be advantageous. Thus, although a standard technique for removal of the benzyloxycarbonyl group involves treatment with hydrogen bromide in acetic acid,[11] the homobenzyloxycarbonyl function is stable in this reagent over a period of 24 h at room temperature. Hydrogen chloride in ether readily cleaves the *t*-BOC group of entry 11 (Table I)[9] or trifluoroacetic acid the *tert*-butyl ester function of the protected pentapeptide of entry 12 without affecting the β-phenylethyl ester or hZ functions, respectively. The stability of the hZ group toward acids is further demonstrated by the conversion of protected amino acids to the corresponding acyl chlorides which can be used as coupling agents (Table I, entries 4 and 5).

In cases where the catalytic deblocking of hZ functions proceeded slowly, reaction could be speeded up by increasing the ratio of catalyst to substrate, sonication,[12] and/or heating to 50–65 °C. When incorporated in ester form the β-phenylethyl residue is cleaved less readily than the corresponding urethane structure. Evidence for the relative stability of β-phenylethyl glycinate toward catalytic hydrogenolysis has been cited previously.[13] Steric or other factors may influence the deblocking process. Thus, in the case of the methyl ester related to the dipeptide derivative of entry 4 (Table I), catalytic transfer hydrogenolysis removed the hZ group within 20 h at room temperature whereas the *tert*-butyl ester survived reaction under the same conditions.

In view of the ready availability[14] and shelf stability of β-phenylethyl chloroformate, the homobenzyloxycarbonyl amino-protecting group promises to be of significant potential applicability in organic synthesis. Synthesis of hZ derivatives of amino acids follows standard procedures. The derivative of glycine has been reported in another connection.[15]

Preparation of Catalyst. To 10 mL of ice-cold methanol was added 100 mg of 5 or 10% Pd–C catalyst (Pfaltz and Bauer or Fluka). The mixture was stirred magnetically and treated immediately with 100 mg of palladium acetate and 300 mg of ammonium formate. After about 1 min a flocky suspension of the catalyst was formed as the color of the palladium salt disappeared. The substrate to be deblocked (100–500 mg)[16] was added and the mixture stirred at room temperature until the starting material was consumed (TLC, HPLC). Filtration to remove the catalyst was followed by evaporation of ammonia, methanol, and volatile NH_4OCHO at atmospheric or reduced pressure. The residue was purified in an appropriate manner. For examples see the table.

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(10) (a) Noda, K.; Terada, S.; Izumiya, N. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 1883. (b) Yamashiro, D.; Li, C. H. *J. Am. Chem. Soc.* **1973**, *95*, 1310. (c) Blaha, K.; Rudinger, J. *Collect. Czech. Chem. Commun.* **1965**, *30*, 585. For studies on the relative stability of β-phenylethyl esters toward acidic conditions, see: Tronow, B. W.; Ssibgatullin, N. C. *Chem. Ber.* **1929**, *62*, 2850.

(11) Ben-Ishai, D.; Berger, A. *J. Org. Chem.* **1952**, *17*, 1564.

(12) Ultrasound has previously been used to enhance the rate of catalytic hydrogenation processes. For examples and a general discussion, see: (a) Boudjouk, P. *Nachr. Chem. Tech. Lab.* **1983**, *31*, 798. (b) Boudjouk, P.; Han, B.-H. *J. Catal.* **1983**, *79*, 489. (c) Han, B.-H.; Boudjouk, P. *Organometallics* **1983**, *2*, 769.

(13) Taylor-Papadimitriou, J.; Yovanidis, C.; Paganou, A.; Zervas, L. *J. Chem. Soc. C* **1967**, 1830. See, however, entries 3 and 6 of the table.

(14) Najer, H.; Chabrier, P.; Giudicelli, R. *Bull. Soc. Chim. Fr.* **1955**, 1189.

(15) Barltrop, J. A.; Schofield, P. *J. Chem. Soc.* **1965**, 4758.

(16) In order to maintain a reasonable rate of hydrogenolysis for reactions run at room temperature, a greater weight of active palladium is generally required over that needed for comparable benzylic systems. For deblockings run at or somewhat below the reflux temperature of methanol, or under sonication, less catalyst may be used. Under reflux in methanol, ammonium formate collects in the condenser and should be pushed back into the reaction mixture occasionally. For some substrates optimal results require freshly precipitated palladium whereas in other cases an additional quantity of the commercial palladium–carbon catalyst is sufficient. More active as well as more selective catalysts are being sought.

