Supplementary Material Available: Experimental and spectral data (mp, IR, ^{1}H NMR, and MS) for **3**–**6** and (*S*,*S*)-enantiomers of **7** and **8** and spectral data for **15** (R_f, IR, and ^{1}H NMR) and for **1** (mp, R_f, and ^{1}H NMR) (5 pages). Ordering information is given on any current masthead page.

A Practical and Efficient Method for Enantioselective Allylation of Aldehydes

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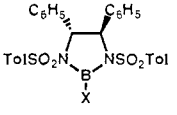
The enantioselective addition of allyl groups to the carbonyl function of aldehydes to form chiral secondary homoallylic alcohols is a highly useful synthetic operation for multistep synthesis since the resulting adducts serve as precursors of β-hydroxy and γ-hydroxy carboxylic acid derivatives.[1] Subsequent to early studies on the use of allylic boranes in this reaction by Hoffmann,[2] many groups have made important contributions to the steady improvement in this methodology.[1,3] Nonetheless, each of the published approaches suffers from major disadvantages, for example, because of destruction of expensive chiral reagents or the reliance on impractical reagents or intermediates. Described herein is a new method which is believed to be superior to earlier procedures, especially for work on larger scale. The process utilizes the readily available and easily recoverable (*R*,*R*)- or (*S*,*S*)-1,2-diamino-1,2-diphenylethane (stien) controller group, which is also the subject of the preceding communication.[4]

Reaction of the bis-*p*-toluenesulfonyl derivative of (*R*,*R*)-stien[4] in dry CH_2Cl_2 with 1 equiv of BBr_3, at 0 °C or below initially and then at 20 °C for 40 min, afforded, after removal of solvent and HBr under reduced pressure, the bromoborane **1** (CAUTION: moisture sensitive). Treatment of a solution of **1** in dry CH_2Cl_2 at 0 °C initially and at 23 °C for 2 h with allyltributyltin resulted in generation of the chiral allylborane **2**. Reaction of **2** in CH_2Cl_2



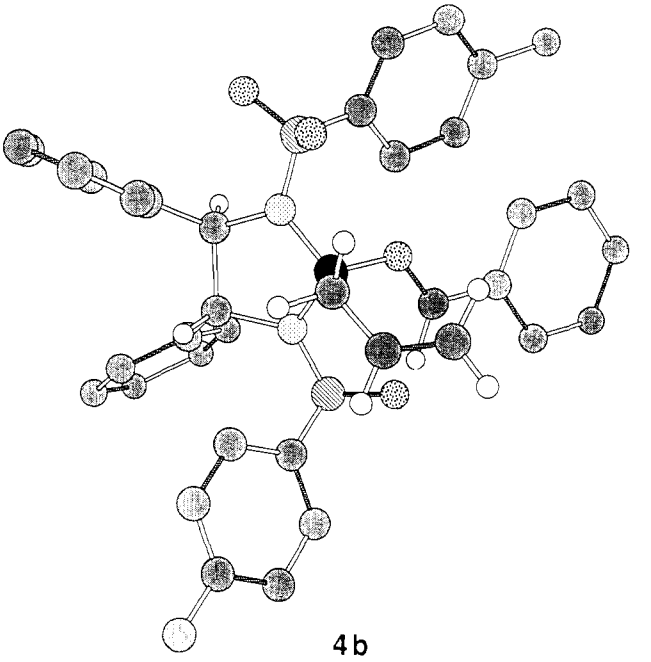
1 X = Br
2 X = $CH_2CH{=}CH_2$

or toluene solution at −78 °C with a variety of aldehydes (0.9 equiv) produced the corresponding homoallylic alcohols **3** in the optical purities indicated in Table I. The product **3** was isolated in >90% yield and ca. 97% purity by addition of aqueous pH 7 buffer, removal of CH_2Cl_2, addition of ether to precipitate the bis-*p*-toluenesulfonamide of (*R*,*R*)-stien, filtration, removal of tin halide (by washing the ethereal filtrate with 50% aqueous potassium fluoride), and removal of solvent. Final purification of **3** can be effected by silica gel chromatography or distillation, depending on scale. In each case enantiomeric excess (ee) values were determined by 500 MHz ^{1}H NMR analysis of the (*R*)-(+)-α-methoxy-α-(trifluoromethyl)phenyl acetate (MTPA) ester,[5] and absolute configuration was established by measurement of optical rotation and comparison with literature data.[6]

Table I. Reaction of Aldehydes with Chiral Allylborane **2**, (*R*,*R*)-Form, at −78 °C To Give Homoallylic Alcohols **3**

R of RCHO	solvent	% ee of **3**	abs config
C_6H_5	CH_2Cl_2	94	*R*
C_6H_5	toluene	95	*R*
(*E*)-$C_6H_5CH{=}CH$	CH_2Cl_2	98	*R*
(*E*)-$C_6H_5CH{=}CH$	toluene	97	*R*
c-C_6H_{11}	CH_2Cl_2	93	*R*
c-C_6H_{11}	toluene	97	*R*
n-C_5H_{11}	CH_2Cl_2	90	*S*
n-C_5H_{11}	toluene	95	*S*

The observed preference for absolute configuration **3** for the homoallylic alcohols from the (*R*,*R*)-allylborane reagent **2** was predicted on the basis of a chair-like transition state with optimum stereoelectronics and minimum steric repulsion between appendages on the five-membered ring, the optimum arrangement being as depicted in line drawing **4a** and three-dimensional representation **4b**.



