TRIZMA base, 1 mM Na, EDTA, pH 8.0). Gilvocarcin V was dissolved in DMSO to a concentration of 1 mg/mL. In a darkened room, 1 mL of the gilvocarcin V solution was added to each sample of DNA solution. After vigorous shaking, the samples were placed in the center chamber of a double-jacketed photolysis apparatus. The outer chamber contained a precooled 40% solution of cobalt nitrate in water to act as a filter and as a temperature buffer. The samples were photolyzed for 30 min in a Rayonet photochemical reactor equipped with 16 General Electric F8T5-BLB 75-W lamps. After photolysis, 3 mL of saturated NaCl solution was added, and the mixture was poured into 70 mL of cold ethanol. The resulting precipitate was wound onto a glass rod and pressed to remove additional ethanol. Control experiments were conducted both with drug while omitting light exposure and with light while omitting drug. The precipitated DNA pellets were white for the control without drug and yellowish off-white for the control excluding light. The experimental pellets were a yellow-orange color. HPLC analysis of the ethanol supernatant revealed that, in comparison to the light excluded control, 75% of the added gilvocarcin V was bound to the DNA precipitate after light exposure and that the unbound gilvocarcin V was unchanged.

DNA adducts were isolated by hydrolyzing the combined DNA pellets from 16 photolysis experiments with 10 mL of 0.1 N HCl at 100 °C for 2 h. This solution was filtered through Waters C-18 Sep-Pak cartridges. The cartridges were rinsed with water and increasing percentages of methanol in water. Adducts containing the gilvocarcin M chromophore eluted with 60-70% methanol in water. In practice, after eluting with 40% methanol, the cartridges were washed with 100% methanol to elute the desired fraction in a small volume which was concentrated under vacuum. HPLC analysis revealed a mixture of four isomers in a ratio of 6:73:11:11. These were fractionated by semipreparative reverse-phase MPLC using an EM Science LoBar C-8 size A column, eluting with 50% methanol-water at 3 mL/min. The major component **8** was separated from the other isomers. The latter two isomers were characterized by NMR analysis of the mixture as the furanose isomers. The minor component was not obtained in sufficient quantity for further characterization.

Gilvocarcin V-DNA Photoadduct. β-Fucopyranose isomer **8**: HPLC (HP-ODS column 3.4 mm × 100 mm, 60% methanol in water, 1 mL/min, 260-nm detection) 1.7 min; ^{1}H NMR (d_4-methanol, 300 MHz) δ 8.61 (s, 1 H), 7.88 (d, 1 H, J = 8.4 Hz), 7.87 (br s, 1 H), 7.40 (br s, 1 H), 6.99 (d, 1 H, J = 8.7 Hz), 5.85 (d, 1 H, J = 9.3 Hz), 4.36 (q, 1 H, J = 6.0 Hz), 4.17 (s, 6 H), 4.14 (m, 1 H), 3.82 (m, 2 H), 3.54 (m, 2 H), 2.75 (m, 1 H), 2.59 (m, 1 H), 1.62 (s, 3 H), 1.23 (d, 3 H, J = 6.3 Hz); ^{1}H NMR (10% d_4-methanol in $CDCl_3$, 400 MHz) δ 8.59 (s, 1 H), 7.89 (br s, 1 H), 7.88 (d, 1 H, J = 8.5 Hz), 7.30 (d, 1 H, J = 1.7 Hz), 7.04 (d, 1 H, J = 8.4 Hz), 5.83 (d, 1 H, J = 9.6 Hz), 4.40 (q, 1 H, J = 6.6 Hz), 4.19 (t, 1 H, J = 10 Hz), 4.19 (s, 3 H), 4.17 (s, 3 H), 4.12 (br s, 2 H), 3.89 (s, 1 H), 3.87 (dd, 1 H, J = 10, 3.5 Hz), 3.81 (t, 1 H, J = 8.0 Hz), 3.51 (dd, 1 H, J = 11.5, 8.0 Hz), 2.78 (ddd, 1 H, J = 11.5, 8.0, 8.0 Hz), 2.61 (ddd, 1 H, J = 11.5, 11.5, 8.0 Hz), 1.68 (s, 3 H), 1.28 (d, 3 H, J = 6.6 Hz); FAB MS (argon bombardment in a matrix of glycerol-thioglycerol) m/z M^+ ($C_{32}H_{32}O_{11}N_2$) 620.09 (54), $[M + Na]^+$ 643.1 (10), 517.05 (26), 487.05 (100).

