group in the alkaline decomposition of **6**;[19] a consideration of VSEPR effects in the reagents, transition states, and products,[1] and the principle of microscopic reversibility as applied to these systems.[20]

The kinetics measurements and product ratio determinations were carried out essentially as described previously,[13] allowance being made for the presence of the basic dimethylamino groups. The amount of *N*,*N*-dimethylaniline formed was determined by both potentiometric titration of the acidified solution by standardized aqueous sodium hydroxide and by VPC analysis. The amount of benzene formed was determined by VPC analysis. The presence (or absence) of toluene was also determined by VPC analysis. Benzyldiphenylphosphine oxide (**5**), mp 191–192 °C, was collected by filtration and its physical and spectral properties compared with those of an authentic sample.[21]

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

---

(19) McEwen, W. E.; Janes, A. B.; Knapczyk, J. W.; Kyllingstad, V. L.; Shiau, W.-I.; Shore, S.; Smith, J. H. *J. Am. Chem. Soc.* **1978**, *100*, 7304.

(20) McDowell, R. S.; Streitwieser, A., Jr. *J. Am. Chem. Soc.* **1985**, *107*, 5849.

(21) Michaelis, A.; LaCoste, W. *Chem. Ber.* **1885**, *18*, 2109.

S. M. Cairns, W. E. McEwen*

Department of Chemistry
University of Massachusetts
Amherst, Massachusetts 01003

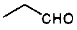
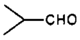
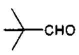
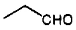
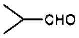
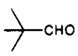
Received July 7, 1987

Asymmetric Addition of (*E*)- and (*Z*)-Crotyl-*trans*-2,5-dimethylborolanes to Aldehydes

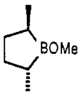
Summary: Reactions of homochiral (*E*)- and (*Z*)-crotyl-*trans*-2,5-dimethylborolanes with aldehydes proceed to provide homoallylic alcohols with excellent diastereo- and enantioselectivity.

Sir: The stereoselective construction of the 3-hydroxy-2-methylcarbonyl structural units,[1] often embedded in natural products of propionate origin such as macrolides,[2] continues to attract attention. While the aldol methodology[1] is considered the most direct approach toward this synthetic objective, asymmetric crotylboration[3,4] has emerged as an effective and practical alternative. In this connection it is timely to record herein the titled reagents derived from *B*-methoxy-(*R*,*R*)- and *B*-methoxy-(*S*,*S*)-2,5-dimethylborolanes [(*R*,*R*)-**1**, (*S*,*S*)-**1**].[1a,5] The new reagents equal or surpass the enantioselectivities of the boron reagents thus far recorded in the literature.[3,4] Diastereoselectivities observed in the reactions with chiral aldehydes conform to the rule of double asymmetric synthesis.[6]

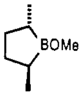
Table I. Reaction of Cortylborolanes (*E*)-(*R*,*R*)-2 and (*Z*)-(*R*,*R*)-2 with Representative Achiral Aldehydes

entry	crotylborane	aldehyde	yield,^{a} %	anti/syn^b ratio	major product	% ee^c
1	(*E*)-2		81	93/7	**4a**^{d}	96
2	(*E*)-2		76	96/4	**4b**^{e}	97
3	(*E*)-2		72	96/4	**4c**^{e}	95
4	(*Z*)-2		73	7/93	**6a**^{d}	86
5	(*Z*)-2		70	4/96	**6b**^{f}	93
6	(*Z*)-2		75^g	5/95	**6c**^{h}	97

