ORGANIC
LETTERS

2000
Vol. 2, No. 18
2813−2815

Equilibrium Constants between Boron Trifluoride Etherate and Carbonyl Compounds in Chloroform Solution

J. J. Gajewski* and P. Ngernmeesri

Department of Chemistry, Indiana University, Bloomington, Indiana 47401

gajewski@indiana.edu

Received June 20, 2000

ABSTRACT

$$>C{=}O \quad + \quad BF_3\text{-}OEt_2 \leftrightarrows \quad >C{=}O\text{-}BF_3 \quad + \quad OEt_2$$

Equilibrium constants for boron trifluoride complexation with carbonyl compounds relative to diethyl ether were determined in $CDCl_3$. With benzaldehyde the equilibrium constant is 0.208. There is a 1.28-fold preference for BF_3 bonding to benzaldehyde-D over benzaldehyde-H. The ρ^+ value for complexation with substituted benzaldehydes is –2.0. Equilibrium constants with cyclohexanone and isobutyraldehyde were found to be not very different from those predicted from the heats of addition of BF_3 relative to that for diethyl ether. The heats of addition can be correlated with Taft's β values and with β' values.

Since various additions to aldehyde carbonyl groups involve Lewis acid catalysis and often the use of boron trifluoride etherate,[1] it would appear to be appropriate to determine the equilibrium constant for relevant aldehydes under more or less synthetic chemistry reaction conditions. Of further concern should be the rate of the equilibration, substituent effects, and, because of interest in studying the mechanism of these additions by determination of deuterium kinetic isotope effects, the effect of deuterium at the carbonyl carbon on the equilibrium.[2]

The benzaldehyde−BF_3 complex has been prepared and characterized by X-ray crystallography.[3] It has the BF_3 moiety bound to an oxygen lone pair in a *transoid* (*E*) fashion. The same is true of 2-heptenal in methylene chloride solution.[4] Calorimetric determination of the heats of complexation of benzaldehyde and diethyl ether with BF_3 in methylene chloride solution indicate an enthalpy difference of ca. 1 kcal/mol favoring boron trifluoride etherate over benzaldehyde−boron trifluoride.[5] However, entropy differences, while not expected to be large, could modify this preference. Additions to other aldehydes and unhindered ketones were also found to be only slightly endothermic relative to addition to diethyl ether,[5] and similar questions about entropy differences can be posed.

In the hope of detecting a change in the chemical shift of either benzaldehyde or diethyl ether upon reaction assuming rapid exchange, which is the case for BF_3 in excess diethyl ether,[6] 1 equiv of benzaldehyde was added to 0.23 M boron trifluoride (BF_3) etherate in deuteriochloroform solution. While the spectrum resembled benzaldehyde with only a slight downfield shift of the ortho protons[4] and a modestly downfield shifted triplet for the diethyl ether methyl protons, the methylene protons appeared as a broad singlet at 3.98 ppm downfield from TMS. Under these same conditions, the spectrum of boron trifluoride etherate alone consists of a quartet at 4.20 ppm and a triplet at 1.4 ppm. For comparison, the methylene quartet of diethyl ether itself appears at 3.478 ppm in deuteriochloroform at room temperature. It therefore appears that boron trifluoride rapidly interchanges its position on ether and benzaldehyde at normal probe temperatures. Confirmation that the broad signal is due to rapid equilibration comes from the spectrum recorded at −60 °C in which the broad singlet is replaced by two quartets separated by 0.70 ppm. Calculation of the equilib-

---

[1] (a) Cornel, V. in *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. P., Ed.; John Wiley & Sons: New York, 1995 (under boron trifluoride). (b) Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1976**, *16*, 1295. (c) Yamamoto, Y. *Aldrichimca Acta* **1987**, *20*, 45.

[2] Gajewski, J.J.; Bocian, W.; Harris, N. J.; Olson, L. P.; Gajewski, J. P. *J. Am. Chem. Soc.* **1999**, *121*, 326.

[3] Reetz, M. T.; Hullmann, M.; Massa, W.; Berger, S.; Rademacher, P. Heymanns, P. *J. Am. Chem. Soc.* **1986**, *108*, 2405.

[4] Denmark, S. E.; Almstead, N. G. *J. Am. Chem. Soc.* **1993**, *115*, 3133.

[5] Gal, J.-F.; Maria, P.-C. *Prog. Phys. Org. Chem.* **1990**, *17*, 159.