α-Fucofuranose isomer: HPLC 2.1 min; ^{1}H NMR (d_4-methanol, 300 MHz) δ 8.52 (s, 1 H), 7.85 (d, 1 H, J = 8.1 Hz), 7.84 (br s, 1H), 7.38 (br s, 1 H), 6.95 (d, 1 H, J = 8.4 Hz), 6.07 (d, 1 H, J = 0.9 Hz), 4.15 (s, 6 H), 3.82 (m, 1 H), 2.77 (m, 1 H), 2.59 (m, 1 H), 1.64 (s, 3 H), 1.32 (d, 3 H, J = 6.6 Hz).

β-Fucofuranose (natural) isomer: HPLC 2.6 min; ^{1}H NMR (d_4-methanol, 300 MHz) δ 8.51 (s, 1 H), 8.11 (d, 1 H, J = 8.4 Hz), 7.82 (br s, 1 H), 7.35 (br s, 1 H), 6.96 (d, 1 H, J = 8.7 Hz), 6.34 (d, 1 H, J = 3.9 Hz), 4.16 (s, 6 H), 3.82 (m, 1 H), 2.77 (m, 1 H), 2.59 (m, 1 H), 1.64 (s, 3 H), 1.41 (d, 3 H, J = 6.6 Hz).

Acknowledgment. Helpful discussions with Drs. Y. C. Tse-Dinh, David Eaton, and Pat N. Confalone are greatly appreciated. Thanks are also extended to Drs. Derek Ovenall (NMR), Rod Farlee (NMR), and Joe Lazar (MS) of the analytical division of Du Pont Central Research and to Frank Dobson for technical assistance.

Supplementary Material Available: Figures of the HPLC traces of the DNA hydrolysis reactions and the UV, FAB MS, and NMR spectra of compound **8** (9 pages). Ordering information is given on any current masthead page.

Chiral Synthesis via Organoboranes. 24. *B*-Allylbis(2-isocaranyl)borane as a Superior Reagent for the Asymmetric Allylboration of Aldehydes

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Contribution from the H. C. Brown and R. B. Wetherill Laboratories of Chemistry, Purdue University, West Lafayette, Indiana 47907. *Received July 17, 1989*

Abstract: Hydroboration of (+)-2-carene, readily available via the base-induced isomerization of (+)-3-carene, provides bis(2-isocaranyl)borane, which can be readily transformed into *B*-allylbis(2-isocaranyl)borane (2-^{d}Icr$_2$BAll). This new reagent undergoes asymmetric allylboration with a variety of aldehydes and affords the corresponding homoallylic alcohols in 94-99% ee. The enantioselectivities realized with this reagent are significantly higher than those realized with the previously explored reagents, *B*-allyldiisopinocampheylborane (^{d}Ipc$_2$Ball) and *B*-allylbis(4-isocaranyl)borane (4-^{d}Icr$_2$BAll).

Over the past few years, asymmetric allyl- and crotylboron reagents have proven to be exceptionally valuable in the context of acyclic stereoselection. Driven by the rapidly growing demand for highly enantiomerically pure substances in multistep natural product syntheses,[1] the development of superior allylboron reagents, which can achieve enantio- and diastereoselectivities approaching 100%, has evidently become both desirable and challenging.[2] Consequently, in continuation of our efforts in this

