Secondary Deuterium Kinetic Isotope Effects in Irreversible Additions of Allyl Reagents to Benzaldehyde

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The competitive kinetics of additions of allyl to benzaldehyde-*h* and -*d* from allyltributyl tin, from diisopropyltartrylallyl boronate, and from allyl bromide and zinc dust in aqueous tetrahydrofuran have inverse secondary deuterium kinetic isotope effects, SDKIEs. These inverse SDKIEs are in contrast to the normal SDKIEs that were obtained with allyl lithium and allyl Grignard, suggesting rate-determining single-electron transfer in these cases. By various MO calculations the transition state for addition of allyl boronate occurs with substantial B−O bond formation and little C−C bond formation. The magnitudes of the SDKIEs with the other two allylating reagents, when compared with reasonable equilibrium isotope effects for the addition, suggest transition states with substantial C−C bond formation.

Introduction

Addition of allylic nucleophiles to the carbonyl group is of major importance in organic chemistry.[1] The mechanism of this process is therefore of concern, particularly in connection with questions of face selectivity.[2] Three extreme mechanisms can be envisioned where the rate-determining step can be (1) a direct attack of the base with its two electrons on the carbocation-like carbonyl carbon, sometimes called the polar mechanism, (2) a single-electron transfer (SET) from the base to generate a carbonyl radical anion−base radical cation pair which collapses to the tetrahedral adduct,[3] or (3) Lewis acid complexation of the carbonyl oxygen (Scheme 1). A partial distinction can be made between them on the basis of the secondary deuterium kinetic isotope effect, SDKIE, at the carbonyl carbon. An inverse effect ($k^H/k^D < 1.0$) is expected if the rate-determining step is a polar addition[4a] or Lewis Acid complexation;[4b] however, for rate-determining single-electron transfer the SDKIE should be normal ($k^H/k^D > 1.0$).[4a]

The SDKIEs in metal hydride and methyl lithium and methyl Grignard additions to benzaldehyde are inverse, while those of allyl lithium and allyl Grignard additions are normal.[4a] Therefore, single-electron transfer appears to occur only with the more easily oxidized allyl reagents,[5] while all others appear to be nucleophilic additions. Indeed, with hydride reagents the inverse SDKIE is more

Scheme 1
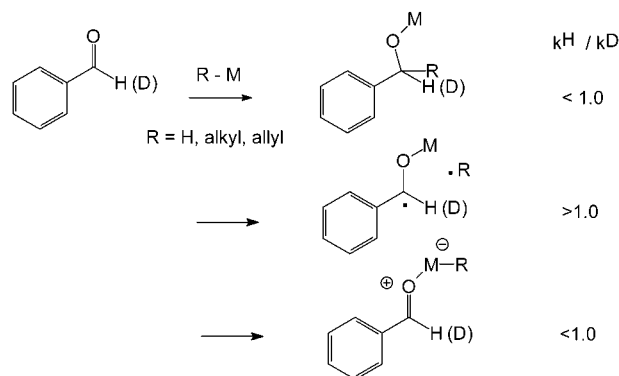
inverse with the less reactive reagent, suggesting later transition states in those cases.[4a] The possibility of rate-determining Lewis acid complexation in these additions was ruled out on the expectation that the SDKIE for this pathway would be near unity since the carbonyl carbons in the starting material and complex would appear to have similar charges. However, subsequent work in our laboratory has revealed that BF_3 complexation with benzaldehyde is accompanied by a substantial inverse isotope effect.[4b] This then makes more difficult a distinction between mechanisms 1 and 3, although in weak acid-catalyzed additions of oxygen nucleophiles to aldehydes, proton transfer appears much less advanced than nucleophilic addition in the transition state.[6] Further, MP2/6-311+G** calculations of proton and hydronium ion

(1) *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vols. 1 and 2.

(2) Eliel, E. L.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*; John Wiley & Sons: New York, 1994; pp 875−888. Coxon, J. M.; Houk, K. N.; Luibrand, R. T. *J. Org. Chem.* **1995**, *60*, 418 (for calculations with AlH₃). Wu, Y.-D.; Houk, K. N.; Paddon-Row: M. N. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1019 (for caculations with LiH).

