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ESSENTIALLY HOMOCHIRAL 1-SILYL ALCOHOLS FROM THE REDUCTION OF ALIPHATIC ACYLSILANES WITH CHLORODIISOPINOCAMPHEYLBORANE

John A. Soderquist,* Charles L. Anderson,[1] Edgar I. Miranda,[2] Isaac Rivera[2]
Department of Chemistry, University of Puerto Rico
Rio Piedras, Puerto Rico 00931

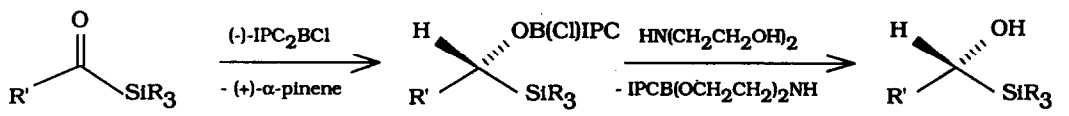
and

George W. Kabalka
Department of Chemistry, University of Tennessee
Knoxville, Tennessee 37996

Abstract: *The enantioselective reduction of aliphatic acylsilanes with (-)-B-chlorodiisopinocampheylborane ((-)-IPC$_2$BCl) provides (R)-1-silylated alcohols (3) in high enantiomeric excess (96-98%) in good isolated yields (59-67%).*

The chemistry of organoboranes spans the entire spectrum of both functional group conversions and carbon-carbon bond-forming reactions.[3] Among the most important of these transformations has been in the selective reductions of carbonyl compounds.[4] While both borohydride and borane reagents can be employed, Midland's discovery[5] that the β-hydride from a *tertiary* chiral center can be transferred through an electrocyclic process to a prochiral aldehyde or ketone in a very highly enantioselective manner, engendered widespread interest in these reductions. More recently, Brown[6] introduced IPC$_2$BCl which combines a highly asymmetric reaction environment with the high Lewis acidity of chloroboranes to provide 2° alcohols in very high ee from prochiral ketones which contain sterically dissimilar groups.

In connection with the preparation of silyl-substituted organoboranes,[7] we developed efficient borane-based routes to 1-silyl alcohols (**3**), compounds which were obtained with modest optical purities (*i.e.* 24-40% ee) from the hydroboration of the appropriate alkenylsilanes with monoisopinocampheylborane (IPCBH$_2$).[7g] Other routes to **3** which give higher product ee's have since been reported,[8] including the asymmetric reduction of selected aryl substituted acylsilanes[8a] with Itsuno's chiral borane reagent. In this Letter, we report the remarkable selectivity of (-)-IPC$_2$BCl which produces **3** from **1** in nearly homochiral form (*cf.* Table 1).



1 **2** **3**

Table 1. The Asymmetric Reduction of **1** with (-)-IPC_2BCl.

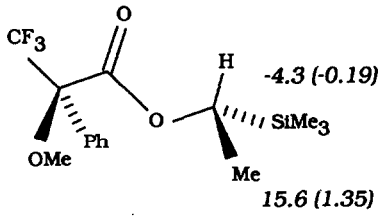
	1		Conditions	Yield of **3**	% ee	$[\alpha]_D^{27}$	bp[a,c]
	R	R'	Temp[a] (Time)[b]	Isolated (GC)[d]			(Torr)
a	Me	Me	-35 (3)	67 (91)	96[e]	+21.57	115-118 (760)
b	Me	Et	-35 (3)	62 (80)	98[f]	+17.16	105 (25)
c	Me	*t*-Pr	25 (120)	60 (81)	98[e]	+14.36	74-76 (0.4)
d	*n*-Bu	Me	25 (4)[g]	59 (93)	96[e]	+11.53	82 (36)
e	*t*-Pr	Me	25 (3)	64 (82)	98[e]	+17.92	75-79 (25)
f	*t*-Bu	Me	N.R.[h]				

[a] °C. [b] h. [c] see ref. 7c,h. [d] The reaction was monitored by GC after the addition of diethanolamine. This process was slow and the reported GC yields were recorded after the following reaction (alcoholysis) times: **3a**: 24 h, **3b**: 5 h, **3c**: 98 h, **3d**: 48 h, **3e**: 4 h. [e] Determined by NMR ((+)-Eu(tfc)$_3$). [f] Determined by NMR ((+)-Eu(hfc)$_3$). [g] At 0°C, **3d** was obtained in 98% ee, but with reduced yield (*i.e.* 40%). [h] No significant reduction was detected after 1 month at 25°C.