(1) (a) Roush, W. R.; Harris, D. J.; Lesur, B. M. *Tetrahedron Lett.* **1983**, 2227. (b) Moret, E.; Schlosser, M. *Ibid.* **1984**, 4491. (c) Roush, W. R.; Peseckis, S. M.; Walts, A. E. *J. Org. Chem.* **1984**, *49*, 3429. (d) Ditrich, K.; Bube, T.; Stürmer, R.; Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1028. (e) Hoffmann, R. W.; Endesfelder, A. *Liebigs Ann. Chem.* **1986**, 1823, (f) Roush, W. R.; Michaelides, M. R.; Tai, D. F.; Chong, W. K. *J. Am. Chem. Soc.* **1987**, *109*, 7575. (g) Roush, W. R.; Palkowitz, A. D. *Ibid.* 953. (h) Khandekar, G.; Robinson, G. C.; Stacey, A. N.; Steel, P. G.; Thomas, E. J.; Rather, S. *J. Chem. Soc., Chem. Commun.* **1987**, 877. (i) Merrifield, E.; Steel, P. G.; Thomas, E. J. *Ibid.* 1826.

(2) (a) Hoffmann, R. W.; Herold, T. *Chem. Ber.* **1981**, *114*, 375. (b) Brown, H. C.; Jadhav, P. K. *J. Am. Chem. Soc.* **1983**, *105*, 2092. (c) *J. Org. Chem.* **1984**, *49*, 4089. (d) Roush, W. R.; Walts, A. E.; Hoong, L. K. *J. Am. Chem. Soc.* **1985**, *107*, 8786. (e) Brown, H. C.; Bhat, K. S. *Ibid.* **1986**, *108*, 293. (f) Roush, W. R.; Hatterman, R. L. *Ibid.* 294. (g) Brown, H. C.; Bhat, K. S.; Randad, R. S. *J. Org. Chem.* **1987**, *52*, 319. (h) *Ibid.* 3701. (i) Garcia, J.; Kim, B. M.; Masamune, S. *Ibid.* 4831. (j) Brown, H. C.; Jadhav, P. K.; Bhat, K. S. *J. Am. Chem. Soc.* **1988**, *110*, 1535. (k) Roush, W. R.; Banfi, L. *Ibid.* 3979. (l) Roush, W. R.; Ando, K.; Powers, D. B.; Halterman, R. L.; Palkowitz, A. D. *Tetrahedron Lett.* **1988**, 5579. (m) Reetz, M. T.; Zierke, T. *Chem. Ind.* **1988**, 663. (n) Hoffmann, R. W. *Pure Appl. Chem.* **1988**, *60*, 123, and its references. (o) Short, R. P.; Masamune, S. *J. Am. Chem. Soc.* **1989**, *111*, 1892. (p) Corey, E. J.; Yu, C.-M.; Kim, S. S. *J. Am. Chem. Soc.* **1989**, 5495. (q) Brown, H. C.; Racherla, U. S.; Pellechia, P. J. *J. Org. Chem.*, in press.

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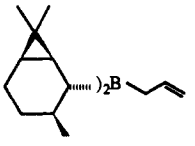
Table I. Comparison of the Asymmetric Allylborations of Representative Aldehydes with Chiral *B*-Allyldialkylboranes **1**–**3** at −78 °C

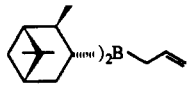
aldehyde	alcohol	reagent (% ee)		
		^{d}Ipc$_2$BAll[a] (**2**)	4-^{d}Icr$_2$BAll (**3**)	2-^{d}Icr$_2$BAll (**1**)
acetaldehyde	4-penten-2-ol	*R*, 92[b] (93)	*R*, 94[b] (99)	*S*, 98[b]
propionaldehyde	5-hexen-3-ol	*R*, (86)	*R*, (91)	*S*, 94[d]
n-butyraldehyde	1-hepten-4-ol	*R*, 86[c] (87)	*R*, 88[c] (89)	*S*, 94[c]
2-methylpropionaldehyde	2-methyl-5-hexen-3-ol	*S*, 88[b] (90)	*S*, 95[b] (97)	*R*, 94[b]
2,2-dimethylpropionaldehyde	2,2-dimethyl-5-hexen-3-ol	*S*, (83)	*S*, (88)	*R*, 99[b]
acrolein	1,5-hexadien-3-ol	*S*, 92[b]	*S*, 93[b] (86)	*R*, 95[b]
benzaldehyde	1-phenyl-3-buten-1-ol	*S*, 94[b] (96)	*S*, 87	*R*, 95[b]

[a] Use of ^{l}Ipc$_2$BAll [derived from (−)-α-pinene] provides the opposite enantiomer. [b] Determined by capillary GC analysis of the corresponding + Mosher ester. [c] Determined by capillary GC analysis of the corresponding menthyl carbonates. See ref 10b. [d] Determined by capillary GC analysis of the corresponding TPC ester. See ref 10c. Values in parentheses are percent enantiomeric excess of the corresponding alcohols based on comparison of optical rotations.

