involving inward rotation of the heteroatom lone pair results in a stabilization of the σ* orbital and a lower TS than for outward rotation.

The TSs for the electrocyclic reactions of 1–6 are asynchronous and early. The breaking of the double bond lags behind the formation of the new double bonds.

The N compounds 4–6 are all unstable with respect to their open-chain isomers. Since the barrier to ring opening is not large, isolation of these species will be difficult. On the other hand, the P analogues 1–3 are stable with respect to their open-chain isomers, and many examples of derivatives of 1 and 2 are known. The possibility of the dihydrodiphosphetes acting as masked diphosphabutadienes is discounted since the rings are much lower in energy than the open chains. However, bulky substituents that can sterically disfavor the ring and stabilize P=C bonds may alter the equilibrium in favor of the open chains.

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Supplementary Material Available: Optimized geometries in the form of Z matrices for all structures at the HF/6-31G* level (4 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Solid-State and Solution Conformational Analysis of Tartrate-Derived 1,3-Dioxolanes and 1,3,2-Dioxaborolanes

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Solid-state (X-ray) and solution conformational analyses of tartrate ester derived 1,3-dioxolanes and 1,3,2-dioxaborolanes are described. The solid-state conformation of dimethyl benzylidenetartrate (**5**) was found to be one in which the two carbomethoxy groups are pseudoaxial and the ester carbonyls eclipse the adjacent dioxolane C–O bonds. This parallels exactly the conformation previously proposed for the 1,3,2-dioxaborolane unit in the transition state of the reactions of tartrate ester modified allylboronates 1–3 and aldehydes. A correlation was developed between the solution and solid-state conformations of 1,3-dioxolanes 5–7 based on the observed $J_{4,5}$ coupling constants and the H_4–C–C–H_5 dihedral angle obtained from the X-ray crystal structures. A high resolution variable-temperature ^{1}H NMR study of 1,3-dioxolane **5** in THF-d_8 revealed that $J_{4,5}$ decreased from 3.72 Hz at 23 °C to 2.91 Hz at −80 °C, providing evidence that the diaxial conformation is increasingly favored as the temperature is decreased. A high resolution variable-temperature ^{1}H NMR study of ortho ester **12**, prepared from dimethyl tartrate and trimethyl orthoacetate, in THF-d_8 similarly revealed $J_{4,5}$ = 5.25 Hz at 23 °C and $J_{4,5}$ = 4.60 Hz at −80 °C. An analogous solution conformation analysis was also performed with 1,3,2-dioxaborolane derivatives **16** and **17** prepared from methyl trifluoroethyl tartrate (**15**). Variable-temperature ^{1}H NMR analysis of **17** in toluene-d_8 revealed that $J_{4,5}$ decreased to a value of $J_{4,5}$ = 5.0 Hz at 23 °C to $J_{4,5}$ = 4.3 Hz at −60 °C. The significance of these data to the mechanism of asymmetric induction in the reactions of the tartrate ester modified allylboronates 1–3 and aldehydes is discussed.

The asymmetric allylboration reaction has been extensively studied over the past several years.[2,3] We have contributed the tartrate ester modified allylboronates 1–3 to this rapidly evolving field and have applied this technology in the synthesis of several stereochemically complex systems.[4,5] While these applications clearly define the synthetic utility of 1–3, the mechanism of asymmetric induction remains a topic of considerable interest, especially with respect to the design of more highly enantioselective chiral auxiliaries.[6] We have suggested that reagents 1–3 preferentially react with aldehydes by way of transition state **A** in which (i) the aldehyde and the two tartrate ester units occupy axial positions with respect to the dioxaborolane unit, and (ii) the tartrate esters are syn coplanar to the adjacent dioxaborolane C–O bonds. We have suggested further that the stereochemically favored transition state **A** is stabilized by a favorable dipole–dipole

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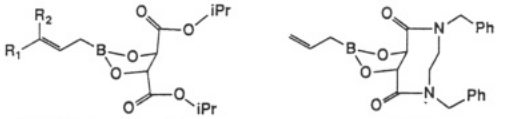
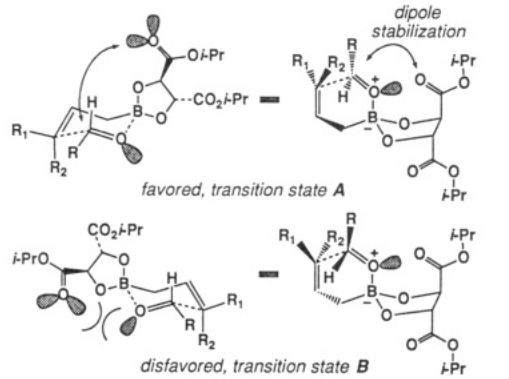
interaction between the aldehyde carbonyl carbon (δ^+) and the proximate ester carbonyl oxygen (δ^-), while the alternative transition structure **B** is destabilized by unfavorable interactions between the nonbonding electrons on the ester carbonyl and the boron-complexed aldehyde.[4] The significant dependence of enantioselectivity on temperature ($\Delta\Delta G^{\ddagger}$ = 1–1.1 kcal mol^{-1} for reactions of **1** and $C_6H_{11}CHO$ at −78 °C, but only 0.5 kcal mol^{-1} at 23 °C) has been rationalized in terms of conformational heterogeneity of the tartrate auxiliary.[4c] Other, presumably less enantioselective, transition structures are available in which the two ester units occupy pseudoequatorial positions or in which the ester carbonyls are not aligned syn to the adjacent C–O bonds. This model is supported by our observation that reagent **4**, incorporating the conformationally rigid tartramide auxiliary, is substantially more enantioselective than the parent tartrate allylboronate **1**. In addition, $\Delta\Delta G^{\ddagger}$ is temperature independent for reactions of **4** and cyclohexanecarboxaldehyde.[6]