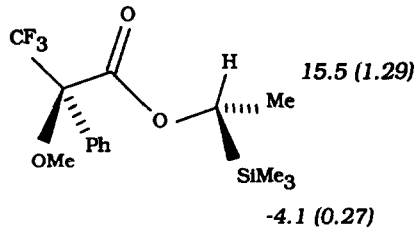
The following procedure for the preparation of **3a** is representative:

To (-)-IPC_2BCl (15.04 g, 46.9 mmol) in THF (10 mL) at -35°C, under a nitrogen atmosphere, was added acetyltrimethylsilane (4.98 g, 42.9 mmol), dropwise. After 3 h, methanolysis of a small aliquot revealed the complete reduction of **1a** (^{11}B NMR δ 29 ppm). The mixture was allowed to reach 25°C, and the THF and α-pinene were removed *in vacuo* (30 Torr (25°C), then 8 h at 0.2 Torr (50 °C)). The residue was dissolved in ether (100 mL) and diethanolamine (14.8 g, 140 mmol) was added. After 24 h, the mixture was filtered and the solid complex was washed with pentane (5 x 15 mL). The combined solutions were were distilled at atmospheric pressure to give 3.37 g of **3a** (67%, 97% GC purity), bp 115-118°C. The spectroscopic properties were identical with those of the racemic material. Treatment of the racemic **3a** with (+)-Eu(tfc)$_3$ revealed that baseline resolution of the ^1H NMR signals for the Me (δ 4.7 and 4.5 ppm). and TMS groups (δ 2.3 and 2.1 ppm). Integration of these signals with the product produced from IPC_2BCl revealed both sets of signals to be in a 98:2 ratio, respectively. In all cases, the major enantiomer was shifted more downfield than the minor enantiomer.

The silyl alcohols, **3**, were prepared in racemic form by our standard borane procedure.[7b,j] In previous studies, we developed the analytical methodology to resolve these enantiomers based upon their behavior toward optically-active shift reagents (*vide ultra*).[7g] From (-)-IPC_2BCl, **3** was obtained as essentially a single enantiomer, having a positive rotation in all cases. Earlier studies[7g] had provided enantiomerically-enriched samples of both (+)-**3e** and (-)-**3e** formed from the hydroboration of isobutenyltrimethylsilane with the (+)-(sesqui)terpene-derived reagents, dilongifolylborane and $IPCBH_2$, respectively. This selectivity correlated well to that of structurally-related trisubstituted alkenes, such as 2-methyl-2-butene. Based upon the enantiomeric preference observed in the reduction of 3-methyl-2-butanone, we expected **1e** to give (+)-**3e** which proved to be the case. With (+) shift reagents, the (+) enantiomer was consistently shifted more downfield than its (-) counterpart. Their Mosher's esters (**4**) were prepared from (R)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid ((+)-MTPA) and, while neither capillary GC nor ^{19}F nor ^{29}Si NMR were generally diagnostic, both ^1H (300 MHz) and ^{13}C



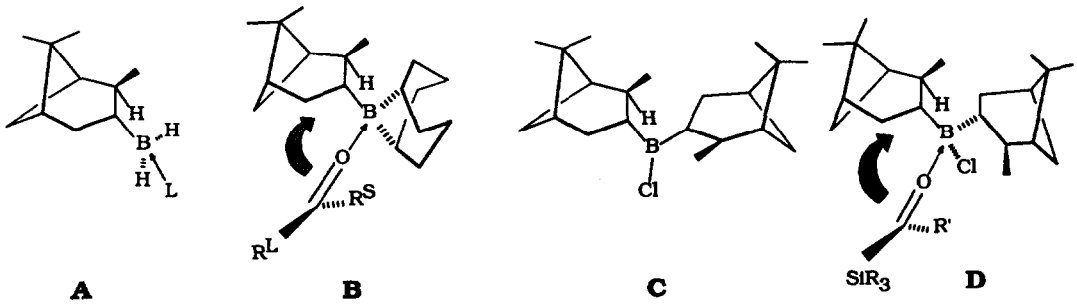
4a (R,R)



