Tetrahedron Letters,Vol.30,No.11,pp 1357-1360,1989
Printed in Great Britain

0040-4039/89 $3.00 + .00
Pergamon Press plc

NEW LEWIS ACID CATALYSTS FOR THE DIELS-ALDER REACTION

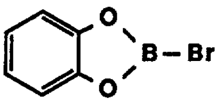
T. Ross Kelly*, Sanat K. Maity, Premji Meghani and Nizal S. Chandrakumar

Department of Chemistry, Boston College, Chestnut Hill, MA 02167 USA

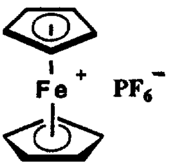
Abstract. *Catechol boron bromide (1) and ferrocenium hexafluorophosphate (2) function as Lewis acid catalysts for the Diels-Alder reaction.*

The development of chiral Lewis acids as catalysts for the asymmetric induction of Diels-Alder and other reactions is a subject of current interest. Recent years have seen some progress,[1,2] but no general solutions have yet emerged. In the course of studies aimed at the rational design of such catalysts it seemed useful to have new, structurally and conformationally defined sites of Lewis acidity capable of being embedded within a larger organic framework in a spatially defined manner. By appropriate manipulation of the contours of the organic scaffolding, one should then be able to design tunable, chiral environments around the Lewis acid center.

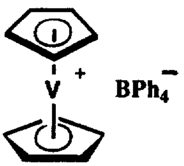
We now report that catechol boron bromide (1)[3] and ferrocenium hexafluorophosphate (2)[4] both function as Lewis acid catalysts for the Diels-Alder reaction. They also exhibit turnover. The results are summarized in Tables 1 and 2 on the following pages. For comparison purposes, both tables include reaction conditions required in the absense of catalysis.



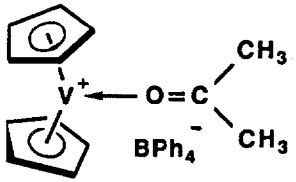
1



2



3



4

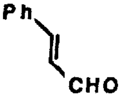
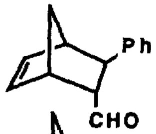
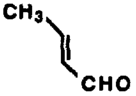
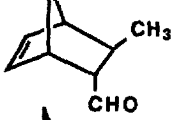
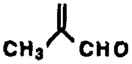
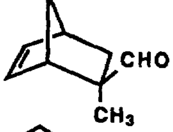
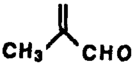
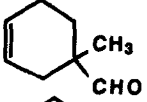
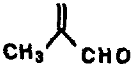
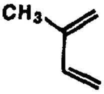
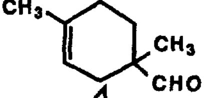
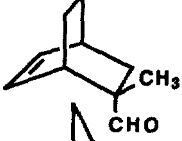
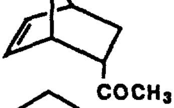
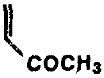
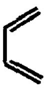
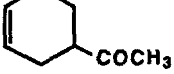
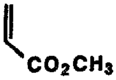
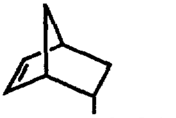
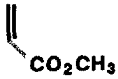
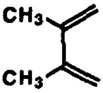
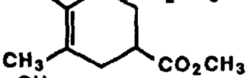
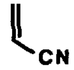
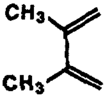
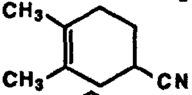
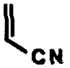
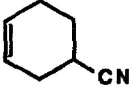
The potential of **1** to function as a Lewis acid catalyst was suggested by its ability to cleave ethers.[5] That ability is presumed[5] to depend in part on the Lewis acid nature of the boron atom. Examination of Table 1 reveals (i) that **1** is very effective as a catalyst with a wide variety of dienophiles and (ii) that **1** exhibits turnover with all dienophiles tested except, apparently, acrylonitrile.