4b

High and predictable diastereoselectivity was also observed in the allylation of chiral aldehydes by reagent **2**. Thus aldehyde **5** was converted by reaction at −78 °C for 2 h with (*R*,*R*)-**2** in 80% yield principally to **6** (ratios **6**:**7** of 25.3:1 in CH_2Cl_2 and 20.2:1 in toluene), whereas its enantiomer, **8**, was transformed mainly into **9** (ratios **9**:**10** of 39:1 in CH_2Cl_2 and 51.6:1 in toluene).[7]

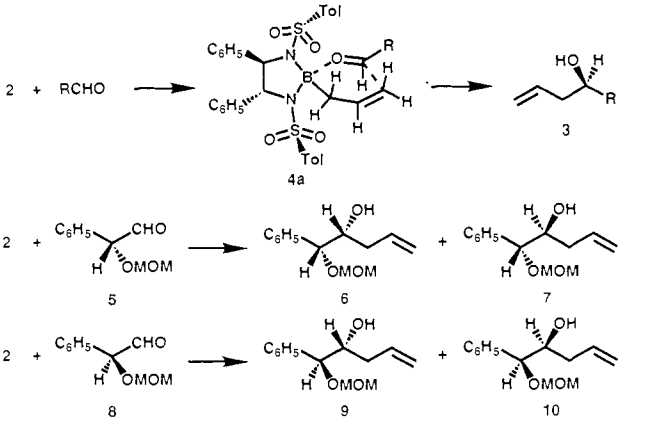


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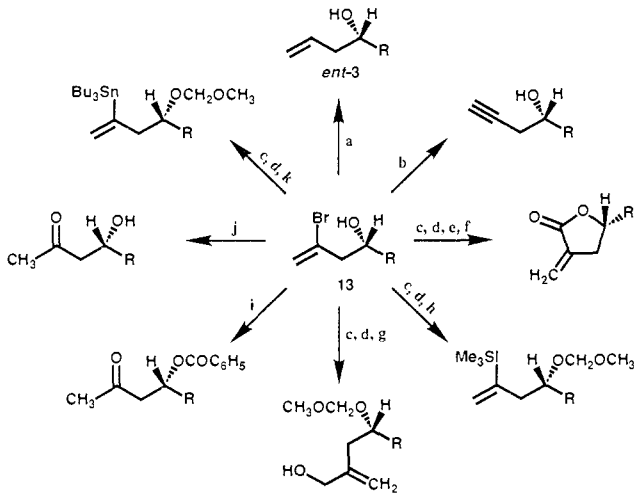
Table II. Reaction of Aldehydes with Chiral 2-Haloallyl Boranes **11** and **12** (*S,S*)-Forms, at −78 °C in CH_2Cl_2 To Give Alcohols **13** and **14**, Respectively

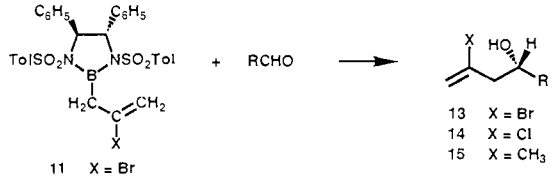
R of RCHO	reagent	% yield of **13** or **14**	% ee of **13** or **14**	abs config
C_6H_5	**11**	73	79	*S*
C_6H_5	**12**	79	84	*S*
(*E*)-C_6H_5CH=CH	**11**	79	87	*S*
(*E*)-C_6H_5CH=CH	**12**	84	92	*S*
c-C_6H_{11}	**11**	75	94	*S*
c-C_6H_{11}	**12**	81	99	*S*
n-C_5H_{11}	**11**	71	94	*R*
n-C_5H_{11}	**12**	77	99	*R*

Scheme I[a]



[a] Transformations of **13**, R = cyclohexyl, reagents and conditions: (a) 3.3 equiv of *t*-BuLi, Et_2O, −78 °C, 2 h; H_2O, 75%; (b) 2.5 equiv of *t*-BuOK, THF, 0 °C, 1 h, 91%; (c) CH_3OCH_2Cl, *i*-Pr_2NEt, CH_2Cl_2, 23 °C, 10 h, 95%; (d) 2.1 equiv of *t*-BuLi, THF, −78 °C, 2 h; (e) CO_2, THF, 0 °C, 1 h, 73%; (f) 4 N HCl, 15:1 H_2O-THF, 60 °C, 2 h, 94%; (g) CH_2O, THF, −10 °C, 1 h, 95%; (h) 2 equiv of Me_3SiCl, THF, 0 °C, 1 h, 87%; (i) C_6H_5COCl, pyridine, 23 °C, 1 h, 95%; 2 equiv of $Hg(OCOCF_3)_2$, CH_3NO_2, 23 °C, 1 h; pH = 1, H_2O-THF, 1 h, 89%; (j) 2 equiv of $Hg(OCOCF_3)_2$, CH_3NO_2, 23 °C, 1 h; 10 equiv of K_2CO_3, H_2O-THF, 23 °C, 2.5 h, 91%; (k) (*n*-Bu)$_3$SnOTf, THF, −78 °C, 1 h, 82%.