(R,R)-**1**, $R_1 = R_2 = H$
(R,R)-**2**, R_1 = Me, $R_2 = H$
(R,R)-**3**, $R_1 = H$, R_2 = Me

(R,R)-**4**

We provide herein evidence from solution ^1H NMR and solid-state X-ray structural studies that the preferred conformations of tartrate ester derived acetals (1,3-dioxolanes) and tartrate alkylboronate derivatives (1,3,2-dioxaborolanes) are indeed ones in which the alkoxycarbonyl groups preferentially occupy axial positions, as already presumed for transition structure **A**.



Attempts to gain insight into the validity of this mechanistic proposal by spectroscopic observation of reaction intermediates have been unsuccessful, in part due to the high reactivity of **1**–**3**.[4b,7] The reactions of simple aldehydes and **1**–**3** are virtually instantaneous at concentrations of 0.2 M at −78 °C. Moreover, attempted spectroscopic (^1H and ^{11}B NMR) observation of ate complexes between *B*-benzyl-1,3,2-dioxaborolane-4,5-dicarboxylic acid diisopropyl ester (i.e., diisopropyl tartrate modified benzylboronate) and phenylacetaldehyde at temperatures between 23 °C and −60 °C were unsuccessful,[8] indicating that the equilibrium constant for complexation of the aldehyde by the Lewis acidic boron atom is very small. Similar unsuccessful attempts at the spectroscopic observation of ate complexes between aldehydes and alkylboronates have been reported by Hoffmann.[9] Finally, attempts to prepare

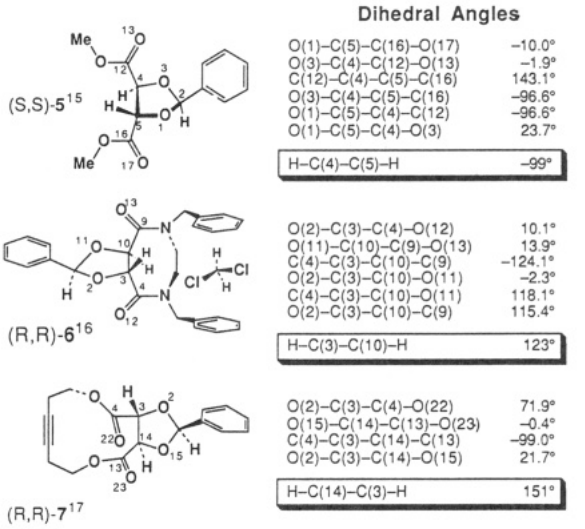


Figure 1.

crystalline tartrate allyl- or alkylboronate derivatives suitable for X-ray structure analysis have not been fruitful.

In view of our lack of success in gaining structural and conformational information concerning intermediates in the allylboration reaction, we decided to determine the solid-state conformations of the crystalline tartrate-derived benzylidene acetals **5**–**7**.[10] While caution obviously must be exercised when extrapolating from data for ground-state structures to transition states for the reaction of interest, even greater caution is called for when model compounds are used in the analysis, as is the case here. Our intent was simply to determine if the conformational features proposed for the allylboration transition state **A** could be verified for *any structure*. We assumed that the structures of 1,3-dioxolanes **5**–**7** would *roughly approximate* the geometry and conformations of the 1,3,2-dioxaborolane ate complex of interest (e.g., **A**) based on the following considerations. First, ab initio calculations for the reaction of formaldehyde and allylboronic acid[11] and X-ray crystal structures of intramolecular ate complexes of boronates and carbonyl groups reveal the boron atom to be tetrahedral.[12] Second, the B–OH bond lengths are calculated to be 1.42 and 1.45 Å in the allylboronic acid–formaldehyde transition state,[11] while the B–O bonds are 1.43–1.45 Å in the X-ray structures of triethanolamine borate.[13] B–O bonds in other ate complexes are slightly longer (mean = 1.48 Å).[12] By way of comparison, the average C–O bond length in acetals is 1.43 Å. This evidence suggests that 1,3-dioxolanes may be reasonable structural models for a 1,3,2-dioxaborolane ate complex. Of course, the analogy between ate complex **A** and dioxolanes **5**–**7** breaks down in that the boron atom of **5** has geminal substituents, while the acetal centers of **5**–**7** do not. We note, however, that the boron to carbonyl oxygen bond length in ate complexes is relatively long (1.57 Å, both experimentally and computationally)[11,12] and that 1,3-interactions in 1,3-dioxolanes are generally rather small.[14]

Chem3D structures of **5**–**7** generated from the X-ray coordinates appear in Figure 1.[15–17] *We were indeed de-*

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(8) Roush, W. R.; Halterman, R. L. Unpublished research, 1986.
(9) Hoffmann, R. W.; Wolff, J. J. *Chem. Ber.* **1991**, *124*, 563.
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(14) Willy, W. E.; Binsch, G.; Eliel, E. L. *J. Am. Chem. Soc.* **1970**, *92*, 5394.