4a (R,S)

NMR (75 MHz), proved quite useful, providing resolved signals for the R,R and R,S diastereomeric esters (*vide ultra*). A correlation between the absolute configuration of 2° alcohols and the ^{1}H NMR shifts of the alkyl groups in the alcohol portion of the ester has been derived[9] and, like Linderman,[8b] we found the TMS group to be upfield (*cf.* **4a**: -0.46 ppm) in the R,R diastereomer. The methyl group in **4a** is downfield (+0.06 ppm) in the R,R diastereomer. Taking into account that group priorities are reversed upon switching from *t*-Bu to TMS, this NMR behavior correlates precisely with that of the methyl-*tert*-butylcarbinyl esters of (+)-MTPA.[9] In **4**, we observed that the ^{13}C NMR signal for the TMS group was upfield in the R,R isomer (*e.g.* **4a**: -0.2 ppm).[10] All of the above are wholly consistent with an R configuration at C-1 for the (+) enantiomers.[11]

The selectivity of terpene-derived organoborane reagents has been demonstrated to be remarkably consistent, being governed largely by steric factors. Midland[5] found that the selectivity of 3-pinanyl-9-BBN (Alpine-Borane™) could be best explained by a boat-type transition state, a model also used by Brown[6b] to explain the similar selectivity of IPC_2BCl. The uniform, predictable nature of all of the asymmetric processes involving α-pinene-derived borane reagents leads one to the inescapable conclusion, that they must all be based upon a common, general process. Clues to the nature of this process were supplied by the X-ray structure of the crystalline 2:1 complex of $IPCBH_2$ with *N, N, N', N'*-tetramethylethylenediamine (L).[7h] Nitrogen complexation occurs on the *exo* face of 3-pinanyl ring deflected away from the methyl group at C-2 (*cf.* **A** below). With Reetz's discovery[12] of the *anti* relationship of the phenyl group to the BF_3 in the PhCHO-BF_3 complex, we are led to conclude that the initial complexation of carbonyl compounds with the borane reagents such as Alpine-Borane™ or IPC_2BCl may resemble **B** and



D, respectively. In these structures, the larger group in the aldehyde or ketone (*i.e.* R^L or SiR_3) is *anti* to the boron. The X-ray structure[6b] of IPC_2BCl, represented by **C**, reveals its monomeric nature and C_2 symmetry with each of the large IPC groups in **C** occupying the *exo* position with respect to the other's ring. Compared to **A**, the additional boron substitution must further deflect the entering carbonyl compound toward the reacting IPC group as is depicted in **D**. The formation of **D** from **C** clearly results in considerable B-strain as well as an unavoidable interaction of the ketone with the proximate methyl in the non-reacting IPC group.[13] At the time of complexation, this IPC group is effectively bulkier than the other and is likely to be *anti* to the ketone. With only a minor rotation, the carbonyl carbon is positioned for *beta* hydride transfer. No intermediates are observed prior to the formation of **2** from **C**, suggesting that once **D** forms, the subsequent conversion to product is kinetically rapid.

In summary, this study has provided **3** in nearly homochiral form and advanced a model of the reduction process which explains the selectivities observed with 3-pinanylboranes.

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REFERENCES AND NOTES

1. Graduate student supported by the NIH-MBRS Program (RR08102).

2. Graduate student supported by the NSF EPSCoR Program of Puerto Rico.

3. Pelter, A.; Smith, K.; Brown, H. C. *Borane Reagents*; Academic Press: London, 1988 and references cited therein.

4. Srebnik, M.; Ramachandran, P. V. *Aldrichimica Acta* **1987**, *20*, 9.

5. (a) Midland, M. M.; Greer, S.; Tramontano, A.; Zderic, S. A. *J. Am. Chem. Soc.* **1979**, *101*, 2352. (b) Midland, M. M. *Chem. Rev.* **1989**, *89*, 1553 and references cited therein.

