroxide and oxidized with 30% hydrogen peroxide in the usual manner[9] to give the corresponding alcohol, which was characterized by ^1H NMR, IR and GC, as shown in eqn. (2); the results are summarized in Table 1.



(2)

The data in Table 1 reveal that the hydroboration of terminal alkenes with SMB prepared *in situ* is slow at room temperature (25 °C). Fortunately at a moderate temperature (60 °C) the hydroboration becomes sufficiently rapid to be practical as a synthetic procedure. It is noteworthy that the hydroboration of terminal alkenes with diborane or SAB proceeds in a regioselective manner to place 94 or 95% of the boron atoms at the terminal position respectively.[5,10] SMB,

DOI: 10.1039/b100228g

Table 1 The hydroboration of alkenes with SMB

Alkene	T/°C	t/h	Regioselectivity of oxidation products[a]		Yield[b] (%)
			1 position	2 position	
1-Octene	25	36	97.5	2.5	88
1-Heptene	60[c]	5	98	2	79.5[d]
2-Methyl-2-butene	25	16	—	—	30.3
Cyclohexene	Reflux	16	—	—	10
1-Heptene + cyclohexene[e]	60[c]	5	97	3	68.5[d]

[a] Determined by GC analysis using an E-30 column; 1 and 2 indicate the positions of carbon atoms of corresponding terminal alkenes. [b] The overall yield of the mixture of alcohols determined by GC using an E-30 column. [c] The temperature of the oil bath. [d] The isolated yield of the mixture of alcohols by distillation. [e] Using an equimolar mixture of 1-heptene and cyclohexene as starting materials for the hydroboration. The reaction mixture was oxidized with alkaline hydrogen peroxide to give the products 1- and 2-heptanol; cyclohexanol was undetected by GC analysis.

however, is more regioselective than diborane or SAB in the hydroboration of terminal alkenes. For example, under optimum conditions, hydroboration in THF using a 10% excess of SMB and the reaction flask immersed in an oil bath at 60 °C for 5 h, terminal alkenes such as 1-heptene undergo hydroboration to place 98% of boron on the terminal position with 2% at the 2 position. On the other hand, trisubstituted and cyclic internal alkenes such as 2-methyl-2-butene and cyclohexene are hydroborated considerably more slowly than terminal alkenes by SMB, which is probably due to steric hindrance involving the approach of the bulky SMB to the olefinic center.

Consequently, the higher reactivity of the reagent SMB toward terminal as compared with internal alkenes including trisubstituted and cyclic olefins makes possible the selective hydroboration of terminal alkenes in the presence of internal alkenes. For example, the competitive hydroboration of 1-heptene and cyclohexene with SMB was carried out using a THF solution of 12.6 mmol of malonic acid added to a reaction flask containing 12.6 mmol each of 1-heptene, cyclohexene and NaBH$_4$ in THF in an oil bath at 60 °C for 5 h, followed by oxidation with alkaline hydrogen peroxide and work-up following the general procedure. The products were purified by distillation and 1-heptanol as major product was obtained in 68.5% yield with 97% isomeric purity by GC analysis, and cyclohexanol was undetected. It is clear that selective hydroboration of terminal alkene in a mixture of terminal alkene and cyclohexene or of a terminal double bond in a structure containing both terminal and cyclic double bonds could be achieved.