lighted to discover that the conformation of the dimethyl tartrate residue of 5 in the solid state is identical to that proposed for the dioxaborolane units of 1–3 in the allylboration transition state A. The tartrate esters are clearly pseudoaxial [the C(12)–C(4)–C(5)–C(16) dihedral angle is 143°; hydrogen atoms were located exactly, and the H–C(4)–C(5)–H dihedral angle is found to be 99° in this structure] and both carbonyls are essentially coplanar with the adjacent dioxolane C–O bonds [dihedral angles of −10° and −2°, respectively; data are summarized in Figure 1]. Other X-ray structures have revealed a preference for conformationally unconstrained α-alkoxy groups to adopt syn-coplanar relationships with carbonyl groups,[18] and recent calculations by Houk and Trost indicate that the syn-coplanar conformation is the lowest energy one for methoxyacetic acid.[19]

It is interesting to compare these data with those obtained for (*R,R*)-**6**: the tartrate C–C bond is essentially eclipsed [C(4)–C(3)–C(10)–C(9) dihedral angle is −124°; the H–C(3)–C(10)–H dihedral angle is 123°], indicating that the amide carbonyls are closer to the equatorial plane of the dioxolane unit compared to the carbomethoxy groups of **5**. The tartramide C=O groups again are essentially coplanar with the adjacent dioxolane C–O bonds [dihedral angles of 10° and 14°, respectively]. Finally, it is noteworthy that the conformation of the tartrate residue in acetal **7** differs significantly from that of **5** and **6**. The "diaxial diester" conformation analogous to that in **5**/**6** apparently is strained by the fusion to the unsaturated

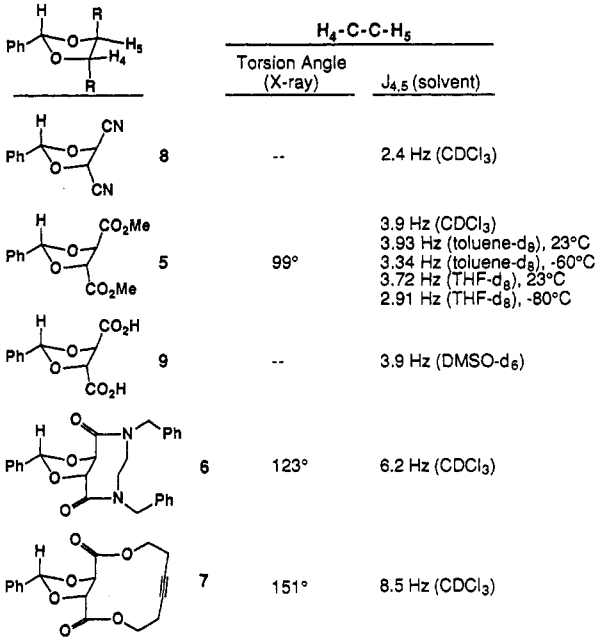

Figure 2.

12-membered ring and a conformation with the ester groups in pseudoequatorial positions is favored [C(4)–C(3)–C(14)–C(13) dihedral angle is 99°; the H–C(14)–C(3)–H dihedral angle is 151°]. In addition, one of the two ester carbonyl groups is twisted some 72° out of the plane of the adjacent C–O bond, also probably to relieve strain within the 12-membered ring.

The striking observation that acetal **5** exists in an eclipsed, diaxial diester conformation in the solid state prompted us to determine the conformation of **5** in solution. Correlations between $J_{4,5}$ and the H_4–H_5 angle, and hence the conformation of the tartrate unit, are possible in view of the considerable body of data provided by Eliel and Anteunis who have extensively documented the conformational preferences of 1,3-dioxolanes.[14,20] Coupling constants for trans H_4–H_5 relationships in alkyl-substituted 1,3-dioxolanes are typically 5.9–8.5 Hz, corresponding to H_4–C–C–H_5 torsional angles of 125–150°.[14] As a point of reference, $J_{4,5}$ for 2-phenyl-*trans*-4,5-dimethyl-1,3-dioxolane is 6.0 Hz (CD_2Cl_2, 23 °C).[21] It is remarkable, therefore, that $J_{4,5}$ = 3.9 Hz for acetal **5** in both $CDCl_3$ or toluene-d_8 at 23 °C. Even more striking is $J_{4,5}$ = 2.4 Hz observed for dinitrile **8**.[22] While it is conceivable that the electronegative methoxycarbonyl and nitrile substituents of **5** and **8** may have an effect on the Karplus curves that describe the angle dependence of the coupling constant in these systems,[23] the considerably larger coupling constants for tartramide acetal **6**[6] ($J_{4,5}$ = 6.2 Hz) and especially dilactone acetal **7**[10b] ($J_{4,5}$ = 8.5 Hz) strongly suggest that the

(15) (a) X-ray crystal structure data for dimethyl benzylidenetartrate (**5**): space group $P2_12_12_1$; cell dimensions (at −144 °C), a = 8.463 (2), b = 8.302 (2), and c = 17.771 (5) Å; Z (molecules/cell) = 4; volume = 1248.57 Å^3; calculated density = 1.416 g/cm^3; wavelength = 0.71069 Å; linear absorption coefficient, 1.058 cm^{-1}. The structure was solved using a combination of direct methods and Fourier techniques and was refined to final residuals $R(F)$ = 0.039 and $R_w(F)$ = 0.389 for 4307 independent reflections ($F > 3\sum(F)$) of 2335 unique intensities collected in the range $6° \le 2q \le 55°$. Details of the data collection and structure solution, atomic positional and thermal parameters, complete bond distance and bond angle data, and a listing of F_{obs} vs F_{calc} are provided in the supplementary material or may be obtained directly from the Indiana University Molecular Structure Center. Request report No. 89061. (b) The X-ray crystal structure determination of **5** was carried out by Dr. William E. Streib of the Indiana University Department of Chemistry Molecular Structure Center, Indiana University, Bloomington, IN 47405.