6. (a) Brown, H. C.; Chandrasekharan, J.; Ramachandran, P. V. *J. Org. Chem.* **1985**, *50*, 5446. (b) Brown, H. C.; Chandrasekharan, J.; Ramachandran, P. V. *J. Am. Chem. Soc.* **1988**, *110*, 1539.

7. (a) Hassner, A.; Soderquist, J. A. *J. Organomet. Chem.* **1977**, *131*, C1. (b) Soderquist, J. A.; Hassner, A. *J. Organomet. Chem.* **1978**, *156*, C12. (c) Soderquist, J. A.; Brown, H. C. *J. Org. Chem.* **1980**, *45*, 3571. (d) Soderquist, J. A.; Hassner, A. *J. Org. Chem.* **1983**, *48*, 1801. (e) Soderquist, J. A.; Shiau, F.-Y.; Lemesh, R. A. *J. Org. Chem.* **1984**, *49*, 2565. (f) Soderquist, J. A.; Najafi, M. R. *J. Org. Chem.* **1986**, *51*, 1330. (g) Soderquist, J. A.; Hwang-Lee, S.-J. *Tetrahedron* **1988**, *44*, 4033. (h) Soderquist, J. A.; Hwang-Lee, S.-J.; Barnes, C. L. *Tetrahedron Lett.* **1988**, *29*, 3385. Soderquist, J. A.; Negron, A. *J. Org. Chem.* **1989**, *54*, 2462. (i) Soderquist, J. A.; Colberg, J. C.; Del Valle, L. *J. Am. Chem. Soc.* **1989**, *111*, 4873. (j) Soderquist, J. A.; Rivera, I.; Negron, A. *J. Org. Chem.* **1989**, *54*, 4051. (k) Soderquist, J. A.; Santiago, B. *Tetrahedron Lett.* **1989**, *30*, 5693. (l) Soderquist, J. A.; Colberg, J. C. *SynLett* **1989**, *1*, 25. (m) Soderquist, J. A.; Santiago, B. *Tetrahedron Lett.*, submitted for publication. (n) Soderquist, J. A.; Vaquer, J. *Tetrahedron Lett.*, submitted for publication.

8. (a) Buynak, J. D.; Strickland, J. B.; Hurd, T.; Phan, A. *J. Chem. Soc., Chem. Commun.* **1989**, 89. (b) Linderman, R. J.; Ghannam, A. *J. Am. Chem. Soc.* **1990**, *112*, 2392.

9. Yamaguchi, S. in *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983, pp 125-152 and references therein.

10. This phenomenon is also observed for other TMS derivatives of **3** (Linderman, R. J., private communication).

11. The opposite selectivity (*i.e.* (1S)-**3**) has been found from the reduction of aryl derivatives of related acylsilanes with IPC_2BCl which was prepared from (-)-α-pinene (Buynak, J. D.; Strickland, J. B. *Abstract of Papers*, 199th National ACS Meeting, Boston, Massachusetts, April 22-27, 1990, ORGN 297.

12. (a) Reetz, M. T.; Hullmann, M.; Massa, W.; Berger, S.; Rademacher, P.; Heymanns, P. *J. Am. Chem. Soc.* **1986**, *108*, 2405. (b) See also: Denmark, S. E.; Henke, B. R.; Webber, E. *J. Am. Chem. Soc.* **1987**, *109*, 2512.

13. Compared to **C**, IPC(*t*-Bu)BCl has the reverse selectivity (Brown, H. C., private communication). Replacing a 2° (IPC) group with a 3° (*t*-Bu) group clearly increases the B-strain in the corresponding ketone complex. We propose that all of the above factors are operative except that, in this case, the preferred attack is changed to the methyl side of the IPC ring to minimize this strain (*i.e.* Interactions of CH_3 (C-4) *vs* CHMe (C-2) with *t*-Bu).

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