(3) For a review with a penetrating analysis see: Walling, C. *J. Am. Chem. Soc.* **1988**, *110*, 6846.

(4) (a) Gajewski, J. J.; Bocian, W.; Harris, N. J.; Olson, L. P.; Gajewski, J. P. *J. Am. Chem. Soc.* **1999**, *121*, 326. In a polar addition it is assumed that the carbonyl oxygen has a counterion or a proton nearby or there is strong hydrogen bonding to the carbonyl oxygen in the transition state. (b) Gajewski, J. J.; Ngernmeesri, P. *Org. Lett.* **2000**, *2*, 2813. (c) Harris, N. J. *J. Phys. Chem.* **1995**, *99*, 14689.

(5) (a) Holm, T. *Acta Chem. Scand.* **1983**, *B37*, 569. E_o(rel SHE): allyl-MgBr, −1.16 V; MeMgBr, −0.25 V (in diethyl ether at 25 °C). For phenyl-MgBr E_o = 0. Eberson, L. *Acta Chem. Scand.* **1984**, *B38*, 439. (b) Jaun, B.; Schwanz, J.; Breslow, R. *J. Am. Chem. Soc.* **1980**, *102*, 5741. Approximate E_o(rel SCE, E_o(rel SHE) = 0.242 V): allyl-Li, −1.24 V; BuLi, −1.41 V; MeLi, −0.72 V; PhLi, −0.34 V (all in THF at −60 °C except allyl at −25 °C).

(6) Jencks, W. P. *Acc. Chem. Res.* **1976**, *9*, 425−32. Funderburk, L. H.; Aldwin, L.; Jencks, W. P. *J. Am. Chem. Soc.* **1978**, *100*, 5444−59. Hill, E. A.; Milosevich, S. A. *Tetrahedron Lett.* **1976**, 4553−54. The possibility that both protonation and nucleophilic attack are reversible with the rate-determining step involving general base catalysis in the removal of a proton, which would also give rise to gas, is not involved.
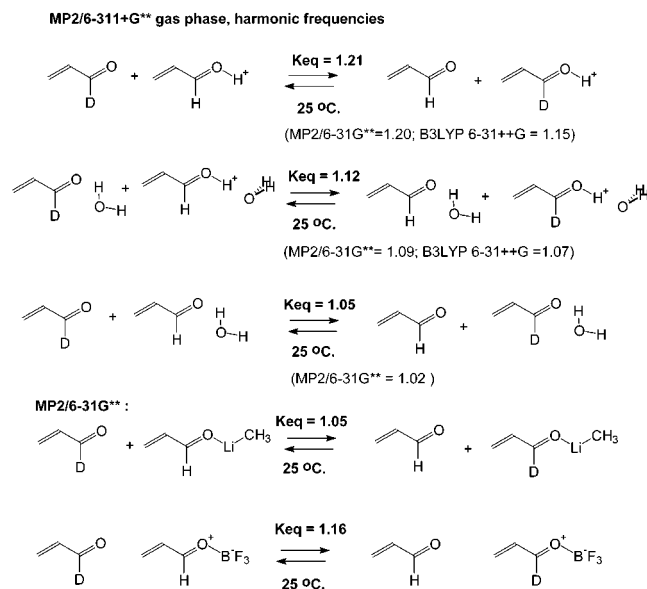
Figure 1. Calculated equilibrium isotope effects in the complexation of acrolein. The geometries are reasonably accurately rendered. Other levels of theory are given in the parentheses.

complexes of acrolein reveal a substantially smaller equilibrium isotope effect with one additional water, all in the gas phase, Figure 1. Calculations at this level reasonably reproduced equilibrium fractionation factors with respect to acetylene which were derived from experimentally determined infrared frequencies.[4c] Finally, the equilibrium isotope effect with a methyl lithium complex is substantially smaller than that with BF_3, at the MP2/6-31G** level, Figure 1.[4b,7,8]

A further utility of the SDKIE is its ability to reflect the extent of bond formation at the site bearing deuterium provided that its value can be compared with the isotope effect expected for complete bond formation. This latter value may be the equilibrium isotope effect for the overall process, a value interpolated from tables of deuterium fractionation factors between various types of carbon, or a value calculated from molecular orbital theory using calculated harmonic frequencies and the Bigeleisen equation assuming complete bond formation.[9] Care needs be exercised in the selection of models for equilibrium effects, because, as we have shown pre-

Figure 2. Addition of an *O*-silyl ketene *N,O*-acetal to benzaldehyde.