(16) X-ray crystal structure data for (*R,R*)-**6**: crystallized as a 1:1 molecular complex with CH_2Cl_2: space group $P2_1/a$; cell dimensions (at −155 °C); a = 11.698 (3) Å, b = 11.249 (2) Å, c = 14.093 (3) Å, β = 125.56 (1)°; Z (molecules/cell) = 4; volume = 1508.71 Å^3; calculated density = 1.393 g/cm^3; wavelength, 0.71069 Å; linear absorption coefficient, 0.992 cm^{-1}. The structure was solved using a combination of direct methods and Fourier techniques and was refined to final residuals $R(F)$ = 0.0361 and $R_w(F)$ = 0.0421 for 2392 independent reflections ($F > 2.33\sum(F)$) of 2662 unique intensities collected in the range $6.0° \le 2q \le 50°$. Details of the data collection and structure solution, atomic positional and thermal parameters, complete bond distance and bond angle data, and a listing of F_{obs} vs F_{calc} are provided in the supplementary material or may be obtained from the Indiana University Molecular Structure Center. Request report No. 89059.

(17) X-ray crystal structure data for (*R,R*)-**7**: space group $P\bar{1}$; cell dimensions (at −155 °C): a = 9.837 (2) Å, b = 9.966 (2) Å, c = 8.198 (2) Å, α = 111.85 (1)°, β = 99.45 (1)°, γ = 89.51 (1)°; Z (molecules/cell) = 2; volume = 734.66 Å^3; calculated density = 1.430 g/cm^3; wavelength, 0.71069 Å; linear absorption coefficient, 1.019 cm^{-1}. The structure was solved using a combination of direct methods and Fourier techniques and was refined to final residuals $R(F)$ = 0.0557 and $R_w(F)$ = 0.0719 for 1813 independent reflections ($F > 2.33\sum(F)$) of 1922 unique intensities collected in the range $6.0° \le 2q \le 45°$. Details of the data collection and structure solution, atomic positional and thermal parameters, complete bond distance and bond angle data, and a listing of F_{obs} vs F_{calc} are provided in the supplementary material or may be obtained from the Indiana University Molecular Structure Center. Request report No. 88215.

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(21) Denmark, S. E., private communication.

(22) Dinitrile **8** was synthesized by Dr. Luca Banfi by treatment of benzylidenetartramide with oxalyl chloride in DMF (83% yield). Unfortunately, attempts to deprotect **8** in order to use the resulting *threo*-dihydroxysuccinonitrile as an auxiliary for the asymmetric allylboration reaction were thwarted by the instability of the bis-cyanohydrin.

(23) (a) Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, 2nd ed.; Pergamon Press: New York, 1972. (b) Karplus curve modified for 1,3-dioxolanes: Lemieux, R. U.; Stevens, J. D.; Fraser, R. R. *Can. J. Chem.* **1962**, *40*, 1955.

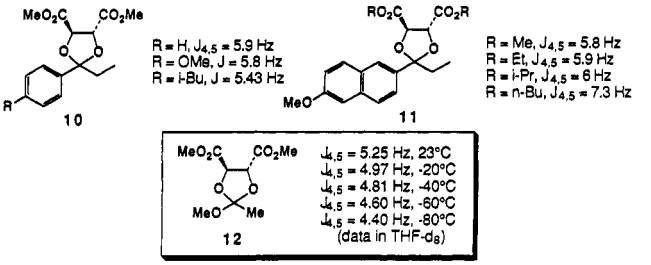
major contribution to the range of observed Js is conformational and not electronic in nature (Figure 2). The conformationally rigid tartramide derivative **6** provides a critical point of comparison with previously characterized systems, since there is little doubt that the conformation of this system is very similar, if not identical, in solution and the solid state: the coupling constant ($J_{4,5}$ = 6.2 Hz) and torsion angle (123°) are consistent with predictions based on the data provided by Eliel and Anteunis.[14,20] One can only conclude, therefore, that the *average* H_4–C–C–H_5 torsional angle is considerably greater in dilactone acetal **7** than in tartramide acetal **6**[24] and that the *average* H_4–C–C–H_5 angle is considerably smaller in **5** than in **6**. *That is, the observed H_4–H_5 coupling constants appear to correlate with the torsion angles determined by the X-ray structure analyses.*

While the coupling constant data for acetal **5** ($J_{4,5}$ = 3.9 Hz) indicates that the preferred conformation in solution is one in which the two methoxycarbonyl groups are pseudoaxial, it is probable that the coupling constant reflects contributions of both diaxial (note J = 2.4 Hz for dinitrile **8**) and diequatorial conformations. Indeed, a variable-temperature ^{1}H NMR study of **5** in toluene-d_8 performed under high resolution conditions revealed that $J_{4,5}$ decreased from 3.93 Hz at 23 °C to 3.34 Hz at −60 °C.[25] Because the −60 °C data were difficult to obtain owing to the viscosity of toluene at this temperature, a parallel set of variable-temperature ^{1}H NMR studies was performed with **5** in THF-d_8, again under high resolution conditions.[25] These measurements revealed $J_{4,5}$ = 3.72 Hz at 25 °C, 3.43 Hz at −20 °C, 3.26 Hz at −40 °C, 3.10 Hz at −60 °C, and 2.91 Hz at −80 °C; the error limit on each measurement is ±0.01 Hz.[26]

It is clear from these data that the diaxial diester conformation of **5** is increasingly favored as the temperature is decreased. For the sake of argument, if one assumes that the $J_{4,5}$ data for dinitrile **8** (2.4 Hz) and dilactone **7** (8.5 Hz) define the limiting J values for dioxolanes with "maximal" diaxial and diequatorial conformations, respectively, then the variable-temperature NMR data suggest that **5** is a ca. 75:25 mixture of diaxial and diequatorial conformers at room temperature and a ca. 90:10 mixture at −80 °C. If one assumes a larger $J_{4,5}$ for the diequatorial conformation, say 9.5 Hz,[24] then the conformational equilibrium is even more heavily slanted in favor of the diaxial conformation at any given temperature.