^{a} Combined yield for syn and anti products. Unless otherwise noted yields were based on the amount of borolane reagent used and calculated by capillary GC analysis (5% phenylmethylsilicone, 0.20 mm × 12 m) of the alcohols using an internal standard. ^{b} Determined by capillary GC analysis (see footnote *a*). ^{c} Determined by HPLC analysis (Chemcosorb Si60 3 µm 4.6 × 250 mm) of bis[(*R*)-MTPA] esters of the corresponding 1,3-diols obtained from ozonolysis of **4** and **6** followed by reductive workup. Values are corrected for the purity of (*R*,*R*)-**1** (97.9% ee). ^{d} Bis[(*R*)-MTPA] esters of the corresponding 1,3-diols (see footnote *c*) from the products were compared with authentic samples obtained from the crotyl derivatives of (−)-Ipc$_2$BH, see ref 4a. ^{e} The absolute configuration of the products was determined by the comparison of bis[(*R*)-MTPA] derivatives of the corresponding 1,3-diols (see footnote *c*) with those of authentic diols provided from our previous work. See ref 1a. ^{f} $[\alpha]^{25}_{\mathrm{D}}$ −7.54° (*c* 0.83, CHCl$_3$) for the corresponding 1,3-diol (lit. $[\alpha]^{25}_{\mathrm{D}}$ +10.29° (*c* 0.91, CHCl$_3$) for the antipode. Masamune, S.; Choy, W.; Kerdesky, F. A. J.; Imperiali, B. *J. Am. Chem. Soc.* **1981**, *103*, 1566). ^{g} Yield was based on the amount of the aldehyde used. ^{h} The absolute configuration was assumed and in accordance with predicted ^{1}H NMR and HPLC behavior of the bis[(*R*)-MTPA] derivaive of the corresponding 1,3-diol. See: Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.



(*R*,*R*)-1



(*S*,*S*)-1

Reaction of (*E*)- and (*Z*)-Crotyl-(*R*,*R*)-2,5-dimethylborolanes [(*E*)-(*R*,*R*)-2 and (*Z*)-(*R*,*R*)-2] with Aldehydes. The preparation of the crotylborolanes (*E*)-(*R*,*R*)-**2** and (*Z*)-(*R*,*R*)-**2** adopted the Schlosser procedure[7] modified by Brown[4a,b] as shown in Scheme I.[8] Thus,

---

(1) For a review, see: (a) Masamune, S.; Sato, T.; Kim, B. M.; Wollmann, T. A. *J. Am. Chem. Soc.* **1986**, *108*, 8279 and its supplementary material. (b) Heathcock, C. H. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1984; Vol. 3, p 111. (c) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. Stereochem.* **1982**, *13*, 1. (d) Mukaiyama, T. *Org. React. (N.Y.)* **1982**, *28*, 203.

(2) (a) Masamune, S.; McCarthy, P. In *Macrolide Antibiotics*; Omura, S., Ed.; Academic: New York, 1984; Chapter 4. (b) Paterson, I.; Mansuri, M. M. *Tetrahedron* **1985**, *41*, 3569.

(3) (a) Roush, W. R.; Adam, M. A.; Walts, A. E.; Harris, D. J. *J. Am. Chem. Soc.* **1986**, *108*, 3422. (b) Roush, W. R.; Palkowitz, A. D.; Palmer, M. A. J. *J. Org. Chem.* **1987**, *52*, 316. (c) Roush, W. R.; Palkowitz, A. D. *J. Am. Chem. Soc.* **1987**, *107*, 953. (d) Roush, W. R.; Halterman, R. L. *Ibid.* **1986**, *108*, 294.

(4) (a) Brown, H. C.; Bhat, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 293. (b) Brown, H. C.; Bhat, K. S. *Ibid.* 5919.

(5) (a) Masamune, S.; Kim, B. M.; Petersen, J. S.; Sato, T.; Veenstra, S. J.; Imai, T. *J. Am. Chem. Soc.* **1985**, *107*, 4549. (b) Imai, T.; Tamura, T.; Yamamuro, A.; Sato, T.; Wollmann, T. A.; Kennedy, R. M.; Masamune, S. *Ibid.* **1986**, *108*, 7402. (c) Masamune, S.; Kennedy, R. M.; Petersen, J. S.; Houk, K. N.; Wu, Y.-d. *Ibid.* 7404.