The possibility that metallocenes might function as Lewis acid catalysts was inferred from the report[6] that vanadocenium tetraphenylborate (**3**) can be crystallized as the O-bonded, acetone complex **4**. The ferrocenium cation **2** was examined instead of **3** because of its easier synthesis.[4] A number of commercially available metallocene derivatives (zirconocene dichloride, titanocene dichloride, hafnocene dichloride, cobaltocenium hexafluorophosphate, and ferrocene itself) were also examined, but none exhibited Lewis acid catalysis under the assay system used.[7]

Ferrocenium hexafluorophosphate (**2**) is not so active a catalyst as **1** (Table 2), but it is less corrosive. Perhaps more importantly, the demonstration that **2** behaves as a Lewis acid raises the possibility that other metallocene derivatives may also exhibit useful Lewis acid behavior.

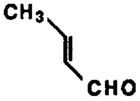
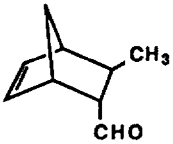
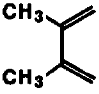
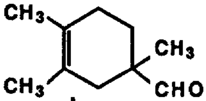
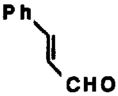
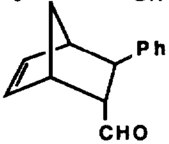
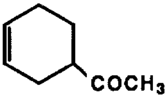
Attempts to incorporate **1** and **2** and related units into asymmetric frameworks with the objective of preparing rationally designed chiral Lewis acids are currently underway.

Table 1. Catalysis by Catechol Boron Bromide.

Entry	Dienophile	Diene	Reaction Conditions temp/time/equiv. of catalyst[a]	Isolated Yield(%)	Isomer Ratio[b] endo/exo	Product(s)[c,d]	Conditions for Uncatalyzed Reaction[1e]
1			-78°C / 5h / 0.25	80	86/14		No reaction at 20°C[8]
2			-78°C / 1.5h / 0.25	70	85/15		100°C / 4h[9]
3			-78°C / 0.5h / 0.25	95	10/90		100°C / 2-3h[10]
4			0°C / 4h / 0.25	68	-		150°C / 5h[11]
5			20°C / 2h / 0.25	89	e		180°C / 3h[12]
6			- 40°C / 9h / 0.25	42	82 /18		100°C / 3h[13]
7			-78°C / 1h / 0.25	94	e		0°C / 5h[14]
8			0°C / 5h / 0.25	62	-		140°C / 8h[15]
9			-78°C / 3h / 0.25	98	e		0°C / 2h[16]
10			0°C / 5h / 0.25	78	–		140°C / 3h[17]
11			0°C / 6h / 0.25 0°C / 6h / 1.0	29 91	– –		100°C / 20h[18]
12			20°C / 6h / 0.25	20	–		135°C / 12h[19]

(a) Catalyst : dienophile ratio, with the diene being in excess. (b) Determined by ^{1}H NMR analysis. (c) Major isomer shown. (d) All products were purified by flash column chromatography on silica gel and structures assigned are consistent with their spectra. (e) Other isomer was not detected by ^{1}H NMR spectroscopy.

Table 2*. Catalysis by Ferrocenium Hexafluorophosphate.

Entry	Dienophile	Diene	Reaction Conditions temp/time/equiv. of catalyst[a]	Isolated Yield(%)	Isomer Ratio[b] endo/exo	Product(s)[c,d]	Conditions for Uncatalyzed Reaction[1e]
1			0°C / 3h / 0.5	78	81/19		100°C / 4h[9]
2			20°C / 48h / 0.5	67	-		150°C / 5h[11]
3			0°C / 20h / 0.2	59	88/12		No reaction at 20°C[8]
4			20°C / 36h / 0.5	80	-		140°C / 8-10h[15]

* See notes to Table 1.

Acknowledgments. Support of this work by the National Institutes of Health (grant CA17631) is gratefully acknowledged. We thank Dr. L.B. Kool for several helpful conversations and Dr. J.A. Gladysz for an informative discussion and a preprint of reference 6c. P. M. thanks the Fulbright Program for a travel award.