It is tempting to speculate that the conformational behavior of **5** is relevant to the mechanism of asymmetric induction of the tartrate-ester-modified allylboronates, especially in view of the temperature dependence of enantioselectivity that we have already interpreted in terms of conformational heterogeneity of the dioxaborolane unit in the transition state.[4c] However, as already noted, the structural analogy between **5** and transition structure **A** breaks down in that the boron center of **A** is geminally substituted, whereas the acetal carbon of **5** is not. Although 1,3-interactions in 1,3-dioxolanes are generally regarded as small,[14] and while the boron to carbonyl oxygen bond in ate complexes like **A** is expected to be relatively long (1.57 Å),[11,12] the question remains as to how serious the 1,3-interaction between the axial -CO_2iPr and -O=CHR actually may be. That is, could a diequatorial diester conformation of the dioxaborolane be favored instead of the diaxial conformation as formulated in **A**?

We have attempted to address this question as follows. First, the literature reveals that $J_{4,5}$ is usually in the range of 5.4–6 Hz ($CDCl_3$) for a series of ketals (e.g., **10**, **11**) prepared from ethyl aryl ketones and dialkyl tartrates.[27] The magnitude of these coupling constants suggests that, on average, the tartrate esters adopt pseudoaxial positions. It is recalled that $J_{4,5}$ = 6.2 Hz for the conformationally rigid tartramide derivative **6**, for which the H–C(4)–C(5)–H dihedral angle is 123°. Moreover, the corresponding allylboronate **4** is substantially more enantioselective than the parent tartrate ester derivatives.[6] Thus, conformation preferences inferred for **10** and **11** based on these $J_{4,5}$ data are in line with the mechanistic model presented in the introduction to this paper. More striking, however, are high resolution variable-temperature $J_{4,5}$ data obtained for other ester **12**, which was easily prepared by treatment of dimethyl tartrate with trimethyl orthoacetate. Ortho ester



12 more closely "models" the transition state for the allylboration reaction than **10** or **11**, since **12** has a C(2)-alkoxy group that is a closer mimic to the boron bound carbonyl oxygen unit present in **A**. *Significantly, ortho ester 12 shows $J_{4,5}$ = 5.25 Hz at 23 °C and $J_{4,5}$ = 4.40 Hz at −80 °C (measurements in THF-d_8).*[25]

Having established that tartrate ester derived acetals, ketals, and ortho esters prefer a conformation in which the two carbomethoxy groups adopt axial or pseudoaxial positions, we decided to determine the conformational preferences of tartrate-derived 1,3,2-dioxaborolanes. Although H_4 and H_5 are chemically equivalent in tartrate-ester-derived 1,3,2-dioxaborolanes such as **1–3**, it is conceivable that the desired $J_{4,5}$ value could be obtained by observation of the ^{13}C satellites.[23a] We elected, however, to break the symmetry of the tartrate ester, thereby rendering H_4 and H_5 nonequivalent and enabling us to measure $J_{4,5}$ directly. This was accomplished as follows. Partial base hydrolysis of **5** provided a mixture of monoacids **13** (diastereomeric at the acetal center) in 80% yield that was directly esterified by treatment with carbonyl diimidazole (CDI) and trifluoroethanol in THF (78%). Deprotection of **14** was accomplished by hydrogenation (10% Pd/C, H_2) in trifluoroethanol as solvent (97%). Conversion of diol **15** to 1,3,2-dioxaborolane derivatives **16** and **17** was then accomplished by treatment of **15** with

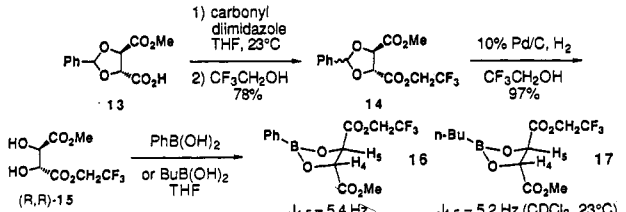
(24) As another point of comparison, Anteunis has reported $J_{4,5}$ = 9.25 Hz for *trans*-2,2-bis(trifluoromethyl)-4,5-dimethyl-1,3-dioxolane and concluded that this corresponds to a torsion angle of 160–165° (Anteunis, M.; Van Cauwenberghe, R.; Becu, C. *Bull Soc. Chim. Belg.* **1973**, *82*, 591). Consequently, our conclusion that the solution ($J_{4,5}$ = 8.5 Hz) and solid-state conformations (X-ray derived torsion angle = 151°) of **7** are similar is reasonable.

(25) (a) High resolution variable-temperature ^{1}H NMR analyses were performed on a Varian 400 MHz instrument typically with a spectral window of 775–820 Hz centered around the H_4 and H_5 resonances (ca. 4.1–5.8 ppm), 131 072 data points were collected. The digital resolution of all such high resolution measurements was ±0.012 Hz. The high resolution variable-temperature data for **5** and **12** were reproducible to ±0.01 Hz in duplicate runs. (b) We thank Dr. K. J. Moriarty and Dr. J. C. Park for assistance with initial variable-temperature ^{1}H NMR studies with **5** and **17**.

