Tetrahedron Letters, Vol. 33, No. 46, pp. 6945-6948, 1992
Printed in Great Britain

0040-4039/92 $5.00 + .00
Pergamon Press Ltd

THE STRUCTURE OF THE 2-METHYLACROLEIN BORON TRIFLUORIDE COMPLEX IN THE CRYSTALLINE PHASE AND IN SOLUTION

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Summary: *A crystalline 1 : 1 complex of BF_3 and 2-methylacrolein has been isolated and shown to have molecular structure* ***1****. ^1H NMR molecular dynamics and NOE studies have demonstrated that the same s-trans structure of the complex predominates at 185 K in CD_2Cl_2 solution. The relevance of these results to the enantioselectivity of Diels-Alder reactions with chiral Lewis acids is discussed.*

The detailed understanding of the reaction mechanisms of enantioselective organic reactions, especially those involving chiral catalysts acting on achiral substrates, is important for the future evolution of this field. Recently a number of interesting enantioselective Diels-Alder reactions have been reported involving acrolein or 2-methylacrolein, cyclopentadiene and various chiral Lewis-acids as catalysts.[1] Although the observed enantioselectivities vary widely, higher values have generally been observed with 2-methylacrolein than with acrolein. Also, different face selectivities have been noted for these two aldehydes with a particular catalyst. The understanding of enantioselectivity, which clearly is much more feasible when enantioselectivity is high (>95 : 5), requires a knowledge of the detailed structure and concentration of each aldehyde-Lewis acid complex which is present in equilibrium and the relative rates for reaction of each with the diene. Even if the catalyst has a single fixed geometry in the complex with the α,β-enal, it is necessary to know the proportion of *s-cis* and *s-trans* α,β-enal complexes, since these will lead to enantiomeric products. As a first step toward obtaining such information we have studied the structure of the complex of boron trifluoride with 2-methylacrolein both in the crystalline state and in solution, with the results reported herein.[3]

A crystalline 1 : 1 complex of 2-methylacrolein and BF_3 was prepared as follows. A solution of 3 mmol of 2-methylacrolein in 3 ml of CH_2Cl_2 under dry N_2 was treated with 1 equiv of $BF_3 \bullet Et_2O$ and the resulting solution was overlayered with 8 ml of hexane at 23 °C and stored at -60 °C. After several days large colorless prisms were formed. A crystal of dimensions 0.34 x 0.36 x 0.50 mm was cut from a larger crystal (at -20 °C under dry Ar) and used for X-ray structure determination at -100 °C which revealed structure **1** for the complex.[2] The salient features of this structure are as follows: (1) the α,β-enal is in the *s-trans* geometry; (2) coordination of BF_3 is to the lone pair syn to the formyl proton with <BOC = 123.8°; (3) as compared to

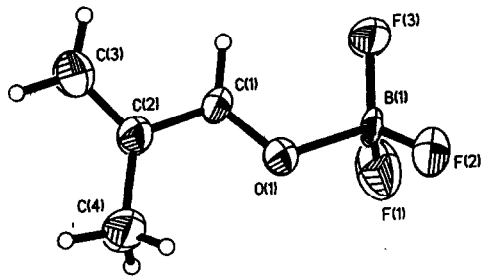
free acrolein, the O–C(1) bond in complex **1** is lengthened by 0.05 Å, the C(1)–C(2) bond is shortened by 0.03 Å and the C(2)–C(3) bond is almost unchanged.[4,5]

^{1}H NMR studies in CD_2Cl_2 solution have shown clearly that the same *s-trans* 2-methylacrolein–BF_3 complex overwhelmingly predominates in solution as well. Uncomplexed 2-methylacrolein is known to be more stable in the *s-trans* form than in the *s-cis* form by 2.2 kcal per mole,[6] and this is supported by ^{1}H NMR NOE studies in CD_2Cl_2 at 200 K which reveal the NOE enhancements shown in **2**. Similar NOE studies of 2-methylacrolein in the presence of excess BF_3 in CD_2Cl_2 at 200 K clearly indicate the presence of the static *s-trans* complex **3** with the NOE enhancements indicated. Variable temperature 500 MHz ^{1}H NMR studies of a 2 : 1 mixture of 2-methylacrolein and BF_3 in CD_2Cl_2 show that reversible complexation becomes slow on the NMR time scale below 243 K, with the result that discrete sharp spectra of the free α,β-enal and the α,β-enal–BF_3 complex are observed between 243 K and 185 K. The NOE data clearly indicate the presence of the *s-trans* complex **3** but not of the *s-cis* rotomer and the predominance of the former. It is certainly possible that a small fraction of complex is in the *s-cis* form, with the *s-trans* and *s-cis* forms in rapid equilibrium on the NMR time scale at 180 K, but the barrier to interconversion would have to be less than *ca.* 5 kcal per mole.

Low temperature ^{1}H NMR studies at 500 MHz were also carried out for a 1 : 1 mixture of 2-methylacrolein and BF_3•Et_2O. The reaction between them becomes slow on the NMR time scale at or below 200 K. The ratio of complexed and non-complexed 2-methylacrolein was found to be 27 : 73 and NOE studies again showed the presence of the *s-trans* complex but not its *s-cis* rotomer.