Figure 3. Face selectivity in the Yamamoto addition of allyl tin reagents to benzaldehyde.

viously,[4a] the fractionation factor at the carbonyl carbon depends on the substitution at the carbonyl oxygen.

Other previous work in this area has been published by Myers[10] and by Streitwieser.[11] Myers measured a very large inverse SDKIE (0.76) in the addition of an (*S*)-prolinol-derived *O*-silyl ketene *N,O*-acetal to benzaldehyde-*h/d*, a reaction that proceeds with high selectivity to give the (2*S*,3*R*)-*anti*-aldol product in nonbasic solvents, Figure 2.

The results were interpreted in terms of a very late transition state for addition, a conclusion that is reinforced by a large positive Hammett ρ value (3.5) for addition to substituted benzaldehydes. The late transition state is also consistent with high stereoselectivity observed in this reaction. Gung found, via theory, a cyclic transition state with pentavalent silicon for addition of enol silane trihydride to formaldehyde at the MP2/6-31G* level and found a 2.07 Å C−C bond being formed with a substantial inverse SDKIE (0.80).[12] Streitwieser measured a large inverse secondary deuterium equilibrium isotope effect (0.74) in the addition of a lithium enolate to benzaldehyde, but on the basis of HF/6-31++g* calculations on simpler model systems, the transition state for the addition appears early because the C−C bond being formed was found to be very long; however, the isotope effect calculated is large and inverse.

Because allyl lithium and Grignard reagents add via single-electron transfer,[4a] little face selectivity would be expected, and is rarely found except in highly biased systems, in the subsequent ketyl−allyl radical combination. However, allylstannanes add to aldehydes with Lewis acid catalysis, and the addition occurs in a highly stereoselective fashion in the sense of an open transition state.[13] Thus, with crotyl stannane addition to benzaldehyde, *SR* and *RS* products dominate, Figure 3.

(7) The isotopic harmonic frequencies for formation of the complexes were calculated and were used unscaled in the Bigeleisen equation to calculate the equilibrium preferences: Bigeleisen, J.; Mayer, M. G. *J. Chem. Phys.* **1947**, *15*, 261. Wolfsberg, M. *Acc. Chem. Res.* **1972**, *5*, 225. Hout, R. F., Jr.; Wolfsberg, M.; Hehre, W. J. *J. Am. Chem. Soc.* **1980**, *102*, 3296. The calculations reveal that the major frequency change from aldehyde to tetrahedral carbon is the C−H stretch not the C−H bend. Indeed, the bending frequency in aldehydes is approximately the same as that of hydrogens attached to tetrahedral carbons.

(8) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.6; Gaussian, Inc.: Pittsburgh, PA, 1998.
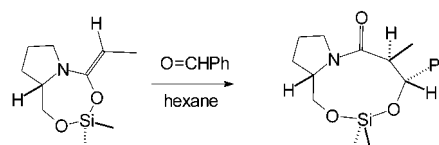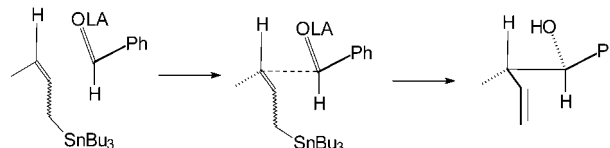
(9) (a) Shiner, V. J., Jr.; Neumann, T. E. *Z. Naturforsch.* **1989**, *44a*, 337. (b) For earlier work on fractionation factors see: Hartshorn, S. R.; Shiner, V. J., Jr. *J. Am. Chem. Soc.* **1972**, *91*, 9002. (c) For an example of a transition-state calculation of SDKIEs see: Delmonte, A. J.; Haller, J.; Houk, K. N.; Sharpless, K. B.; Singleton, D. A.; Strassner, T.; Thomas, A. A. *J. Am. Chem. Soc.* **1997**, *119*, 9907.