(26) The data from a duplicate high resolution variable-temperature NMR analysis of **5**, performed on a separate day, are as follows: $J_{4,5}$ = 3.70 Hz at 25 °C; 3.43 Hz at −20 °C; 3.27 Hz at −40 °C; 3.09 Hz at −60 °C; and 2.92 Hz at −80 °C.

(27) Castaldi, G.; Cavicchioli, S.; Gioardano, C.; Uggeri, F. *J. Org. Chem.* **1987**, *52*, 3018.

phenylboronic acid or butylboronic acid, respectively.[28] Analysis of the ^1H NMR spectra of these compounds revealed $J_{4,5}$ = 5.2–5.4 Hz in $CDCl_3$ at 23 °C and $J_{4,5}$ = 5.0 Hz for the spectrum of **17** measured in toluene-d_8. Variable-temperature NMR analysis of **17** under low resolution conditions (i.e., ±0.2 Hz) revealed that $J_{4,5}$ decreased to a value of $J_{4,5}$ = 4.3 Hz at −60 °C.[25b] Thus, even though the boron atom is sp^2 hybridized in **16** and **17**, causing the dioxaborolane ring system to be nearly planar[29a] and the B–O bonds in **16–17** to be considerably shorter (1.36–1.39 Å)[29b] than in the ate complexes cited previously,[11-13] it is remarkable that the alkoxycarbonyl groups of **16–17** still prefer to adopt axial (or pseudoaxial) conformations similar to those of the tartrate-derived acetals, ketals, and ortho ester presented earlier in this paper.



In summary, the structural information provided herein strongly supports the conclusion that the preferred conformation of tartrate-ester-derived 1,3-dioxolanes **5** and **10–12** and 1,3,2-dioxaborolanes **16** and **17** is one in which the two alkoxycarbonyl groups occupy axial (or pseudoaxial) positions with respect to the heterocyclic ring systems. The variable-temperature ^1H NMR data for **5**, **12**, and **17** are also indicative of conformational equilibria between diaxial and diequatorial conformers, with the diaxial one being increasingly favored at low temperatures. While, as already noted in the introduction to this paper, caution must be exercised when extrapolating from ground-state structures to transition states for the allylboration reaction, the data presented here suggests that the conformational features previously assumed[4] for the allylboration transition state **A** are indeed reasonable. These conformational arguments are further strengthened by data previously reported for allylboronate **4**: the tartramide auxiliary has no choice but to adopt the conformation indicated in transition structure **A** (cf., X-ray structure of **6**) and **4** is substantially more enantioselective than **1**.[6] We have also published results indicating that the increased enantioselectivity of **4** is related to its conformation and not to the functional group change of esters in **1** to lactams in **4**.[7a]

We anticipate that the data presented here will prove useful in the design of more effective chiral auxiliaries for the asymmetric allylboration reaction.

Experimental Section

General. All reactions were conducted in oven-dried (125 °C) or flame-dried glassware under atmospheres of dry argon or nitrogen. Analytical thin-layer chromatography (TLC) was performed by using 2.5-cm × 10-cm plates coated with a 0.25-mm thickness of silica gel containing PF 254 indicator (Analtech). Flash chromatography was performed as described by Still using Kieselgel 60 (230–400 mesh) or Kieselgel 60 (70–230 mesh).[30] Unless otherwise noted, all compounds purified by chromatography are sufficiently pure (by ^1H NMR analysis) for use in subsequent reactions.

^1H NMR spectra were measured on commercially available instruments at the indicated field strengths. Residual chloroform (δ = 7.26 ppm) was used as internal reference for spectra measured in $CDCl_3$. High resolution variable-temperature ^1H NMR experiments were performed as described in ref 25. Low and high resolution mass spectra were measured at 70 eV. The X-ray crystal structure determinations of **5–7** were performed as summarized in refs 15–17. Details of the data collection and structure solution, atomic positional and thermal parameters, complete bond distance and bond angle data, and a listing of F_{obs} vs F_{calc} for each structure are provided in the supplementary material.

(4*R*,5*R*)-4,5-Bis(methoxycarbonyl)-2-methyl-2-methoxy-1,3-dioxolane (12). To a solution of dimethyl (*R*,*R*)-tartrate (0.5 g, 2.8 mmol) in 4 mL of benzene were added trimethyl orthoacetate (430 μL, 3.4 mmol) and catalytic pyridinium *p*-toluenesulfonate. The solution was refluxed for 2 h and then was diluted Et_2O and washed with saturated aqueous $NaHCO_3$ solution. The organic phase was washed with additional $NaHCO_3$ solution and brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. This provided 336 mg (51%) of **12** as a colorless liquid that was sufficiently pure for use in the variable-temperature ^1H NMR studies described in the text: ^1H NMR ($CDCl_3$, 400 MHz) δ 5.14 [d, *J* = 5.1 Hz, 1 H], 4.81 [d, *J* = 5.1 Hz, 1 H], 3.89 [s, 3 H]; 3.87 [s, 3 H], 3.65 [s, 3 H], 1.72 [s, 3 H]; ^1H NMR (THF-d_8, 400 MHz, 23 °C) δ 4.90 [d, *J* = 5.25 Hz, 1 H], 4.74 [d, *J* = 5.26 Hz, 1 H], 3.74 [s, 3 H], 3.73 [s, 3 H], 3.24 [s, 3 H], 1.54 [s, 3 H]; ^{13}C NMR ($CDCl_3$, 400 MHz) δ 170.3, 76.9, 76.5, 53.1, 53.0, 50.9, 20.7; IR ($CDCl_3$) 3000, 2960, 1750 (br), 1440, 1390, 1360, 1340, 1230, 1050, 880, 810 cm^{-1}; high resolution mass spectrum, calcd for $C_9H_{13}O_7$ (M^+ − 1) 233.0619, found 233.0672.