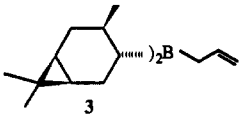
direction, we report a new reagent, *B*-allylbis(2-isocaranyl)borane (**1**), that undergoes reaction with a variety of aldehydes to furnish the corresponding homoallylic alcohols in 94–99% ee. The enantioselectivies realized with this reagent are significantly higher than those realized previously with *B*-allyldiisopinocampheylborane (^{d}Ipc$_2$BAll, **2**) and *B*-allylbis(4-isocaranyl)borane (4-^{d}Icr$_2$BAll, **3**).



1



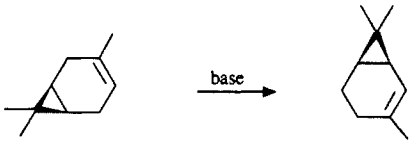
2



3

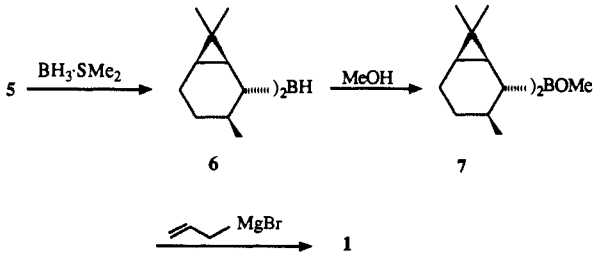
Results and Discussion

(+)-2-Carene (**5**) is readily available via the base-induced isomerization of (+)-3-carene[3,4] (**4**, eq 1).



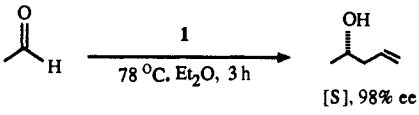
4 **5** (1)

Hydroboration of (+)-2-carene (**5**) with $BH_3{\cdot}SMe_2$ in tetrahydrofuran provides a white crystalline solid of bis(2-isocaranyl)borane (**6**) of essentially 100% optical purity,[5] which can be readily methanolzyed. Treatment of the methoxy derivative (**7**) with allylmagnesium bromide provides *B*-allylbis(2-isocaranyl)borane (2-^{d}Icr$_2$BAll, **1**) in ≥85% overall yield (eq 2).



6 **7** (2)

As this new reagent, 2-^{d}Icr$_2$BAll (**1**), possesses a relatively hindered boron atom that is flanked on both sides by substituents, in contrast to our previous reagents ^{d}Ipc$_2$BAll (**2**) and 4-^{d}Icr$_2$BAll (**3**), we hoped to achieve greater enantioselectivities on allylboration. Indeed, we were gratified to observe that **1** reacts with acetaldehyde at −78 °C to give, after oxidation and workup, (*S*)-(+)-4-penten-2-ol in 98% ee, the highest yet achieved in such asymmetric allylboration (eq 3). Under similar conditions, ^{d}Ipc$_2$BAll (**2**) and 4-^{d}Icr$_2$BAll (**3**) react with acetaldehyde to provide (*R*)-(−)-4-penten-2-ol (the opposite enantiomer) in 92% and 94% ee, respectively.[6]



[S], 98% ee (3)

The remarkable ease of the preparation of *B*-allylbis(2-isocaranyl)borane (**1**), together with its exceptionally enantioselective condensation with acetaldehyde, prompted us to examine the full scope of this reagent against representative aldehydes. In all cases, 2-^{d}Icr$_2$BAll (**1**) achieved higher asymmetric inductions (in the range of 94–99% ee) than either ^{d}Ipc$_2$BAll or 4-^{d}Icr$_2$BAll.