(10) Myers, A. G.; Widdowson, K. L.; Kukkola, P. J. *J. Am. Chem. Soc.* **1992**, *114*, 2765.

(11) Abu-Hasanayn, F.; Streitwieser, A. *J. Org. Chem.* **1998**, *63*, 2954. The calculated IEs are for gas-phase, unsolvated species.

(12) Gung, B. W.; Zhu, Z.; Fouch, R. A. *J. Org. Chem.* **1995**, *60*, 2860.

(13) Yamamoto, Y.; Yatagai, H.; Naruta, Y. Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 7107. Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31−47.
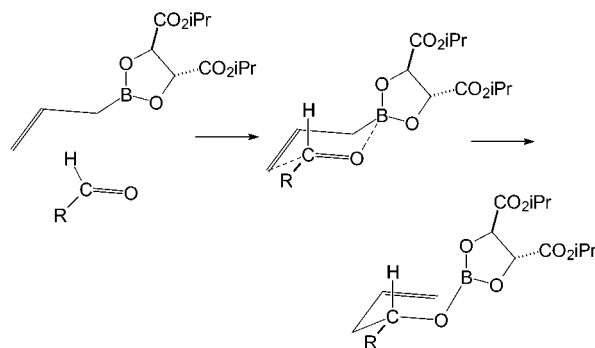
Figure 4. Face selectivity in the Roush addition of diisopropyltartrylallyl boronate to benzaldehyde.

Further, allyl boranes and boronates[14] have been used to add to aldehydes, giving, in many cases, not only high diastereoselectivity in the sense of a cyclic, chairlike transition state[15] but also high face selectivity when optically active ligands are attached to the boron, Figure 4.

Given these observations, it is reasonable to expect substantial C−C bond formation in the allyl borane−aldehyde transition state, yet ab initio calculations, albeit with small basis sets and no electron−electron correlation, suggest relatively long forming C−C bonds in a highly simplified model transition state.[16]

Finally, an allylating reagent that has been used in aqueous solution is an allyl zinc species derived from allyl bromide and zinc dust,[17] and it is related to the indium reagent first generated by Chan[18] that provides substantial face selectivity in carbonyl additions.[19] All of these additions of allyl metal reagents can be either two-electron, polar additions or single-electron transfer, so a determination of the SDKIEs in these systems would appear appropriate.

Results

The KIEs for various additions were determined by reaction of a mixture of benzaldehyde-*h* and -*d* with a deficiency (approximately 0.1 equiv) of reagent in either ethereal solvents or methylene chloride or toluene at −78 °C.[4] The 1-phenyl-3-buten-1-ol product from addition of allyltributyl tin catalyzed by BF_3 etherate,[13] from diisopropyltartrylallyl boronate reagents,[14b] and from allyl bromide/zinc in aqueous tetrahydrofuran[17] was obtained by literature procedures and converted to the previously characterized[4a] methyl ether by reaction with sodium hydride followed by treatment with methyl iodide. The H/D content at C-1 of the methyl ethers was determined by ^1H NMR. Care was taken to use 20 s delay times between RF pulses in the ^1H NMR to minimize saturation effects. The composition of the initial mixture of aldehyde-*h* and -*d* was determined from a reaction with an excess of reagent and analysis of the derivative of the product by the same techniques used for the competition

(14) (a) Brown, H. C. Randad, R. S. *Tetrahedron* **1990**, *46*, 4457 and references therein. (b) Roush, W. R.; Hoong, L. K.; Palmer, M. A. J.; Park, J. C. *J. Org. Chem.* **1990**, *55*, 4109 and references therein.
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(16) Li, Y.; Houk, K. N. *J. Am. Chem. Soc.* **1989**, *111*, 1236−40.
(17) Petrier, G.; Luche, J. L. *J. Org. Chem.* **1985**, *50*, 910. Breton, G. W.; Hughey, C. A. *J. Chem. Educ.* **1998**, *75*, 85.
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(19) Li. C.-J.; Chan, T.-H. *Tetrahedron* **1999**, *55*, 11149.