(4*R*,5*R*)-4-(Methoxycarbonyl)-5-[(2,2,2-trifluoroethoxy)carbonyl]-2-phenyl-1,3-dioxolane (14). To a solution of diester **5** (4.44 g, 16.7 mmol) in 50 mL of methanol under argon was added a solution of KOH (0.94 g, 16.7 mmol) in 20 mL of methanol over a 1-h period. The resulting mixture was allowed to stir for 8 h at 25 °C and then MeOH was removed in vacuo. The thick colorless liquid was dissolved in 100 mL of saturated NaCl and extracted with Et_2O (2 × 100 mL) to remove residual **5**. The aqueous phase was acidified to pH = 3 using 1 N HCl (saturated with NaCl) and extracted with EtOAc (4 × 100 mL; the pH of the aqueous phase was adjusted to pH = 3 before each extraction). The combined organic extracts were dried with Na_2SO_4, filtered, and concentrated to give a clear viscous liquid. The crude product was purified on a column of silica gel using 9:1 Et_2O/EtOAc, giving 3.35 g (80% yield) of monoacid **13** as a mixture of diastereomers: R_f 0.05 (9:1 Et_2O/EtOAc); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.57–7.56 [m, 4 H], 7.44–7.41 [m, 6 H], 6.17 [s, 1 H], 6.15 [s, 1 H], 5.05 [d, *J* = 3.4 Hz, 2 H], 4.93–4.91 [m, 2 H], 3.90 [s, 3 H], 3.84 [s, 3 H]; IR (neat) 3250–2700 (br), 3025, 2990, 2960, 2400, 1755, 1745, 1465, 1440, 1410, 1380, 1115, 1045, 975, 675 cm^{-1}.

A solution of **13** (0.50 g, 1.98 mmol) in 12.5 mL of dry THF under argon was treated with carbonyl diimidazole (0.48 g, 2.97 mmol) at room temperature for 2 h. Trifluoroethanol (0.29 mL, 3.96 mmol) was then added dropwise via syringe and the resulting solution was stirred for 8 h. The solvent was removed in vacuo with a bath temperature not exceeding 30 °C. The resulting liquid was dissolved in 50 mL of Et_2O and extracted with 1 N HCl (2 × 25 mL), brine (2 × 25 mL), and saturated $NaHCO_3$ (2 × 25 mL). The organic phase was dried over Na_2SO_4, filtered, and concentrated in vacuo to give 0.54 g of a clear liquid. The crude product was purified by flash chromatography (100 g of silica gel, 25% Et_2O–hexane) to give 0.42 g (78% yield) of **14** as a 1:1 mixture of diastereomers: R_f 0.42 (30% Et_2O/hexane); $[\alpha]^{25}_D$ −22.8° (c 13.3, CH_2Cl_2); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.59–7.56 [m, 2 H], 7.43–7.40 [m, 3 H], 6.17 [s, 1 H], 6.15 [s, 1 H], 5.11 and 4.81 [AB, J_{AB} = 4.3 Hz, 2 H], 4.99 and 4.96 [AB, J_{AB} = 3.95 Hz, 2 H], 4.68–4.56 [m, 2 H], 3.89 [s, 3 H], 3.84 [s, 3 H]; ^{13}C NMR ($CDCl_3$, 500 MHz) δ 169.49 [s], 168.77 [s], 168.24 [s], 167.75 [s], 134.95 [s], 134.89 [s], 130.10 [s], 130.06 [s], 128.37 [s], 128.40 [s], 127.75 [q], 127.08 [s], 122.48 [q], 106.95 [s], 77.41 [s], 77.13 [s], 76.89 [s], 76.63 [s], 61.01 [q], 60.99 [q], 52.89 [s]; IR (neat) 3070, 3040, 2960, 2910, 1780, 1765, 1755, 1745, 1610, 1495, 1460, 1440, 1410, 1110, 975, 920, 855, 845, 760, 700, 650 cm^{-1}; high resolution mass

(28) Diol **15** was also converted to the corresponding allylboronate derivative upon treatment with allylboronic acid, but H_4 and H_5 were partially obscured by other protons in the ^1H NMR spectrum.

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spectrum, calcd for $C_{14}H_{13}O_6F_3$ (M^+) 334.0664, found 334.0679. Anal. Calcd for $C_{14}H_{13}O_6F_3$: C, 50.31; H, 3.92. Found: C, 50.49; H, 3.75.