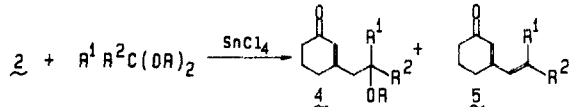
Reactions of 3-[(Trimethylsilyl)methyl]cyclo-2-hexenone with Carbonyl Compounds. Regio- and Chemoselective Condensations

Summary: Under the influence of $SnCl_4$ or trimethylsilyl iodide the title compound reacts with acetals or aldehydes at the γ-position to give the corresponding condensation products, whereas fluoride or base-mediated reactions take place at the α-position to afford α-substituted products selectively.

Sir: Structures of cyclohexenones bearing unsaturated side chains at their 3-position are common carbon frameworks in a wide range of natural products such as vitamin A, retinal, and so on. It appears that such skeletons could be constructed from the corresponding enol silyl ether such as **1**. Enol silyl ethers of unsaturated carbonyl compounds have been used in a wide range of synthetic organic chemistry and a variety of procedures have been developed for the regioselective synthesis of such substrates,[1,2a] but we still could not find any reliable method for the preparation of compounds similar to **1**.[2]

Judging from the mode of reactivities of α-silyl ketones,[3] the keto isomer **2** is expected to behave in a similar manner with **1** in Lewis acid mediated reactions with carbonyl compounds or their acetals. In this paper, we describe a preparative method for keto isomer **2** and its synthetic use for carbon-chain homologation. The silyl ketone **2** can be prepared as follows. Treatment of cyclohexenone with [(trimethylsilyl)methyl]magnesium chloride in the presence of a catalytic amount of CuBr–SMe_2 and chlorotrimethylsilane (1.1 equiv)[4] led to the direct formation of the corresponding enol silyl ether **3** of 3-[(trimethylsilyl)methyl]cyclohexanone. The resulting **3** was converted to the desired **2** by the reaction with $^1/_4$ equiv of palladium acetate and allyl carbonate[5] in good overall yield (Scheme I).

Under the influence of $SnCl_4$, the silyl ketone **2** reacts with various acetals (eq 1). Interestingly, the reaction



(1)

(1) (a) Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths; London, 1981; pp 198–287. (b) Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: Berlin, 1983; pp 206–227. (c) Brownbridge, P. *Synthesis* **1983**, 1.

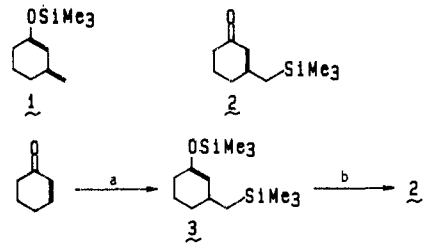
(2) Two procedures were recently published for such purpose: (a) Krafft, M. E.; Holton, R. A. *J. Am. Chem. Soc.* **1984**, *106*, 7619. (b) Kawanishi, M.; Itoh, Y.; Hieda, T.; Kozima, S.; Hitomi, T.; Kobayashi, K. *Chem. Lett.* **1985**, 647.

(3) Inoue, T.; Sato, T.; Kuwajima, I. *J. Org. Chem.* **1984**, *49*, 4671.

(4) Chlorotrimethylsilane has been found to accelerate the conjugate addition of Grignard reagents to afford the corresponding enol silyl ether directly. Horiguchi, Y.; Matsuzawa, S.; Nakamura, E.; Kuwajima, I., submitted for publication.

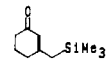
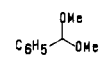
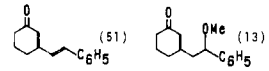
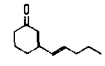
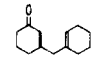
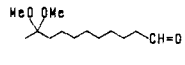
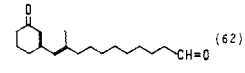
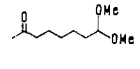
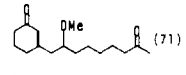
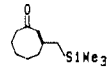
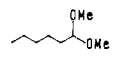
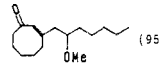
0022-3263/86/1951-1932$01.50/0

Scheme I[a]



[a] (a) Me_3SiCH_2MgCl, Me_3SiCl, catalytic CuBr–SMe_2, THF, −78 °C, 2 h; (b) $Pd(OAc)_2$, $(CH_2{=}CHCH_2O)_2C{=}O$, CH_3CN.