These results are summarized in Table I.

Originally, we relied on a comparison of the optical rotations of the product alcohols with the values that were reported in the literature for presumably 100% enantiomerically pure materials for the determination of asymmetric inductions in allylborations. However, this procedure turned out to be unreliable. Now we establish the optical purities of the product alcohols by the capillary GC analyses of the appropriate diastereomeric derivatives (MTP, MCF, or TPC).[10] This method has proven to be far more reliable and reproducible. For example, the rotation method earlier indicated an optical purity of ≥99% for the product alcohol from acetaldehyde and 4-^{d}Icr$_2$BAll (**3**). However, the capillary GC analysis method now reveals an optical purity of only 94% ee (Table I).

In the case of α-pinene, the + and − forms are readily available, and hence, the synthesis of *R* and *S* enantiomers of the homoallylic alcohols is possible by utilizing either ^{d}Ipc$_2$BAll or ^{l}Ipc$_2$BAll. On the contrary, with 3-carene, only the + isomer is found in nature, and therefore only (+)-2-carene can be obtained via the base-induced isomerization. Fortunately, however, the two reagents, 4-^{d}Icr$_2$BAll (**3**) and 2-^{d}Icr$_2$BAll (**1**), derived from the isomeric terpenes, are complementary to each other and afford opposite enantiomers of products on allylboration. Although these results

(3) Acharya, S. P.; Brown, H. C. *J. Am. Chem. Soc.* **1967**, *89*, 1925. See also: Ohloff, G.; Schulte-Elte, K. H.; Giersch, W. *Helv. Chim. Acta* **1965**, *48*, 1665.

(4) (+)-2-Carene is now available from Aldrich Chemical Co., Milwaukee, WI.

(5) Brown, H. C.; Vara Prasad, J. V. N.; Zaidlewicz, M. *J. Org. Chem.* **1988**, *53*, 2911.

(6) Jadhav, P. K.; Bhat, K. S.; Perumal, P. T.; Brown, H. C. *J. Org. Chem.* **1986**, *51*, 432.

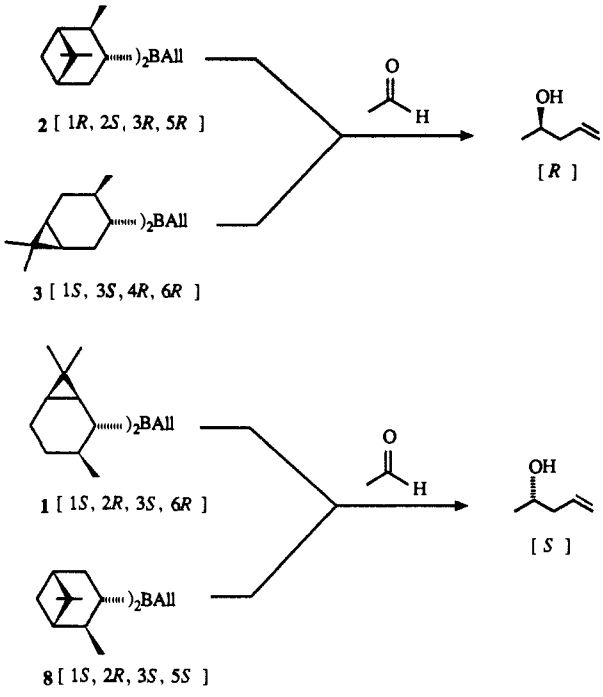
(7) Some of these reagents, such as **9** and **13**, react very slowly at −78 °C. See ref 2q.

(8) The enantioselectivities reported[2o] for reagent **15** are at −100 °C, while those for the rest of the reagents, **1**–**3** and **9**–**14**, are described at −78 °C. It is, therefore, not clear how this reagent actually compares with the others at −78 °C.

(9) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Syntheses via Boranes*; Wiley-Interscience: New York, 1975.

(10) (a) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543. (b) Westley, J. W.; Halpern, B. *Ibid.* **1968**, *33*, 3978. (c) Hoops, E. A.; Peltzer, E. T.; Bada, J. L. *J. Chromatogr. Sci.* **1978**, *16*, 556. See also: Payan, I. L.; Perezrios, R. C.; Fisher, G. H.; Man, E. H. *Anal. Biochem.* **1985**, *149*, 484.