These results have the following implications for enantioselective Diels-Alder reactions of 2-methylacrolein and dienes under catalysis by chiral Lewis acids. Unless the chiral Lewis acid is structured to favor the *s-cis* α,β-enal complex, the *s-trans* complex will predominate and it is this complex which will lead to the major enantiomeric adduct unless there are relatively unfavorable factors which operate in the transition state for its conversion to product.[7] It would appear from this simple result that it might be easier to design a catalyst for enantioselective Diels-Alder reactions through the *s-trans*–α,β-enal–complex pathway. Interestingly however, the most selective catalytic system which has been developed to date appears to function via an *s-cis*–α,β-enal complex.[1f,1g] Future discoveries in this area are certain to be of great interest and significance both to synthetic chemistry and mechanistic theory. This work is being continued to determine quantitatively the position of the Lewis acid–*s-trans* α,β-enal and *s-cis*–α,β-enal complex equilibrium as a function of temperature and structure of the Lewis acid.[8]

X-Ray Structure of 2-Methylacrolein–BF_3Complex (1):



1

Bond Length of **1** (Å):

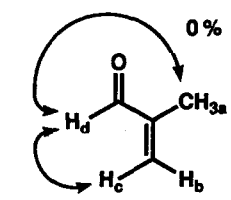
B(1)–O(1)	1.587 (8)	B(1)–F(1)	1.324 (11)
B(1)–F(2)	1.369 (10)	B(1)–F(3)	1.366 (11)
O(1)–C(1)	1.264 (9)	C(1)–C(2)	1.438 (9)
C(2)–C(3)	1.331 (13)	C(2)–C(4)	1.486 (13)

Bond Angles of **1** (°):

O(1)–B(1)–F(1)	103.9 (6)	O(1)–B(1)–F(2)	104.6 (6)
F(1)–B(1)–F(2)	114.3 (7)	O(1)–B(1)–F(3)	106.8 (5)
F(1)–B(1)–F(3)	115.1 (8)	F(2)–B(1)–F(3)	111.1 (7)
B(1)–O(1)–C(1)	123.8 (6)	O(1)–C(1)–C(2)	121.5 (7)
C(1)–C(2)–C(3)	114.7 (7)	C(1)–C(2)–C(4)	119.4 (7)
C(3)–C(2)–C(4)	125.9 (7)		

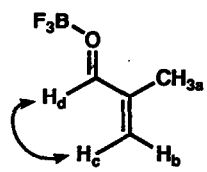
^{1}H NMR DATA for 2 and 3

Compound	T (K)	CH_{3a}	H_b	H_c	H_d
2	297	1.82	6.29	5.88	9.52
2	200	1.81	6.38	6.01	9.51



+8.8%, +8%

2



8%, +9.6%

3

3	297	2.02	7.18	7.00	9.30
3	270	2.02	7.18	7.00	9.28
3	250	2.02	7.17	6.99	9.23
3	215	2.00	7.18	7.01	9.21
3	200	1.98	7.20	7.02	9.20

References and Notes

1. (a) Hashimoto, S. I.; Komeshima, N.; Koga, K. *J. Chem. Soc. Chem. Comm.* **1979**, 437-438; (b) Furuta, K.; Shimizu, S.; Miwa, Y.; Yamamoto, H. *J. Org. Chem.* **1989**, *54*, 1483-1484; (c) Bir, G.; Kaufmann, D. *Tetrahedron Letters* **1987**, *28* 777-780; (d) Takasu, M.; Yamamoto, H. *Synlett* **1990**, 194-196; (e) Sator, D.; Saffrich, J.; Helmchen, G *Synlett.* **1990**, 197-198; (f) Corey, E. J.; Loh, T.-P. *J. Am. Chem. Soc.* **1991**, *113*, 8966-8967; (g) Corey, E. J.; Loh, T.-P.; Roper, T. D.; Azimioara, M. D.; Noe, M. C. *J. Am. Chem. Soc.* submitted May 1992.

2. X-Ray crystallographic data available from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge, CB2 1EZ, UK. Empirical formula $C_4H_6BF_3O$, triclinic, space group $P1^-$, a = 6.591 (2) Å; b = 6.930 (2) Å; c = 7.324 (3) Å, V = 320.4 (11) $Å^3$, Z = 2; D_C = 1.429 Mg/M^3. Bond distances and angles found for **1** were as indicated. Hydrogens were placed at calculated positions (d C–H = 0.96 Å).

3. For review on structures of Lewis acid–carbonyl complexes see (a) Shambayatti, S.; Crowe, W. E.; Schreiber, S. L. *Angew. Chem. Int. Ed. Engl.* **1990**, *29* 256-272; (b) Reetz, M. T.; Hüllmann, M.; Massa, W.; Berger, S.; Rademacher, P.; Heymanns, P. *J. Am. Chem. Soc.* **1986**, *108*, 2405-2408; (c) Loncharich, R. J.; Schwartz, T. R.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 14-23.

4. For data on *s-trans* acrolein in the gas phase see Blom, C. E.; Grassi, G.; Bauder, A. *J. Am. Chem. Soc.* **1984**, *106*, 7427-7431.

5. The lengthening of the O–C(1) bond is 0.03 Å greater than expected from 4-31G or STO-3G calculations on acrolein•BF_3. See, Guner, O. F.; Ottenbrite, R. M.; Shillady, D. D.; Alston, P. V. *J. Org. Chem.* **1987**, *52*, 391-394.

6. Durig, V. R.; Qiu, J.; Dehoff, B.; Littler, J. S. *Spectrochem. Acta* **1986**, *42A*, 89-103.

7. For theoretical calculations on this point, see Birney, D. M.; Houk, K. N. *J. Am. Chem. Soc.* **1990**, *112*, 4127-4133.

8. This research was supported financially by the National Science Foundation and the National Institutes of Health.

(Received in USA 7 July 1992; accepted 20 August 1992)