Pergamon

Tetrahedron Letters, Vol. 35, No. 29, pp. 5141-5144, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)01008-0

Metal Alkoxide Catalysis of Catecholborane and Borane Reductions. Mechanistic Studies.

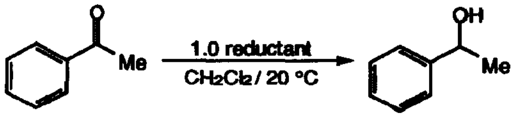
Craig W. Lindsley and Marcello DiMare*

Department of Chemistry, University of California, Santa Barbara, CA, 93106

Abstract: Catalytic quantities of transition metal alkoxides such as Ti(O*i*Pr)$_4$ have been found to accelerate dramatically the rate of catecholborane and BH_3·THF reductions of ketones. Experiments suggest catalysis is achieved by the formation of alkoxyborohydrides.

Catecholborane (CB) and BH_3·THF have garnered attention recently with their use in Group 9[1] and samarium catalyzed[2] olefin hydroboration and oxazaborolidine catalyzed[3] ketone reduction, respectively. Given the Lewis acidic character present in some of these catalyst systems and $TiCl_4$ accelerated BH_3·THF reductions,[4] the examination of Lewis acids in conjunction with these reductants seemed appropriate. We report observations on the accelerating effect of transition metal alkoxides on CB and BH_3·THF reductions of ketones. Interestingly, mechanistic studies suggest that it is the Lewis *basic* rather than acidic character of these amphoteric materials that leads to accelerated reductions.

After surveying a number of transition metal-containing compounds,[5] Ti(O*i*Pr)$_4$, Al(O*i*Pr)$_3$, and Zr(O*i*Pr)$_4$ were found to provide marked accelerations of CB and BH_3·THF reductions of ketones. For example, uncatalyzed CB reduction of acetophenone (0.25 M, CH_2Cl_2, 20 °C) requires ca. 24 h for complete reduction; the addition of 10 mol% Ti(O*i*Pr)$_4$ reduces reaction time to 30 min (93% isolated yield). Similarly, BH_3·THF reduction of acetophenone (0.25 M, CH_2Cl_2, 0 °C) requires 30 min; the addition of 10 mol% Ti(O*i*Pr)$_4$ ensures complete reduction in less than 1 min (95% isolated yield). Given the ready availability of optically pure metal alkoxides and recent mechanistic observations regarding CB chemistry,[6] further studies seemed warranted.



	reaction time	
reductant	uncatalyzed	0.1 Ti(O*i*Pr)$_4$
catecholborane	24 h	30 min
BH_3·THF	30 min	<1 min

Combination of Ti(O*i*Pr)$_4$ and CB 1:10 in the presence or absence of substrate immediately gives dark red solutions when dilute, or red-black precipitates when concentrated, in several solvents.[7] Examination of the supernatant by ^{13}C NMR from a concentrated sample using 1:1 Ti(O*i*Pr)$_4$/CB in $CDCl_3$ shows no signals associated with catechol. Collection and hydrolysis of the corresponding precipitate gives catechol.

UV-VIS spectra of dilute 1:1 $Ti(OiPr)_4$/CB CH_2Cl_2 solutions show absorptions at 242 (ε 7,500) and 380 nm (broad; ε 3,400).[8] ^{11}B NMR spectroscopy was also applied, relying on authentic samples[9] and analogy to literature values[10] to make assignments. The CH_2Cl_2 solutions from 1:5 $Ti(OiPr)_4$ and CB showed unreacted CB (d, J = 193 Hz, 29.0 ppm), $HB(OiPr)_2$ (d, J = 159 Hz, 27.4 ppm), and small amounts of what is consistent with $(C_6H_4O_2)B(OiPr)$ (s, 23.1 ppm). A 1:1 ratio gives predominately $B(OiPr)_3$ (s, 17.7 ppm) and small amounts of $HB(OiPr)_2$.