Table I. $SnCl_4$-Mediated Reactions with Acetals[a]

run	enone	acetal	product[b] (yield, %[c])
1			 (51) (13)
2			 (68)
3			 (81)
4			 (62)
5			 (71)
6			 (95)

[a] The reaction was performed as described in the text. [b] All products were fully characterized by spectral and analytical data. [c] Isolated yield.

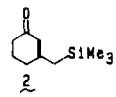
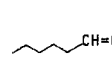
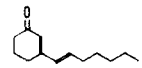
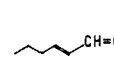
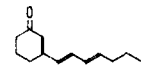
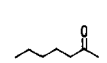
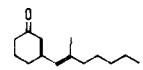
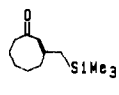
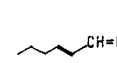
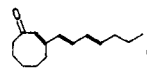
takes place exclusively on the carbon attached to silicon, which is in good contrast to the well established behavior of allylsilanes.[6] Products were usually obtained as a mixture of 3-(2-alkoxyalkyl)cyclohexenone **4** and 3-vinylcyclohexenone **5**, but the former was completely converted to the latter on exposure of the reaction mixture to *p*-TsOH after quenching with water.

Titanium tetrachloride or boron trifluoride etherate are not effective as the catalyst in the above reaction. α,β-Unsaturated acetals fail to react with **2** under the present reaction conditions and give back the parent aldehydes and the desilylated enone. As expected from the above result, aldehydes also do not react with **2** under similar reaction conditions. This characteristic feature has allowed chemoselective carbon-chain homologation on acetal moieties of substrates bearing additional aldehyde or ketone functions as shown in runs 4 and 5 (Table I).

The following procedures are representative. To a dichloromethane (1.5 mL) solution of 3-[(trimethylsilyl)methyl]cyclohexenone (36 mg, 0.2 mmol) and butyraldehyde dimethylacetal (24 mg, 0.2 mmol) was added stannic chloride (104 mg, 0.4 mmol), and the mixture was stirred for 4 h at 0 °C. The reaction mixture was quenched with water and the aqueous layer was extracted with dichloromethane. After organic layers were treated with a small amount of *p*-toluenesulfonic acid for 6 h at room temperature, the mixture was washed with saturated aqueous $NaHCO_3$ and the organic layer was dried. Removal of the solvent followed by purification with column chromatography afforded 3-(1-pentenyl)-2-cyclohexen-1-one (23 mg, 68%).

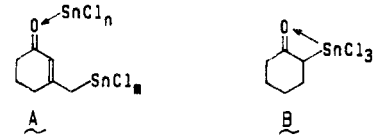
(5) Tsuji, J.; Minami, I.; Shimizu, I. *Tetrahedron Lett.* **1983**, *24*, 5635.
(6) Reference 1a, pp 97–124, and ref 1b, pp 173–205. Chan, T. H.; Fleming, I. *Synthesis* **1979**, 761. Sakurai, H. *Pure Appl. Chem.* **1982**, *54*, 1.

Table II. Me_3SiI-Mediated Reactions with Carbonyl Compounds[a]

run	enone	carbonyl compound	product[b] (yield, %[c])
7			 (63[d])
8			 (81, 68[e])
9			 (23[d])
10			 (81)

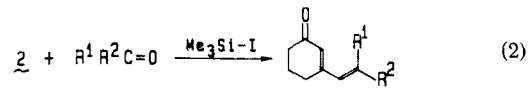
[a] The reaction was performed in the presence of Me_3SiI (1 equiv) in CH_2Cl_2 at 0 °C for 4 h. [b] All products were fully characterized by spectral and analytical data. [c] Isolated yield. [d] Me_3SiI (2 equiv) was used. [e] Me_3SiI (0.1 equiv) was used.

^1H NMR studies on the reaction intermediate have suggested some interesting results. On treatment of **2** with an equimolr amount of $SnCl_4$ in CD_2Cl_2 at −60 °C, a lower field shift of vinyl proton from 5.60 to 6.31 ppm was observed, but a methylene group attached to the silyl group still appeared at 1.89 ppm without any formation of chlorotrimethylsilane in a detectable amount. On warming up to −40 °C, two new absorptions appeared at 6.57 (br s, 1 H) and 3.40 ppm (br s, 2 H), respectively, together with the signal of the silyl chloride. These spectroscopic features apparently support the formation of 3-(stannylmethyl)cyclohexenone (A) coordinated to another Sn(IV) moiety. We previously reported that α-(trichlorostannyl)cyclohexanone (B) adds to aldehydes to afford the



adducts in good yield under similar reaction conditions.[7] A great difference of reactivities between A and B is quite interesting.