[6] Fratiello, A.; Onak, T. P.; Schuster, R. E. *J. Am. Chem. Soc.* **1968**, *90*, 0, 1194. See also the following: Gillespie, R. J.; Hartman, J. S. *Can. J. Chem.* **1968**, *46*, 2147. Childs,. R. F.; Mulholland, D. L.; Nixon, A. *Can. J. Chem.* **1982**, *60*, 801.

10.1021/ol000164k CCC: $19.00

rium constant from the observed chemical shift relative to those of complexed and free diethyl ether at room temperature for reaction 1 gave a value of 0.208 ± 0.011, resulting

$$\mathrm{PhCH{=}O + BF_3{\cdot}OET_2 \leftrightarrows PhCH{=}O{\cdot}BF_3 + OEt_2} \quad (1)$$

from eight separate experiments. The relative heats of reaction of BF_3 with both benzaldehyde and diethyl ether in methylene chloride solution would suggest an equilibrium constant of 0.22 if there were no entropy difference and no solvent effect, and this is remarkably close to the value observed directly in chloroform.

Similar observations were made with benzaldehyde-*carbonyl*-D. However, the methylene protons of diethyl ether appeared at slightly higher field: 3.95 ppm. When seven experiments were averaged, the equilibrium constant was determined to be 0.266 ± 0.020. This allowed calculation of the equilibrium isotope effect or fractionation factor for deuterium between protio and deuterio benzaldehyde (reaction 2) to be 0.78 ± 0.07. Thus, complexation of deuterio benzaldehyde is favored over protio benzaldehyde by a factor of 1/0.78 or 1.28.

$$\mathrm{PhCHO + PhCDO{\cdot}BF_3 \leftrightarrows PhCHO{\cdot}BF_3 + PhCDO} \quad (2)$$

Confirming the magnitude and direction of the fractionation factor for reaction 2 is a 6-31G*/MP2 geometry optimization and harmonic frequency calculation[7a] for acrolein-H and -D and acrolein-H and -D BF_3.[7b] When these unweighted frequencies where inserted into the Bigeleisen equation characterizing a fractionation factor equilibrium,[7c] a value of 0.86 was obtained. The major contributor to this equilibrium isotope effect appears to be the change in the carbonyl-H stretching frequency (from 2997 cm^{-1} in acrolein to 3181 cm^{-1}, uncorrected, in the complex). The recently determined secondary deuterium kinetic isotope effects for hydride reductions and Grignard and lithium reagent addition to benzaldehyde assumed that rate-determining complexation of the Lewis acid portion of the these reagents would result in no large effect.[2] Clearly this is not the case with the strong Lewis acid examined here. Whether or not a large effect would be observed with metal cations has yet to be determined.

Potentially complicating the analyses described above is the possibility that there may be complexation of BF_3 with deuteriochloroform solvent because the methylene protons of diethyl ether appear at approximately 0.02 ppm lower field in 1. M BF_3−etherate in $CDCl_3$. When 1 equiv of benzaldehyde was added, the shift observed allowed calculation of an equilibrium constant which was 0.188. In effect, there was less free diethyl ether produced both before and after addition of benzaldehyde in the more concentrated solution. However, the equilibrium constants determined at the two concentrations are within experimental error which is substantially magnified relative to the difference in the chemical shifts observed because of the squaring of the ratios to obtain the equilibrium constants. Further, the heat of addition of BF_3 to methylene chloride was found[5] to be −2.4 kcal/mol which is much less than the −18.8 kcal/mol for the addition to diethyl ether in methylene chloride solvent so the difference in equilibrium constants is on the order of 7×10^{11}; therefore, even a concentration difference of a factor of 1000 should have little effect on pushing the equilibrium toward a $CDCl_3$−BF_3 complex.

The Hammett ρ^+ value was determined to be −2.0 ($r = 0.999$) from the equilibrium constants for *p*-anisyl (7.24), *p*-tolyl (0.838), and *p*-chloro (0.112) benzaldehyde at the same concentration as benzaldehyde itself in chloroform. The equilibrium constant for the *p*-nitro derivative was also determined, but its very small value (0.009) is subject to very large error so it was excluded from the analysis (its inclusion provides a ρ^+ value of −1.86; $r = 0.998$). The ρ^+ value is relatively small compared with that for solvolysis of cumyl derivatives (−4 to −5).[8] This is not inconsistent with the notion that the carbonyl carbon is strongly positively charged even before complexation.