References and Notes

1. For recent reviews, see: (a) L.A. Paquette In "Asymmetric Synthesis"; J.D. Morrison, Ed.; Academic Press: Orlando, FL, 1984; vol. 3B, p 455. (b) W. Oppolzer, *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 876. (c) G. Helmchen, R. Karge and J. Weetman In "Modern Synthetic Methods"; R. Scheffold, Ed.; Springer-Verlag: Berlin, 1986; Vol. 4, p 262. (d) W. Oppolzer, *Tetrahedron* **1987**, *43*, 1969. (e) For tables of uncatalyzed Diels-Alder reactions see: A.S. Onishchenko, "Diene Synthesis," Israel Program for Scientific Translations, Jerusalem, 1964.
2. Among recent references to chiral Lewis acids, see (a) M.M. Guseinov, I.M. Akhmedov and E.G. Mamedov, *Azerb. Khim. Zh.* **1976**, 46 [*Chem. Abstr.* **1976**, *85*, 176925z]. (b) S. Hashimoto, N. Komeshima and K. Koga, *J. Chem. Soc., Chem. Commun.* **1979**, 437. (c) M. Bednarski and S. Danishefsky, *J. Am. Chem. Soc.* **1983**, *105*, 3716. (d) M. Bednarski and S. Danishefsky, *J. Am. Chem. Soc.* **1983**, *105*, 6968. (e) M. Bednarski, C. Maring and S. Danishefsky, *Tetrahedron Lett.* **1983**, *24*, 3451. (f) T.R. Kelly, A. Whiting and N.S. Chandrakumar, *J. Am. Chem. Soc.* **1986**, *108*, 3510. (g) K. Narasaka, M. Inoue and N. Okada, *Chem. Lett.* **1986**, 1109. (h) K. Maruoka, M. Sakurai, J. Fujiwara and H. Yamamoto, *Tetrahedron Lett.* **1986**, *27*, 4895. (i) K. Narasaka, M. Inoue and T. Yamada, *Chem. Lett.* **1986**, 1967. (j) M.T. Reetz, S.-H. Kyung, C. Bolm and T. Zierke, *Chem. Ind.* **1986**, 824. (k) G. Bir and D. Kaufmann, *Tetrahedron Lett.* **1987**, *28*, 777. (l) M. Quimpere and K. Jankowski, *J. Chem. Soc., Chem. Commun.* **1987**, 676. (m) C. Chapuis and J. Jurczak, *Helv. Chim. Acta* **1987**, *70*, 436. (n) D. Seebach, A.K. Beck, R. Imwinkelried, S. Roggo and A. Wonnacott, *Helv. Chim. Acta* **1987**, *70*, 954. (o) H. Takemura, N. Komeshima, I.

Takahashi, S. Hashimoto, N. Ikota, K. Tomioka and K. Koga, *Tetrahedron Lett.* **1987**, *28*, 5687. (p) K. Narasaka, M. Inoue, T. Yamada, J. Sugimori and N. Iwasawa, *Chem. Lett.* **1987**, 2409. (q) C.J. Northcott and Z. Valenta, *Can. J. Chem.* **1987**, *65*, 1917. (r) K. Maruoka, T. Itoh, T. Shirasaka and H. Yamamoto, *J. Am. Chem. Soc.* **1988**, *110*, 310. (s) K. Furuta, M. Yoshikazu, K. Iwanaga and H. Yamamoto, *J. Am. Chem. Soc.* **1988**, *110*, 6254.