Apparently rapid metathesis takes place when $Ti(OiPr)_4$ and CB are combined, leading to titanium catecholate complexes, known to be deeply colored (red-brown-black) solids with similar UV-VIS spectra,[11] and several boron-containing species depending upon the stoichiometry (eq 1). The formation of $HB(OiPr)_2$, a new potential reductant or catalyst, required evaluation. When acetone and $BH_3 \cdot THF$ are mixed in a 2:1 ratio, $HB(OiPr)_2$ is cleanly generated, as shown by ^{11}B NMR. By itself, however, it is only a modestly better reducing agent than CB, requiring 4 h to reduce acetophenone (0.25 M, CH_2Cl_2), and when added in small amounts to CB and ketones mixtures led to no significant acceleration.

(1)

Unlike CB reductions, the catalysis of $BH_3 \cdot THF$ reductions by $Ti(OiPr)_4$ is dependent on the order of addition. When a solution of ketone and $Ti(OiPr)_4$ is treated with $BH_3 \cdot THF$, reduction requires less than 1 min at 0 °C. When a solution of $Ti(OiPr)_4$ is treated first with $BH_3 \cdot THF$ and then ketone, the reduction rate is the same as the uncatalyzed reaction. Once again, ^{11}B NMR[9,10] showed migration of oxygenated substituents from titanium to boron. The mixing of $Ti(OiPr)_4$ and $BH_3 \cdot THF$ (1:10) leads to the immediate formation of $HB(OiPr)_2$. A 1:1 ratio leads to $HB(OiPr)_2$, $B(OiPr)_3$, and absorptions that are consistent with alkoxyborohydrides (m, -14.6; m, -22.2; m, -29.8).[12]

Additional mechanistic insight was obtained by substituting $KOtBu$ for $Ti(OiPr)_4$ in $BH_3 \cdot THF$ and CB reductions.[13] For both, ketone reduction rates were comparable to those with $Ti(OiPr)_4$ catalysis and independent of addition order, pointing to the Lewis *basic* properties of the other metal alkoxides as the source of catalysis. Presumably, $KOtBu$ and $BH_3 \cdot THF$ combine to give $K[tBuOBH_3]$, which then disproportionates to related alkoxyborohydrides and eventually borohydride, as others have observed (eq 2).[14] Events are probably similar for CB (eq 3), while the overall slower reactions may be due to its lower Lewis acidity ($Ti(OiPr)_4$ alkoxyborohydrides disfavored at equilibrium). Given the direct observation of alkoxyborohydrides when $BH_3 \cdot THF$ and $Ti(OiPr)_4$ are combined 1:1, it is probable that the other metal alkoxides examined behave similarly.

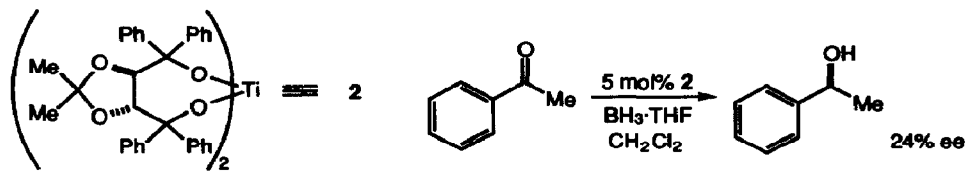
$$BH_3 + KOtBu \longrightarrow [tBuOBH_3]K \longrightarrow [(tBuO)_{4-n}BH_n]K \qquad (2)$$

(3)

A question that arises is why the order of addition is important for $Ti(OiPr)_4$ catalysis of $BH_3 \cdot THF$ reductions. One explanation is that there are two competing processes (eq 4). In the presence of ketone and $BH_3 \cdot THF$, the alkoxyborohydride and ketone react preferentially to give reduction. In the absence of ketone, the alkoxyborohydrides must undergo further modifications by BH_3·THF to such an extent that the titanium can no longer act as a gegenion to an alkoxyborohydride or donate an alkoxide to allow additional alkoxyborohydride generation.[15] That the order of addition is unimportant for $Ti(OiPr)_4$ catalysis of CB reductions probably reflects the reduced Lewis acidity of CB relative to BH_3·THF and the lower concentration of alkoxyborohydrides.

(4)

Concurrent with the mechanistic studies, three optically pure alkoxides were examined as prospective catalysts. Two are titanates of tartaric acid derivatives developed by Seebach, so called TADDOL titanates,[16] and the other a titanate derived from menthol:[17] $(TADDOL)Ti(OiPr)_2$ (**1**), $(TADDOL)_2Ti$ (**2**), and $Ti(O\text{-menthyl})_4$ (**3**). Perhaps not unexpectedly given the mechanistic pathways described, CB and BH_3·THF reductions of acetophenone with these catalysts gave low enantioselectivities. The best (24% ee[18]) was observed, however, with the combination 5 mol% **2** and BH_3·THF in CH_2Cl_2 (eq 5).