The effect of methylene chloride and benzene solvent on the equilibrium constant for benzaldehyde complexation with boron trifluoride etherate was determined at both 0.23 and 1.0 M. The equilibrium constants determined in methylene chloride-D_2 were 0.16 ± 0.015 and 0.14 ± 0.01, respectively, and the equilibrium constants determined in benzene-D_6 were 0.15 ± 0.05 and 0.10 ± 0.03, respectively. The potential origins of these differences are multitudinous; however, the actual changes in chemical shift are not large, indicating that the relative concentrations do not change by more than 10%, i.e., 70:30 vs 75:25 so it is not profitable to pursue these effects at this time.

Finally, the equilibrium constants for complexation of boron trifluoride etherate with cyclohexanone and isobutyraldehyde were determined in chloroform-D to be 0.276 and 0.204, respectively. These equilibrium constants are not very different than those suggested from the heats of addition of BF_3 in methylene chloride solution to acetone and acetaldehyde relative to that of diethyl ether: + 0.6 kcal/mol and +2.1 kcal/mol, respectively, which lead to equilibrium constants of 0.36 and 0.029, respectively. Therefore, the data provided in ref 5 would appear to be a reasonable source for relative complexation preferences with BF_3 in solution. Also of interest is the fact that the relative

---

(7) (a) Gaussian 98. 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.; Baboul, A. G.; 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.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. Gaussian, Inc., Pittsburgh. PA, 1998. (b) Previous work in our laboratory (Harris, N. J. *J. Phys. Chem.* **1995**, *99*, 14689) revealed that this level of theory was necessary to reproduce the fractionation factors for deuterium between small molecules, and it became less accurate with larger molecules. Therefore, our calculations were performed at as high a level as possible on as small a model system as possible rather than performing a suboptimal calculation on benzaldehyde and benzaldehyde−BF_3 with the resources available. (c) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper Collis Publishers: New York, 1987; Chapter 2, Appendix 2.

(8) Reference 7, Chapter 4, Table 4.19.

complexation enthalpies for a wide range of solvent molecules besides methylene chloride, nitromethane, benzonitrile, acetonitrile, methyl acetate, acetone, diethyl ether, 1,4-dioxane, tetrahydrofuran, DMSO, DMF, and HMPA, reported in ref 5 can be correlated with the Taft β values alone ($r = 0.94$)[9] and with β' values ($r = 0.894$).[10] The fact that Taft β values provide a reasonable correlation is probably the result of the fact that these parameters were obtained from the spectroscopy of single molecule−base interactions. Single molecule−BF_3 interactions are being measured in the calorimetry experiment as opposed to a bulk solvent interaction with BF_3. More remarkable is the correlation with β' values which were derived from potassium ion transfer data between bulk solvents.[11]

Acknowledgment. We thank the Department of Energy for support of this work. P.N. thanks the Thai Government for an Undergraduate Scholarship to Indiana University. We also thank Marty Pagel, Ulrike Werner-Zwanziger, and Jeff Frey in the NMR facility of Indiana University for their help.

OL000164K

---

(9) For an excellent summary, see: Abraham, M. H.; Grellier, P. L.; Abboud, J.-L. M.; Doherty, R. M.; Taft, R. W. *Can, J. Chem.* **1988**, *66*, 2673.

(10) Gajewski, J. J. *J. Org. Chem.* **1992**, *57*, 5500. Gajewski, J. J.; Brichford, N. J. In *Structure and Reactivity in Aqueous Solution*; Cramer, C. J., Truhlar, D. G., Eds.; ACS Symposium Series #568; American Chemical Society: Washington, DC, 1994; p 229.

(11) It may be of interest to note that complexation of hydrogen ion with individual solvent molecules in the gas phase reported in ref 5 can be well-correlated with the combination of β' and the Kirkwood−Onsager function of dielectric, i.e., $(\epsilon - 1)/(2\epsilon + 1)$ and the polarizability parameters of ref 7, Chapter 2, Table 2.15, footnote c. However, complexation of lithium and potassium cation with individual solvent molecules in the gas phase (ref 5) can be well-correlated with only the combination of the Kirkwood−Onsager function and the polarizability parameters, that is, β or β' factors do not contribute in these two cases.