Scheme I



are seemingly inconsistent, it is interesting to note that they are in perfect agreement with the predictions based on the analogous configurational relationships of 4-^{d}Icr$_2$BAll (**3**) to ^{d}Ipc$_2$BAll (**2**) and 2-^{d}Icr$_2$BAll (**1**) to ^{l}Ipc$_2$BAll (**8**; Scheme I).

In the recent past, a number of asymmetric allylboron reagents **9–15** have been reported by Hoffmann,[2a] Roush,[2d,k] Reetz,[2m] Masamune,[2i,o] and Corey,[2p] besides our own reagents, that can undergo highly enantioselective condensations with aldehydes.

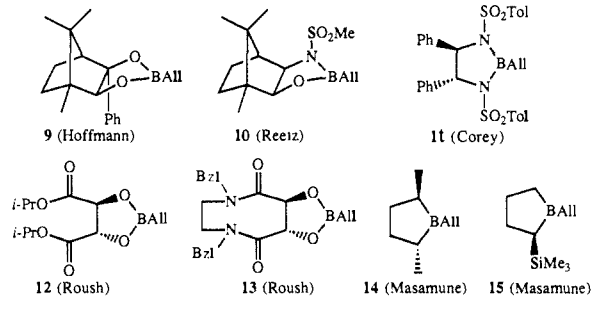


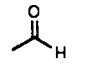
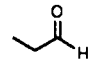
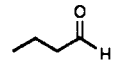
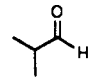
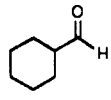
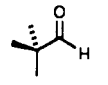
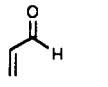
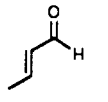
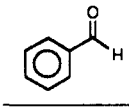
Table II summarizes a comparison of the enantioselectivities achieved by *B*-allylbis(2-isocaranyl)borane (**1**) against those realized from the other reagents. Evidently **1** is among the best of reagents presently known that can consistently achieve exceptionally high (94–99%) enantioselectivities in allylboration.

Further, it must be pointed out that while reagents **10**, **11**, **13**, and **15** also afford comparatively high enantioselectivities,[7,8] each of these reagents require the preparation of the chiral auxiliaries in several steps and some even require resolution.[2o,p] In contrast, *B*-allylbis(2-isocaranyl)borane (**1**) can be prepared highly efficiently from the commercially available (+)-2-carene. In the past, the ease of preparation of Ipc$_2$BAll (**2**) and its crotyl analogues resulted in their rapid adoption for asymmetric allyl- and crotylboration.[1] Preliminary experiments are very promising that the crotyl analogues, 2-^{d}Icr$_2$BCrt, give equally high enantioselectivities. Consequently, it is probable that 2-^{d}Icr$_2$BAll and the crotyl analogues will find similar applications where improved enantioselectivities are desired.

Experimental Section

The reaction flasks and other equipment were stored in an oven at 150 °C overnight and assembled in a stream of dry nitrogen gas. Special techniques used in handling air-sensitive materials are described elsewhere.[9] Borane–methyl sulfide (BMS) purchased from Aldrich Chemical Co. was estimated prior to use.[9] All solvents were distilled and stored under nitrogen. The capillary GC analyses for the determination of optical purities of the derivatized product homoallylic alcohols were performed on a Hewlett-Packard 5890 gas chromatograph.

Table II. Comparison of the Asymmetric Allylborations of Representative Aldehydes with Reagents **9–15** at −78 °C

	reagent (% ee)							
aldehyde	**1**	**9**	**10**	**11**	**12**	**13**	**14**	**15**[a]
	98	86	96					
	94	79	92				93	
	94	72	96	(95)[b]	(79)[c]	(94)[d]	93	96
	94	70	94				85	96
				97	87	97	88	96
	99	45	88		82	96	86	
	95							
				(98)[e]				97
	95		88	95	71	85		

[a] At −100 °C (3 h). See ref 8. [b] Value for 1-hexanal. [c] Value for 1-decanal. [d] Value for (TBDPS)OCH$_2$CH$_2$CHO. [e] Value for cinnamaldehyde.