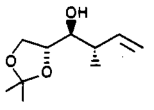
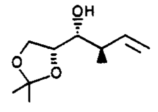
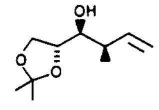
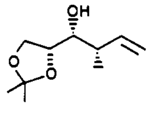
(6) (a) Masamune, S.; Choy, W.; Petersen, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1. For double asymmetric crotylboration, see ref 3a–d. Also for double asymmetric synthesis with *B*-allylboron reagents, see: (b) Roush, W. R.; Walts, A. E.; Hoong, L. K. *J. Am. Chem. Soc.* **1985**, *107*, 8186. (c) Brown, H. C.; Bhat, K. S.; Randad, R. S. *J. Org. Chem.* **1987**, *52*, 319.

(7) Fujita, K; Schlosser, M. *Helv. Chim. Acta* **1982**, *65*, 1258.

(8) Full experimental procedure and spectral data are available in the supplementary material.

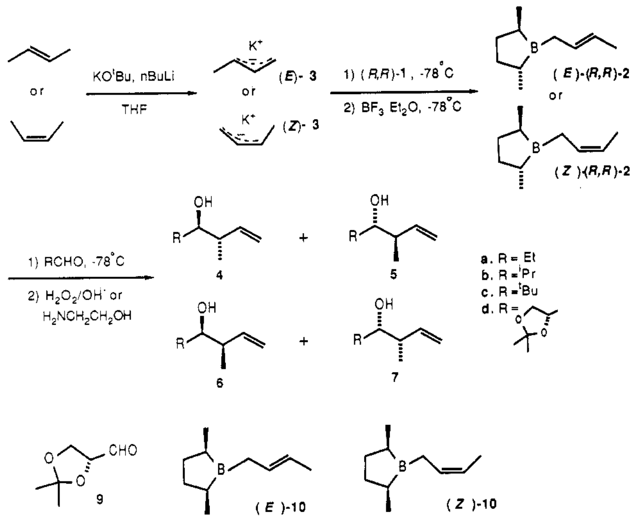
0022-3263/87/1952-4831$01.50/0

Table II. Reaction of Crotylborolanes with 9

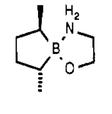
entry	crotyl-borolane	yield,[a] %	product ratio, %[b]				anti/syn ratio	ratio of 4/5 or 6/7	
			 **4d**	 **5d**	 **6d**	 **7d**		obsd	corrected[c]
1	(*E*)-**10**	62[d]	60.6	28.8	9.2	1.3	89.4:10.5	2.1/1	
2	(*Z*)-**10**	57[d]	2.4	1.8	77.5	18.3	4.2:95.8	4.2/1	
3	(*E*)-(*R*,*R*)-**2**	71	96.1[e]	2.8	0.9	0.2	98.9:1.1	34.3/1	48/1
4	(*Z*)-(*R*,*R*)-**2**	66	4.5	2.3	91.6[f]	1.6	6.8:93.2	57.3/1	99/1
5	(*E*)-(*S*,*S*)-**2**	74	12.4	85.6[g]	0.4	1.6	98.0:2.0	1/6.9	1/7.6
6	(*Z*)-(*S*,*S*)-**2**	65	0.5	2.4	15.4	81.7[h]	2.9:97.1	1/5.3	1/5.7

[a] Combined yield of all four possible isomers. Yields were determined by capillary GC analysis (5% phenylmethylsilicone, 0.20 mm × 12 m) using an internal standard. [b] Values were determined by capillary GC analysis (5% phenylmethylsilicone, 0.20 mm × 12 m) of crude products. [c] Corrected values for the composition of the reagents and the diastereofacial selecivity of the aldehyde **9**: 97.9% ee for (*R*,*R*)-**1** (*R*,*R* 98.4%, *R*,*S* 1.11%, and *S*,*S* 0.49%) and 96.1% ee for (*S*,*S*)-**1** (*R*,*R* 1.2%, *R*,*S* 1.5%, and *S*,*S* 97.3%). [d] Yields were not optimized. [e] $[\alpha]^{25}_D$ +6.2° (*c* 0.7, CH_2Cl_2) (lit.[3a] $[\alpha]^{22}_D$ +6.3° (*c* 1.25, CH_2Cl_2)). [f] $[\alpha]^{25}_D$ +45.5° (*c* 1.72, CH_2Cl_2) (li.[3a] $[\alpha]^{23}_D$ +47.6° (*c* 2.1, CH_2Cl_2)). [g] $[\alpha]^{25}_D$ +16.5° (*c* 0.52, CH_2Cl_2) (lit.[3a] $[\alpha]^{23}_D$ +14.5° (*c* 0.95, CH_2Cl_2)). [h] $[\alpha]^{25}_D$ −11.5° (*c* 0.9, $CHCl_3$) (lit.[3a] $[\alpha]^{22}_D$ −11.4° (*c* 0.9, $CHCl_3$)).