3. W. Gerrard, M.F. Lappert and B.A. Mountfield, *J. Chem. Soc.* **1959**, 1529.
4. D.M. Duggan and D.N. Hendrickson, *Inorg. Chem.* **1975**, *14*, 955.
5. (a) P.F. King and S.G. Stroud, *Tetrahedron Lett.* **1985**, *26*, 1415. (b) R.K. Boeckman, Jr. and J.C. Potenza, *Tetrahedron Lett.* **1985**, *26*, 1411.
6. (a) G. Fachinetti, S.D. Nero and C. Floriani, *J. Chem. Soc., Dalton Trans.* **1976**, 1046. X-ray: S. Gambarotta, M. Pasquali, C. Floriani, A. Chiesi-Villa, and C. Guastini, *Inorg. Chem.* **1981**, *20*, 1173. (b) Cationic Cp_2Zr^{IV} alkyl complexes have also been shown to form adducts with THF and MeCN. For x-ray structures and characterization, see: R.F. Jordan, C.S. Bajgur, R. Willett and B. Scott, *J. Am. Chem. Soc.* **1986**, *108*, 7410. R.F. Jordan, W.E. Dasher and S.F. Echols, *J. Am. Chem. Soc.* **1986**, *108*, 1718. R.F. Jordan, C.S. Bajgur, W.E. Dasher and A.L. Rheingold, *Organometallics* **1987**, *6*, 1041. R.F. Jordan, R.E. LaPointe, C.S. Bajgur, S.F. Echols and R. Willett, *J. Am. Chem. Soc.* **1987**, *109*, 4111. (c) For a recent related review see Y.-H. Huang and J.A. Gladysz, *J. Chem. Ed.* **1988**, *65*, 298. (d) For recent examples of cationic rhenium aldehyde and ketone complexes, see J.M. Fernandez, K. Emerson, R.D. Larsen and J.A. Gladysz, *J. Chem. Soc., Chem. Commun.* **1988**, 37. (e) For some recent examples of transition metal Lewis acid catalysis of the Diels-Alder reaction in particular, see: R.V. Honeychuck, P.V. Bonnesen, J. Farahi and W.H. Hersh, *J. Org. Chem.* **1987**, *52*, 5293 and earlier work cited therein.
7. All "reactions" were performed in dichloromethane solution containing cinnamaldehyde (in molar equivalence to the metallocene) and excess cyclopentadiene at temperatures ranging from -78°C to room temperature, assaying for reaction by t.l.c. with an authentic sample of adduct for reference.
8. We observed no reaction in dichloromethane solution in the absence of catalyst over 24 h at room temperature, monitoring by t.l.c. with an authentic sample of adduct for reference.
9. O. Diels and K. Alder, *Ann.* **1929**, *470*, 62.
10. S. Beckmann and R. Bamberger, *Ann.* **1953**, *580*, 198.
11. H. Pines, F.J. Pavlik and V.N. Ipafieff, *J. Am. Chem. Soc.* **1951**, *73*, 5738.
12. G.N. Koshel and M.I. Farberov *Izv. Vysshikh Uchebn. Zavedenii, Khim. i Khim. Tekhnol.* **1964**, *7*, 639, [*Chem. Abstr.* **1965**, *62*, 3997f].
13. O. Diels and K. Alder, *Ann.* **1930**, *478*, 127.
14. We observed complete reaction in a dichloromethane solution containing a 3-fold excess of cyclopentadiene at 0°C after 5 h. See also A.F. Plate and T.A. Merrovich, *Bull. acad. sci. U.R.S.S. Classe sci. Chim.* **1947**, 219 [*Chem. Abstr.* **1948**, *42*, 5440a].
15. A.A. Petrov, *J. Gen. Chem. U.S.S.R.* **1941**, *11*, 309 [*Chem. Abstr.* **1941**, *35*, 5873^6].
16. J.D. Roberts, E.R. Trumbull, Jr., W. Bennett and R. Armstrong, *J. Am. Chem. Soc.* **1950**, *72*, 3116.
17. K. Alder and W. Vogt, *Ann.* **1949**, *564*, 109.
18. A.P. Terent'ev, A.N. Kost and S.M. Gurvich, *Vestnik Moskov Univ.* **6**, No. 12, *Ser. Fiz.-Mat.* i *Estestven. Nauk* **1951**, No. 8, 79 [*Chem. Abstr.* **1953**, *47*, 6878a].
19. J. Gillois-Doucet and R. Rumpf, *Bull. Soc. Chim. Fr.* **1954**, 610.

(Received in USA 30 December 1988)