(2*R*,3*R*)-Methyl Trifluoroethyl Tartrate (15). A mixture of 14 (103 mg, 0.31 mmol) and 10% Pd-C (40.0 mg) in 1.5 mL of CF_3CH_2OH was thoroughly flushed with argon for 15 min. Then a balloon filled with H_2 was attached via a syringe needle to the top of the flask. The mixture was stirred for 12 h at room temperature, filtered through a plug of Celite, and rinsed with acetone. The solvents were removed in vacuo. The resulting liquid was filtered through silica gel using 1:1 EtOAc/hexane to give 70 mg (97% yield) of diol **15** a slightly yellow liquid. When stored in a -20 °C freezer it subsequently crystallized (low melting solid): R_f 0.22 (1:1 EtOAc/hexane); $[\alpha]^{25}_D$ -3.3° (*c* 7.5, CH_2Cl_2); ^{1}H NMR [$CDCl_3$, 300 MHz] δ 4.71-4.54 [m, 4 H], 3.89 [s, 3 H], 3.28 [d, J = 6.2 Hz, 1 H, OH], 3.23 [d, J = 8.2 Hz, 1 H, OH]; ^{13}C NMR [$CDCl_3$, 500 MHz] δ 176.56 [s], 170.12 [s], 122.50 [q], 72.04 [s], 71.94 [s], 61.37 [q], 53.21 [s]; IR (neat) 3610-3430 (br), 2980, 2960, 1765, 1750, 1440, 1410, 1235, 1170, 1120, 1090, 990, 975 cm^{-1}; high resolution mass spectrum, calcd for $C_7H_{10}O_6F_3$ (M^+ + 1) 247.0431, found 247.0440. Anal. Calcd for $C_7H_9O_6F_3$: C, 34.16; H, 3.69. Found: C, 34.43; H, 3.59.

Synthesis of 1,3,2-Dioxaborolane Derivatives 16 and 17. General. To a solution of **15** in anhydrous THF (0.5 mL) was added the boronic acid (1.0 equiv) as a solution in THF (0.5 mL). A small amount of $MgSO_4$ was added to the reaction mixture, which was subsequently stirred for 3 h. The mixture was then filtered and concentrated in vacuo. The products were stored under argon in a -20 °C freezer until the NMR analyses were performed.

Data for phenylboronate 16: ^{1}H NMR [$CDCl_3$, 300 MHz] δ 7.89 [d, J = 7.2 Hz, 2 H], 7.54-7.39 [m, 3 H], 5.20 and 5.08 [AB, J_{AB} = 5 .47 Hz, 2 H], 4.72-4.54 [m, 2 H], 3.87 [s, 3 H]; ^{11}B NMR ($CDCl_3$, 360 MHz] δ 32.0 (br), 29.2 (residual phenylboronic acid from hydrolysis of **16** in the NMR solvent).

Data for butylboronate 17: ^{1}H NMR [$CDCl_3$, 300 MHz; 23 °C] δ 4.98 and 4.87 [AB, J_{AB} = 5.2 Hz, 2 H], 4.67-4.53 [m, 2 H], 1.48-1.43 [m, 2 H], 1.37-1.32 [m, 2 H], 0.99 [t, J = 7.8 Hz, 2 H], 0.89 [t, J = 7.0 Hz, 3 H]; ^{1}H NMR (toluene-d_8, 500 MHz, 23 °C) δ 4.67 [AB, J_{AB} = 5.0 Hz, 1 H], 4.66 [AB, J_{AB} = 5.0 Hz, 1 H], 3.7-3.9 [m, 4 H], 3.20 [s, 3 H], 1.45-1.53 [m, 2 H], 1.25-1.4 [m, 4 H], 0.87 [t, J = 7 Hz, 3 H]; ^{13}C NMR ($CDCl_3$, 500 MHz) δ 169.46, 168.17, 120.22, 77.21, 76.95, 61.17 (q, due to ^{19}F splitting), 53.03, 29.67, 25.57, 25.09, 13.72; ^{11}B NMR ($CDCl_3$, 360 MHz) δ 35.7 (br), 32.9 (residual butylboronic acid from hydrolysis of **17** in the NMR solvent).

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Supplementary Material Available: X-ray crystallographic data and ORTEP drawings of benzylidene acetals **5-7** and ^{1}H NMR spectra of **12**, **16**, and **17** (19 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Enantioselective Synthesis of (*S*)-2-Methyl-1-alkanols via Bakers' Yeast Mediated Reduction of α-Methyl-2-thiophenepropenals

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The bakers' yeast mediated enantioselective reductions of some α-methyl-5-(1-alkyl)-2-thiophenepropenals **3** are described. These furnished (*S*)-β-methyl-5-(1-alkyl)-2-thiophenepropanols **5** in good to high enantiomeric excesses (76-98% ee). An alternative approach to (*S*)-β-methyl-5-(1-alkyl)-2-thiophenepropanols **5d-f** (98% ee) is also described. Raney nickel reduction of their acetates, followed by hydrolysis, provided (*S*)-2-methyl-1-alkanols **2b-f** of unchanged optical purities.

The stereo-, chemo-, and regioselectivities of microbial systems have recently provided easy access to enantiomerically pure compounds for use in synthesis.[1] Bakers' yeast is a convenient reducing microbial system and has been used for the reduction of both carbon-oxygen and carbon-carbon double bonds.[2] Starting materials containing heterocycles has in some cases been used to improve selectivity of product formation[3] or as a means of masking a functional group.[4] In this context some of us recently participated in a study of the enantioselective bakers' yeast reduction of a carbon-carbon double bond in α-methyl-2-furanpropenal (**3a**) to give a high yield of (*S*)-β-methyl-2-furanpropanol (**5a**) in >99% ee where the furan ring served as a masked carboxyl group.[5]

Indeed, simple chiral methyl-branched compounds of high optical purities suitable as starting materials for syntheses are not readily available from the chiral pool. In connection with studies on the pheromone of pine sawflies, which are 3,7-dimethyl-2-pentadecyl esters, we required easy access to compounds of type **1** (* signifies a chiral center) as synthetic intermediates. Especially

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