Preparation of *B*-Allylbis(2-isocaranyl)borane (1). To borane–methyl sulfide (10.3 mL, 9.8 M, 100 mmol) in tetrahydrofuran (200 mL), cooled to −10 °C, was added (+)-2-carene (30 g, 220 mmol), α^{23}_D +92° (neat), over a period of 10 min while the reaction mixture was stirred. Following completion of the addition, stirring was discontinued and the flask containing the reaction mixture was stored at 0 °C for 24 h. White needles of 2-^{d}Icr$_2$BH (**6**) separated out. The supernatant liquid was then decanted by a double-ended needle, and the crystals were washed with anhydrous ether (3 × 50 mL) chilled to 0 °C. The solid was dried under vacuum at room temperature to obtain 2-^{d}Icr$_2$BH (**6**; 24.3 g, 85%) of essentially 100% optical purity.[5] Next, 2-^{d}Icr$_2$BH (14.3 g, 50 mmol) was suspended in tetrahydrofuran (20 mL) and treated with methanol (4 mL) at 0 °C in a dropwise fashion over a period of 20 min while the reaction mixture was vigorously stirred. After the evolution of hydrogen had ceased (0 °C, 6 h), a clear solution formed, indicating completion of the methanolysis. The solvent was stripped off under vacuum (14 mm, 1 h; 1 mm, 2 h) to obtain *B*-methoxybis(2-isocaranyl)borane (**7**, 15.8 g, 100%). Methoxy derivative **7** was dissolved in anhydrous ether (50 mL) and cooled to −78 °C. To this solution was added allylmagnesium bromide in ether (48 mL, 1.0 M, 48 mmol) in a dropwise manner. The reaction mixture was stirred for 15 min at −78 °C and then warmed to room temperature (1 h) to obtain an essentially quantitative yield of *B*-allylbis(2-isocaranyl)borane (**1**). The formation of **1** was confirmed by ^{11}B NMR (δ +80 ppm).

Reaction of 1 with Acetaldehyde. The reaction mixture containing reagent **1** (without removing the precipitated magnesium salts) was cooled to −78 °C, and acetaldehyde in slight excess (2.8 mL, 50 mmol) was added dropwise with stirring. The stirring was continued for 3 h at −78 °C, and the reaction mixture was treated with 3 N NaOH (20 mL) and 30% H_2O_2 (40 mL). The reaction mixture was next refluxed for 3 h to ensure the completion of oxidation. The organic layer was separated, washed with brine, dried over anhydrous magnesium sulfate, and concentrated. The residue was finally fractionally distilled (bp 94 °C (90 mm)) to obtain (*S*)-(+)-4-penten-2-ol, yield 3.2 g (74%). GC analysis of its Mosher ester[10a] on a capillary methyl silicone column (50 m × 0.25

cm) established the compound to be 98% ee.

Allylboration of the Higher Aldehydes. The procedure, essentially as described above, was applied to the other representative aldehydes (Table I). All of the products are known, and the individual isolation procedures have been fully described in our previous publications.[6]

Acknowledgment. The financial support of the National Institutes of Health (Grant GM 10937) and Dow Chemical Co. is gratefully acknowledged. We also thank Dr. Suk Dev (Malti Chem Labs, Baroda, India) for providing us with a generous gift of (+)-2-carene.[4]

Registry No. 1, 124821-92-7; **5**, 4497-92-1; **6**, 114533-27-6; **7**, 124821-93-8; acetaldehyde, 75-07-0; propionaldehyde, 123-38-6; *n*-butyraldehyde, 123-72-8; 2-methylpropionaldehyde, 78-84-2; 2,2-dimethylpropionaldehyde, 630-19-3; acrolein, 107-02-8; benzaldehyde, 100-52-7; (*S*)-4-penten-2-ol, 555563-79-6; (*S*)-5-hexen-3-ol, 62959-96-0; (*S*)-1-hepten-4-ol, 85520-72-5; (*R*)-2-methyl-5-hexen-3-ol, 88691-75-2; (*R*)-2,2-dimethyl-5-hexen-3-ol, 88691-76-3; (*R*)-1,5-hexadien-3-ol, 119596-43-9; (*R*)-1-phenyl-3-buten-1-ol, 85551-57-1.