Table 1. KIEs for Irreversible Additions to PhCHO/PhCDO

reagent[a]	solvent	temp (°C)	KIE[b]	KIE (25 °C)[c]	EIE (25 °C)[d]	*I* (25 °C)[e]
allyl-SnBu₃, BF_3-Et₂O	CH₂Cl₂	78	0.81	0.87	0.71	>0.41
DIPT-allyl boronate	toluene	78	0.69	0.78	0.71	0.73?
DIPT-allyl boronate	THF	78	0.74	0.82	0.71	0.59?
DIPT-allyl boronate	toluene	24	0.85	0.85	0.71	0.48?
allyl zinc	aq THF	25	0.77	0.77	0.71	0.77
allyl lithium (ref 4a)	Et₂O	78	1.095	1.06	0.78	SET

[a] Commercially available reagents were used where available. [b] The average deviation is ±0.03 except as noted. [c] KIE values measured at −78 °C were corrected to 25 °C assuming the KIEs depend only on Δ*H*. [d] Theoretical EIE values from RCHO + RCD(R′)OM ⇌ RCDO + RCH(R′)OM, where R′ = H or alkyl and M = H or Li, from MP2/6-311+G** on acrolein-*1-d*, allyl alcoholate derivatives, acrolein, and allyl-*1-d* alcoholate derivatives. Thus, complete C−C bond formation is the standard here; see ref 4a and the text. [e] The greater than symbol refers to the fact that reactions may occur at higher temperatures, thus providing minimum *i* values. The question mark refers to the possibility that the transition state may be very early with respect to C−C bond formation but is completely complexed with the boron.

experiments. Under these circumstances k^H/k^D equals [H/D product (reagent limiting)]/[H/D product (aldehyde limiting)]. The results from various additions to benzaldehyde-*d* are given in Table 1 along with the previously determined SDKIE for addition of allyl lithium (1.095 at −78° C or 1.06 when extrapolated to room temperature), which is consistent with a rate-determining SET reaction. Also included in the table is the *i* value for the reaction. This is the exponent of a Brønsted-like relationship between the SDKIE and the equilibrium isotope effect, EIE, for the reaction:

SDKIE = EIE^i (or ln SDKIE = *i* ln EIE).[4a,9] To a first approximation, the *i* value should be a measure of progress along the reaction coordinate of the bond being made (or broken) provided that the hydrogen does not become involved extensively in reaction coordinate motion. Under these circumstances, the constant of the usual Brønsted relation is unity.

Discussion

The major point to be made in examining the data of the table is that all the secondary deuterium kinetic isotope effects for the allylations of benzaldehyde are inverse, except for those for the previously reported additions of allyl lithium and Grignard. *So there is no justification for rate-determining electron-transfer mechanisms in any of the reactions reported in this paper on the basis of SDKIEs.*

The additions of allyltributyl tin and allyl boronates to benzaldehyde involve strong Lewis acids, either BF_3 etherate or the boronate itself. So the possibility of rate-determining complexation needs to be examined. It is necessary to recall that BF_3 complexation of benzaldehyde is comparable to that of diethyl ether and that the equilibrium is established rapidly at room temperature such that the methylene protons of ether have an averaged chemical shift at roughly 0.23 M, where the separation of the methylene protons in ether and BF_3 etherate is 200 Hz. However, at −60 °C, the methylene protons of free and BF_3-complexed ether are separately visible. Further, there is a 1.28 ± 0.10 preference for BF_3 complexation of benzaldehyde-*d* over benzaldehyde-*h*. The latter observation suggests that rate-determining

BF_3 complexation would have a maximum KIE of 1/1.28 ± 0.07 at room temperature and would be much more inverse at −78 °C. Finally in this connection, the • value for the equilibria for BF_3 complexation of substituted benzaldehydes from the etherate in deuteriochloroform solution is −2.0.