Scheme I



the methoxyborolane (*R*,*R*)-**1** reacted with (*E*)- and (*Z*)-crotylpotassium [(*E*)-**3** and (*Z*)-**3**] to provide, with the aid of $BF_3 \cdot OEt_2$, (*E*)-(*R*,*R*)-**2** and (*Z*)-(*R*,*R*)-**2**, respectively. After addition of an aldehyde (1.2 equiv) to a 1.0 M solution of each crotylborolane in THF at −78 °C, the solution was stirred 4 h. Addition of 2-aminoethanol (2 equiv) and then warming the solution to room temperature liberated the homoallylic alcohols **4**–**7** and precipitated the borolane moiety as an amino alcohol complex **8**.[9] As



8

summarized in Table I, (*E*)-**2** and (*Z*)-**2** lead to the predominant formation of the anti (**4** + **5**) and syn (**6** + **7**) products, respectively, with an average selectivity of 20:1, and the ee's of the major product range between 95% and 97% for the (*E*)-**2** series and between 86% and 97% for (*Z*)-**2**. Thus, with the exception of entry 4, these crotylboron reagents exhibit exceedingly high enantioselectivities[3,4] with achiral aldehydes varying in steric demand.[10]

Double Asymmetric Reactions. Encouraged by the above results we have carried out several typical double asymmetric reactions[6] using (*E*)-**2** and (*Z*)-**2** and (*R*)-2,3-*O*-isopropylideneglyceraldehyde (**9**) (see Table II). With the aid of achiral reagent (*E*)-**10** and (*Z*)-**10** (see the structures in Scheme I), the diastereofacial selectivity (D.S.) of the aldehyde **9** is estimated to be 2.1/1 for the reaction with (*E*)-crotylborolane (entry 1) and 4.2/1 for that with (*Z*)-crotylborolane (entry 2). The D.S.'s of the reagents (*E*)-**2** and (*Z*)-**2** are approximately 50:1 and 25:1, respectively (Table I).

Entries 3–6 summarizes the results of a series of double asymmetric syntheses using (*E*)- or (*Z*)-(*R*,*R*)-**2** and -(*S*,*S*)-**2**. Reaction of **9** with (*E*)-(*R*,*R*)-**2** and (*E*)-(*S*,*S*)-**2** provided mostly anti alcohols with a diastereomeric ratio of 48:1 (matched, entry 3) and 1:7.6 (mismatched, entry 5), respectively. The formation of syn alcohols prevailed with a diastereomeric ratio of 99:1 (matched, entry 4) and 1:5.7 (mismatched, entry 6), respectively, when (*Z*)-(*R*,*R*)-**2** and (*Z*)-(*S*,*S*)-**2** were employed. The well-established rule of double asymmetric synthesis is once again clearly validated and the diastereoselectivities of the major anti or syn products in the matched cases are among the highest obtained with the known crotylboron reagents.[3]

Acknowledgment. This work was supported by a grant from the National Institutes of Health (GM35879). J.G. is a CIRIT (Generalitat de Catalunya, Spain) fellowship holder.

Supplementary Material Available: Description of experimental details and spectral data (7 pages). Ordering information is given on any current masthead page.

Jordi Garcia, ByeongMoon Kim, Satoru Masamune*

Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

Received July 6, 1987

---

[9] The recovered amino alcohol complex retained full stereochemical integrity and can be reused.

[10] Examples of asymmetric crotylboration with bulky achiral aldehydes, e.g., isobutyraldehyde and 2,2-dimethylpropionaldehyde, were not recorded previously. See ref 3 and 4.