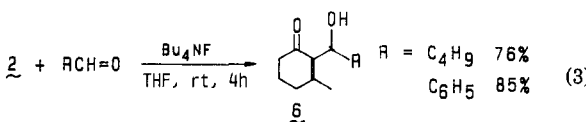
Although $SnCl_4$ did not induce the addition reaction of **2** to aldehydes or ketones (eq 2), use of trimethylsilyl iodide[8] effected the condensation with the former. In the



(2)

presence of the silyl iodide, α,β-unsaturated aldehydes also react to yield the corresponding cyclohexenones bearing dienyl substituents in good yield (runs 8 and 10, Table II).

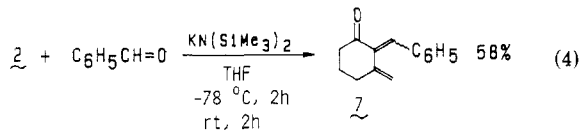
In contrast to the regiochemical outcome as described above, fluoride-catalyzed reaction[3,9] of **2** with aldehydes occurs exclusively at the α-carbon to afford the regioisomeric product **6** (eq 3). Similarly, by using potassium



(3)

(7) Nakamura, E.; Kuwajima, *Chem. Lett.* **1983**, *59*, *Tetrahedron Lett.* **1983**, *24*, 3347.
(8) Sakurai, H.; Sasaki, K.; Hosomi, A. *Tetrahedron Lett.* **1981**, *22*, 745.
(9) Noyori, R.; Yokoyama, K.; Sakata, J.; Kuwajima, I.; Nakamura, E.; Shimizu, M. *J. Am. Chem. Soc.* **1977**, *99*, 1265. Nakamura, E.; Shimizu, M.; Kuwajima, I.; Sakata, J.; Yokoyama, K.; Noyori, R. *J. Org. Chem.* **1983**, *48*, 933.

hexamethyldisilazide,[10] **2** reacts with an aldehyde at the α-position to afford the cyclohexanone **7** having two exo double bonds in good yield (eq 4). The reaction possibly



(4)

proceeds through a C=C bond isomerization of an initially formed aldolate followed by a Peterson-like elimination. Furthermore, these results apparently indicate that the fluoride-catalyzed reaction takes place in a charge-controlled manner like an enolate anion, which may support the generation of *naked enolate anion* from **2**[9,11] in this reaction.

As shown in the tables, the present procedure appears to be applicable to other cyclic enones as well.

Thus, with γ-silyl α,β-unsaturated enones, an appropriate choice of a catalyst or electrophile has allowed several types of synthetically useful regio- and chemoselective condensation reactions with carbonyl compounds or their derivatives.

Acknowledgment. This work is partially supported by a Grant from the Ministry of Education, Science, and Culture of the Japanese Government. We are also indebted to Toray Silicone Co. for the generous supply of chlorotrimethylsilane.

(10) In place of this base, use of lithium diisopropylamide gave much less satisfactory results.
(11) Noyori, R.; Nishida, I.; Sakata, J. *J. Am. Chem. Soc.* **1983**, *105*, 1598.

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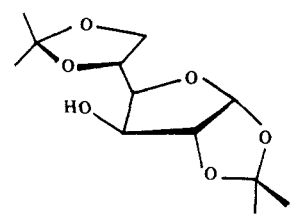
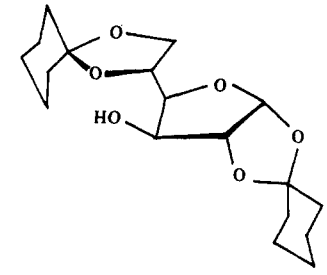
Potassium 9-*O*-(1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranosyl)-9-boratabicyclo[3.3.1]nonane. A New, Effective Chiral Borohydride Reagent[1]

Summary: A convenient and simple synthesis of a new chiral borohydride reagent, potassium 9-*O*-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranosyl)-9-boratabicyclo-[3.3.1]nonane, consisting of a single reducing species, is described. The new reagent is generally effective for the asymmetric reduction of alkyl phenyl ketones and hindered aliphatic ketones.