In the case of BF_3 etherate induced addition of allyltributyl tin to benzaldehyde, it is likely that Lewis acid complexation of the aldehyde occurs before rate-determining C−C bond formation. The fact that these equilibria are established rapidly and that these complexes are formed prior to addition of the tin reagent reinforces the conclusion. Therefore, the SDKIE measured is that for C−C bond formation. If the BF_3 group attached to the benzaldehyde oxygen is like a proton, then the logarithm of the SDKIE can be compared to the logarithm of the equilbrium isotope effect for additions to benzaldehyde in the form of a linear free energy relationship. The equilibrium isotope effects, k^H/k^D, for addition of a hydride to acrolein to give a tetrahedral intermediate with a proton, a lithium ion, and a sodium ion attached to the negatively charged oxygen were calculated previously to be 1/1.28, 1/1.27, and 1/1.12, respectively,[4a] and the equilibrium isotope effect for addition of a carbon nucleophile was assumed to be 10% higher as described previously.[4a] The *i* value so obtained is at least 0.41 so the transition state is midway down the reaction coordinate with respect to C−C bond formation, and it must be late with respect to complexation by the Lewis acid. The *i* value is a minimum value because the actual temperature of the reaction is probably higher than −78 °C, leading to a smaller SDKIE than would be expected at the lower temperature; further, if the equilibrium isotope effect for BF_3 attached to the carbonyl oxygen were more like that of a lithium ion, then the *i* value would also be higher.

In the case of allyl boronate addition, no Lewis acid complex has been observed prior to reaction, so complexation might be rate-determining, and this could provide the very large inverse isotope effect observed. If this is the case, then the transition state leading to the complex with the correct geometry about the carbon−oxygen double bond (*E*) must be lower in energy than the other possibility, and this is not unreasonable. This has led to the suggestion that lone electron pair repulsions are important in a transition state that involves at least some C−C bond formation.[14b] Indeed, early calculations on the allyl borane addition to formaldehyde indicated some C−C bond formation in the transition state.[16]
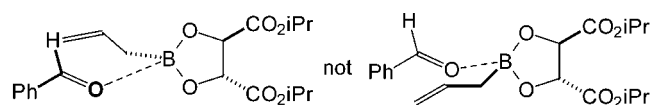
However, the face selectivity is relatively independent of solvent polarity from toluene to tetrahydrofuran, and diastereoselectivity with oxygenated aldehydes also shows no change from carbon tetrachloride to acetonitrile at comparable temperatures, so electrostatic repulsions would not appear to be a factor.

We have performed DFT calculations (6-31+G* basis set)[8] on a model system consisting of allyl ethylene glycol boronate and formaldehyde. The results suggest only weak interaction between the aldehydic carbon and the terminus of the allyl (2.40 A) in a chairlike transition

state which also reveals strong bonding between the aldehydic oxygen and the boron (1.60 A). This would represent an early transition state with respect to C−C bond formation and one that is very similar to the boronate complex of the aldehyde, which is consistent with the equilibrium isotope effects observed for BF_3 complexation of benzaldehyde. Indeed, calculations of harmonic frequencies for the transition state of the model system above as well as one with an axial deuterium and those of formaldehyde-*h* and -*d* allowed calculation of k^H/k^D of 1/1.27 at 25 °C for the model reaction using unscaled frequencies. This is similar to that obtained experimentally for the real system (Table 1). The calculations, however, provide no insight into the face selectivity, which would appear to be the result of steric and not electronic effects, vide infra.

The addition of allyl from what is most likely an allyl zinc species is also a two-electron polar addition judging by the inverse KIE. The contrast between allyl lithium and allyl zinc is important and suggests that the less active metal, not unreasonably, reduces the possibility of single-electron oxidation by benzaldehyde. Furthermore, the magnitude of the KIE suggests a late transition state because the *i* value, assuming that the counterion is a proton, is 0.62. It is useful to compare this addition with those of allyl indium and related reagents, all of which have inverse secondary deuterium kinetic isotope effects as measured by Chan.[20] Thus, none of these additions involve single-electron transfer.[21]

Experimental Section

General Procedures.