In order to study the monohydroborating behavior of SMB, we also examined the hydroboration of 1-heptene with SMB in the molar ratio 2 : 1 in THF at 60 °C, followed by dichlorocarbene insertion using 50% NaOH–CHCl$_3$ under phase transfer conditions and oxidation with alkaline hydrogen peroxide. After the reaction mixture had been worked up as described in the published procedure;[9] the 1-heptanol was isolated by distillation in 75.2% yield with 95.5% isomeric purity by GC analysis and no insertion product, 8-pentadecanone, was obtained. In our previous papers[9] and other groups' work[5,11] it was shown that the insertion of dichlorocarbene into C–B bonds of diorganyl borinates, followed by reaction with alkaline hydrogen peroxide, gave the corresponding ketones. The insertion of dichlorocarbene into the C–B bond of the alkylboronate did not occur. If SMB is a difunctional hydroborating reagent, the insertion of dichlorocarbene into the dialkylborinate, the intermediate of SMB reacting with two mol of 1-heptene, should give 8-pentadecanone. We now can conclude that SMB is a highly regioselective monofunctional hydroborating reagent for terminal alkenes to give monoalkylboron species in high yield even using terminal alkenes and SMB in a 2 : 1 molar ratio.

Experimental

Materials and instrumentation

All alkenes were obtained from Aldrich and reagent grade THF and diglyme were distilled from lithium aluminium hydride and stored under nitrogen. Reagent grade malonic acid and NaBH$_4$ were used without further purification.

All glassware was dried at 140 °C for 10 h prior to use. All reactions were carried out under a static pressure of nitrogen. IR spectra were determined by a Nicolet-170SX FT IR spectrometer, ^{1}H NMR spectra on a Jeol FX-90Q spectrometer. The oxidation products were analyzed by GC using a 102G gas chromatograph. Melting points were determined with an X4 melting point apparatus and are uncorrected.

Preparation of SMB

A solution of malonic acid (1.04 g, 10 mmol) in THF (15 ml) was added dropwise to a suspension of NaBH$_4$ (0.38 g, 10 mmol) in THF (20 ml) with vigorous stirring at room temperature; the hydrogen evolved was measured with a gas buret. After stirring for one hour, the reaction mixture was stirred at 60 °C until no hydrogen was released (about 3 h and 440 mL hydrogen were collected) to give a white precipitate which can be used directly for the hydroboration. A small amount of the precipitate thus obtained was filtered off under vacuum and washed with diglyme, then dried under vacuum to give a sample of SMB for identification. IR (cm^{-1}): 2470, 1688, 1591, 1360, 1077, 1009, 855, 696.

General procedure for the hydroboration of alkenes with SMB

The following procedure for the hydroboration of 1-heptene with SMB is representative. To a suspension containing NaBH$_4$ (1.25 g, 33 mmol) and 1-heptene (2.95 g, 30 mmol) in THF (30 mL), a solution of malonic acid (3.43 g, 33 mmol) in THF (20 mL) was added dropwise over 45 min with efficient stirring at room temperature. After completion of the addition, the reaction mixture was stirred at the same temperature for 1 h. The reaction flask was immersed in an oil bath and heated gradually to 60 °C within 1 h, then maintained at 60 °C for 5 h with vigorous stirring. The reaction mixture was cooled to room temperature and then treated carefully with 20 mL 3 M sodium hydroxide and 3.5 mL 30% hydrogen peroxide. The contents were stirred first for 30 min at room temperature, then for 2 h at 40–50 °C. After cooling to room temperature, the reaction mixture was acidified with 3 M hydrochloric acid. The organic layer was separated and the aqueous phase extracted with diethyl ether (3 × 20 mL). The combined organic phase was washed successively with saturated brine and water, dried over anhydrous sodium sulfate and analyzed by GC for the amounts of isomeric alcohol, 98% 1-heptanol and 2% 2-hepanol. The products, in this case 2.77

g (79.5%), was obtained by distillation, bp 173–176 °C. IR: 3347, 2957, 2926, 2856, 1415, 1395, 1057, 720 cm^{-1}. ^{1}H NMR ($CDCl_3$; TMS, δ 0): δ 3.50–3.68 (t, 2H, CH_2O), 1.70–2.10 (s, 1H, OH), 1.10–1.70 (m, 10H, $5CH_2$), 0.70–1.05 (t, 3H, CH_3).

Acknowledgements

This work was supported by the National Natural Science Foundation of China.

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