Sir: Among a wide variety of naturally occurring chiral synthons, monosaccharide derivative has been one of the most attractive chiral auxiliaries for the modification of sodium borohydride[2] or lithium aluminum hydride.[3] A successful use of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (DIPGF)[2d] or 1,2:5,6-di-*O*-dicyclohexylidene-α-D-glucofuranose (DCHGF)[2e] for modification of sodium borohydride in the presence of carboxylic acids was reported recently to achieve up to 83% enantiomeric excess (ee) in the reduction of propiophenone. Unfortunately, the authors report that their reagent appears to be a complex mixture and they could not assign a specific structure to the reagent which achieved this promising asymmetric reduction. It appeared desirable to undertake the synthesis of a well-defined borohydride derivative which would permit a systematic study of the effect of the structure of the chiral auxiliary on the asymmetric yield achieved.



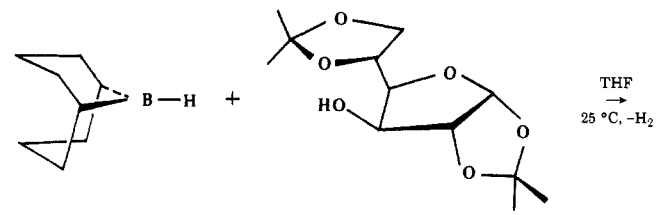
DIPGF



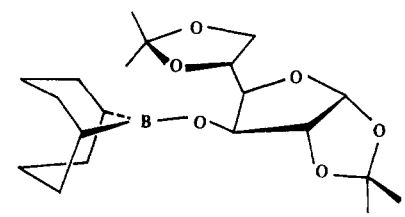
DCHGF

The recent development of a general synthesis of potassium 9-alkoxy-9-boratabicyclo[3.3.1]nonanes[4] by the reaction of potassium hydride with the corresponding borinic esters offered promise for the synthesis of such chirally modified borohydride reagents. Moreover, this class of borohydrides possesses only one hydride per reagent molecule, which should be advantageous for understanding the asymmetric results achieved. With more than one hydride per borohydride unit, it is possible for the stereochemical results to vary with the different hydrides undergoing reaction.

Accordingly, 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (DIPGF, **2**) was selected for study as the chiral auxiliary. The 9-BBN derivative, 9-*O*-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranosyl)-9-borabicyclo[3.3.1]nonane (9-*O*-DIPGF-9-BBN, **3**) was easily prepared by treating this compound with 9-borabicyclo[3.3.1]nonane (9-BBN, **1**) (eq 1). The borinic ester was converted into



9-BBN, 1 DIPGF, 2



(1)

9-*O*-DIPGF-9-BBN, 3

(1) This work was presented at the 190th National Meeting of the American Chemical Society, Chicago, September 1985.

(2) (a) Hirao, A.; Mochizuki, H.; Nakahama, S.; Yamazaki, N. *J. Org. Chem.* **1979**, *44*, 1720. (b) Hirao, A.; Nakahama, S.; Mochizuki, D.; Itsuno, S.; Ohowa, M.; Yamazaki, N. *J. Chem. Soc., Chem. Commun.* **1979**, 807. (c) Hirao, A.; Nakahama, S.; Mochizuki, H.; Itsuno, S.; Yamazaki, N. *J. Org. Chem.* **1980**, *45*, 4231. (d) Hirao, A.; Itsuno, S.; Owa, M.; Nagami, S.; Mochizuki, H.; Zoorov, H. H. A.; Nakahama, S.; Yamazaki, N. *J. Chem. Soc., Perkin Trans. 1* **1981**, 900. (e) Morrison, J. D.; Grandbois, E. R.; Howard, S. I. *J. Org. Chem.* **1980**, *45*, 4229. (f) Review: Midland, M. M. *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2, Chapter 2, and references cited therein.
(3) Review: (a) Haubenstock, H. *Top. Stereochem.* **1983**, *14*, 231 and references cited therein. (b) Grandbois, E. R.; Howard, S. I.; Morrison, J. D. *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2, Chapter 3, and references cited therein.
(4) (a) Brown, H. C.; Cha, J. S.; Nazer, B. *J. Org. Chem.* **1984**, *49*, 2073. (b) Brown, H. C.; Cha, J. S.; Nazer, B.; Brown, C. A. *Ibid.* **1985**, *50*, 549.

0022-3263/86/1951-1934$01.50/0