^{1}H NMR spectra were obtained at 400 MHz. Chemical shifts are reported in δ units relative to that of TMS in chloroform-*d* solution, where chloroform-*h* is the reference, which is assumed to be at δ 7.26 ppm. Column chromatography was performed on 100−200 mesh silica gel, and thin-layer chromatography was performed on 0.25 mm silica gel precoated glass sheets. IR spectra were obtained on a Fourier transform spectrophotometer. Preparative GC was performed using a gas chromatograph with thermal conductivity detection and either a DB-5 (6 ft × 1/4 in.) column or a Carbowax (12 ft × 1/4 in.) column. Dry tetrahydrofuran and diethyl ether were obtained by distillation under N_2 from sodium benzophenone ketyl. All glassware for addition reactions was flame-dried under vacuum with a N_2 purge.

Allyltributyl Stannane and Benzaldehyde.

Boron trifluoride etherate (2 equiv) was reacted with a mixture of benzaldehyde-*h* and -*d* in dry methylene chloride at −78 °C according to the procedures in ref 13. An excess of 1 or 1/10 equiv of allyltributyl stannane was added, and the reaction was allowed to warm to 0 °C. The reaction was quenched with water, and the organic phase was separated, dried, and concentrated to yield the alcohol previously characterized (ref 4a). After conversion to the methyl ether according to ref 4a, the fraction of protium at the α carbon from NMR spectra of the separate reactions was divided to obtain the kinetic isotope effects reported in the table.

Allyl Boronate and Benzaldehyde.

Diisopropyl (*R*,*R*)-2-allyl-1,3,2-dioxaborolane-4,5-dicarboxylate was prepared according to ref 14b and reacted with a deficiency of a mixture of benzaldehyde-*h* and -*d* according to

(20) Chan, T.-H. Paper in preparation for submission to *J. Org. Chem.*

(21) Measurement of secondary deuterium kinetic isotope effects in the additions to benzaldehyde by lithium pinacolate and trimethylsilylcyclohexanone enol catalyzed by Lewis Acids indicates that they are also inverse, revealing no incursion of single-electron-transfer mechanisms. Unpublished work, W. Bocian, Indiana University.

ref 14b. Then the mixture of benzaldehyde-*h* and -*d* was treated with a 10-fold excess of the mixture in toluene and tetrahydrofuran under the same reaction conditions. The resulting alcohol (ref 4a) in each case was treated with sodium hydride and then with methyl iodide according to ref 4a and analyzed by NMR to obtain the fraction of hydrogen at the α carbon in each case. The results were then divided to give the kinetic isotope effects reported in the table.

Allyl Bromide and Zinc and Benzaldehyde in Aqueous Tetrahydrofuran.[17]

To a 100 mL round-bottom flask were added 0.1 g (1.5 × 10⁻³ mol) of untreated zinc powder, 1.5 mL of saturated aqueous ammonium bromide solution, 1.5 mL (15 mM) of benzaldehyde (50:50 H/D), and 10 mL of distilled tetrahydrofuran. The mixture was stirred vigorously while 0.13 mL (1.5 mM) of allyl bromide was added quickly into the reaction mixture at room temperature. The mixture was stirred for 30 min, then 10 mL of diethyl ether was added, and the solution was filtered through a plug of glass wool into a separatory funnel. The organic layer was separated, and the aqueous layer was extracted twice with diethyl ether. The organic phases were combined and stirred with an excess of a saturated aqueous solution of sodium bisulfite for 1 h. The layers were separated, and the aqueous layer was extracted with two portions of diethyl ether. The organic layers were collected, dried, and evaporated under an aspirator vacuum to give a residue of 0.22 g of the alcohol which was characterized previously in ref 4a. The alcohol was converted to the methyl ether by the procedure of ref 4a, and the NMR spectra from three separate experiments were averaged and compared with the ratio of H and D in the product from reactions using a deficiency of benzaldehyde.

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