Synthetic Utility and Mechanistic Studies of the Aliphatic Reverse Brook Rearrangement

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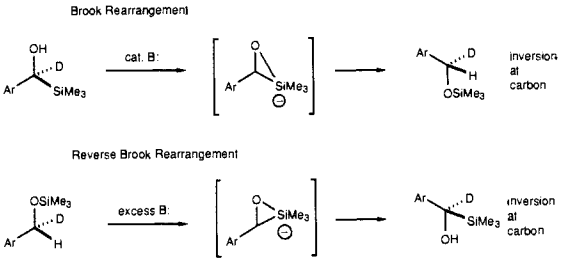
Abstract: The aliphatic reverse Brook rearrangement has been examined in detail. Transmetalation of [α-[(trialkylsilyl)oxy]alkyl]trialkylstannanes occurs via a complex equilibrium favoring the most stable carbanion. The aliphatic reverse Brook rearrangement is driven forward by the rapid migration of silicon from O to C in a transient α-silyloxy carbanion due to the formation of the more stable lithium alkoxide. Cross-over experiments have shown that the rearrangement is an intramolecular process while incorporation of a radical trap revealed that the rearrangement does not involve radical intermediates. Studies of configurationally fixed stannanes derived from 4-*tert*-butylcyclohexanone concluded that the rearrangement occurs with retention of configuration. Preparation and reverse Brook rearrangement of optically active (*S*)-[α-[(trimethylsilyl)oxy]-hexyl]tributylstannane (98% ee) provided 1-(trimethylsilyl)hexanol in 97% ee. The synthetic utility of this method for the preparation of a variety of (α-hydroxyalkyl)trialkylsilanes from aldehydes has also been demonstrated.

The Brook rearrangement[1] is a stereospecific intramolecular migration of silicon from carbon to oxygen which occurs for (α-hydroxybenzyl)trialkylsilanes in the presence of a catalytic amount of base. The rearrangement is driven forward by the increased thermodynamic stability of the silyl ether product relative to the alcohol starting material due to the formation of a Si–O bond in place of a Si–C bond. Brook and co-workers[1b] established that the rearrangement proceeds with inversion of configuration at carbon and retention of configuration at silicon. The reverse or anti-Brook rearrangement,[2] the migration of silicon from oxygen to carbon, has been accomplished by deprotonation of α-(trialkylsilyl)oxy benzyl ethers. Wright and West[2a] studied the reverse rearrangement of (aryloxy)silyl ethers in detail, observing that the reaction is similar to the forward Brook rearrangement in that the migration of silicon is intramolecular and stereospecific. Deprotonation of a homochiral benzyloxy silyl ether and subsequent rearrangement resulted in the homochiral (α-hydroxybenzyl)silane of inverted configuration at carbon. The reverse Brook rearrangement requires excess base and is driven forward due to the stability of the alkoxide anion product relative to the carbanion starting material. These studies are summarized in Scheme I.

More recent studies by Ireland et al.[3a] and Danheiser and co-workers[3b] have illustrated that the reverse Brook rearrangement also occurs for allylic silyl ethers upon deprotonation with strong base. Cohen and Matz[4] had also observed a reverse Brook rearrangement of an allyl anion generated by the reductive lithiation of an allylic phenylthio ether. In all of the above examples, a single regioisomer of the α-hydroxyallyl silane product is produced. We reasoned that the same process should occur for aliphatic systems, in analogy with the Wittig rearrangement,[5] if the requisite carbanion could be easily generated. By incorporating a transmetalation (Sn to Li) as part of the process, we were able to successfully carry out the aliphatic reverse Brook rearrangement via the intermediacy of an [α-[(trialkylsilyl)oxy]alkyl]trialkylstannane.[6] In this paper, we present a full account of this method

Scheme I. Summary of the Brook and Reverse Brook Rearrangement on Aryl-Substituted Species



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