The enantioselective addition of substituted allyl groups to aldehydes at −78 °C has been demonstrated in a number of cases. The 2-haloallyl reagents **11** and **12** were made by reaction of the (*S,S*)-enantiomer of **1** with the corresponding 2-haloallyltri-*n*-butyltin[8] at 0 °C initially and then 23 °C for 20 h. Table II summarizes the results. The absolute configuration of each product was established by dehalogenation to the corresponding allyl carbinols (*ent*-**3**) (reaction with 3.3 equiv of *tert*-butyllithium in ether at −78 °C for 2 h followed by quenching with aqueous acid) and measurement of optical rotation; ee values were determined by 500 MHz ^{1}H NMR analysis of the MTPA esters. In each case the favored transition state for the reaction of aldehydes with **11** or **12** is analogous to **4a**/**4b** although it is apparent that the degree of enantioselectivity diminishes somewhat for the series of chiral borane reagents in the order allyl (**2**) > 2-chloroallyl (**12**) > 2-bromoallyl (**11**).



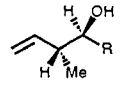
11 X = Br
12 X = Cl

13 X = Br
14 X = Cl
15 X = CH_3

(7) Determined by 500 MHz ^{1}H NMR analysis of the reaction products.

The synthetic utility of the 2-haloallyl carbinols **13** and **14** is clear from a number of transformations which have been demonstrated for both. Scheme I summarizes several of these conversions for the specific case of bromide **13**, R = cyclohexyl; they proceed as well with the corresponding chloride **14**, R = cyclohexyl. The combination of outstanding and predictable enantioselectivity and the versatility of the adducts **13** and **14** suggests that this methodology will be widely useful.

Although the scope of the new enantioselective chemistry described herein is still under investigation, the general pattern of results obtained thus far encourages optimism. The methallyl analogue of **11** or **12**, which is not expected to be as favorable with regard to enantioselectivity, still affords with hexanal adduct **15**, X = CH_3, R = *n*-C_5H_{11} in 88% ee (79% isolated yield). The



16 R = C_6H_5, *E*-C_6H_5CH=CH, cyclo-C_6H_{11}, *n*-C_5H_{11}

trans-crotyl analogue of **2** reacts in THF solution at −78 °C with the four aldehydes listed in Tables I and II to form mainly the anti adducts **16** in 74–82% yield with ee's in the range 91–95%. We believe that the enantioselective allylation of aldehydes, a process of clear synthetic potential, has advanced to a new level of practicality and predictability as a result of the present investigation because of the efficacy and simplicity of the reaction and the ready availability and efficient recovery of the chiral controller.[9]

Supplementary Material Available: An experimental procedure is given for the preparation of **1**, **2**, and **3**, R = C_6H_5 (2 pages). Ordering information is given on any current masthead page.

(8) The preparation of 2-bromoallyltri-*n*-butyltin was accomplished by the following sequence: (1) mesylation of 2-bromo-2-propen-1-ol with 1.1 equiv of methanesulfonyl chloride and 1.5 equiv of triethylamine in methylene chloride at 0 °C for 1 h (91% after distillation); and (2) reaction of this mesylate at −78 °C to 0 °C for 2.5 h with a reagent made from tri-*n*-butyltinlithium (Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481) and 1.0 equiv of cuprous bromide–dimethyl sulfide complex in THF at −78 °C for 2 h to form 2-bromoallyltri-*n*-butyltin in 89% yield. The corresponding 2-chloroallyltin reagent was prepared in the same way.

(9) This research was assisted financially by grants from the National Science Foundation and the National Institutes of Health.

Reactive Dissolution of NO_2 in Aqueous $^{15}NO_2^-$: The First Experimental Determination of a Main-Group Electron-Exchange Rate in Solution

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The rates of electron self-exchange for redox couples of coordination complexes and organic compounds have often been determined directly by using isotope tracer methods and spectroscopic line-broadening methods and indirectly by measuring rates of electron transfer between related complexes and applying the cross relationship of Marcus theory.[1,2] For main-group compounds, however, only indirect measurements have been used. In this way we now have estimates of the self-exchange rate constants for the following systems in aqueous solution: NO_2/NO_2^-,[3] ClO_2/ClO_2^-,[4]

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