(5)

The very recent report by Evans and coworkers[2b] that certain transition metal complexes will accelerate CB hydroboration of alkenes suggested examining this reaction also.[19] By ^{11}B NMR,[9,10] the combination of CB, cycloheptene, and $Ti(OiPr)_4$ in a 2:1:0.1 ratio (THF solution) at first revealed unreacted CB, $HB(OiPr)_2$, $(C_6H_4O_2)B(OiPr)$, and over the course of hours $(C_6H_4O_2)B(OC_7H_{13})$ (s, 23.4) and $(C_7H_{13}O)_nB(OiPr)_{3-n}$ (s, 17.5 ppm). Substitution of Cp_2ZrCl_2 for $Ti(OiPr)_4$ led to the observation of only unreacted CB and $B(OC_7H_{13})_3$ (s, 17.5 ppm). In addition, authentic $(C_6H_4O_2)B(C_7H_{13})$ upon treatment with stoichiometric $Ti(OiPr)_4$ gave no new boron-containing species. No evidence of any intermediate(s) possessing a B-C bond was obtained, for example $(C_6H_4O_2)B(C_7H_{13})$ (s, 36.1 ppm). We are at a loss to explain the absence of B-C bonded intermediates as great pains were taken to exclude O_2, which could oxidize B-C bonded intermediates and prevent their observation.

In conclusion, the acceleration of CB and BH_3·THF reductions by several metal alkoxides has been observed. Our evidence suggests that these accelerations are due to reactions involving the metal alkoxides and reducing agents to produce alkoxyborohydrides or borohydride itself. The large number of species observed and inferred in these reactions of CB and BH_3·THF should serve as a warning to those involved in their chemistry.

Acknowledgment is made to the University of California and to the Donors of The Petroleum Research Fund, administered by the American Chemical Society, for support of this research. MD thanks the American Cancer Society for a Junior Faculty Research Award. Mr. Tim Gross is thanked for his assistance in acquiring the reported ^{11}B NMR data.

References and Notes

1. (a) Burgess, K.; Ohlmeyer, M. J. *Chem. Rev.* **1991**, *91*, 1179-1191 and references therein. (b) Evans, D. A.; Fu, G. C.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1992**, *114*, 6671-6679. (c) Evans, D. A.; Fu, G. C.; Anderson, B. A. *J. Am. Chem. Soc.* **1992**, *114*, 6679-6685. (d) Burgess, K. B.; van der Donk, W. A.; Westcott, S. A.; Marder, T. B.; Baker, R. T.; Calabrese, J. C. *J. Am. Chem. Soc.* **1992**, *114*, 9350-9359.
2. (a) Harrison, K. N.; Marks, T. J. *J. Am. Chem. Soc.* **1992**, *114*, 9220-9221. (b) Evans, D. A.; Muci, A. R.; Stürmer, R. *J. Org. Chem.* **1993**, *58*, 5307-9.
3. For a review, see: Wallbaum, S.; Martens, J. *Tetrahedron: Asymmetry* **1992**, *3*, 1475-1504.
4. Sarko, C. R.; Guch, I. C.; DiMare, M. *J. Org. Chem.* **1994**, *59*, 705-706.
5. Generally, mixed halide and alkoxide metals such as $Ti(O\textit{i}Pr)_2Cl_2$ led to one "turnover", while metal halides such as Cp_2ZrCl_2 showed no catalytic effect.
6. (a) Burgess, K.; Jaspars, M. *Tetrahedron Lett.* **1993**, *34*, 6813-6816; (b) Westcott, S. A.; Blom, H. P.; Marder, T. B.; Baker, R. T.; Calabrese, J. C. *Inorg. Chem.* **1993**, *32*, 2175-2182.
7. Evans and coworkers have noted the same behavior with this combination. Private communication.
8. Mixing $Ti(O\textit{i}Pr)_4$ and catechol 1:1 in CH_2Cl_2 gave essentially the same UV-VIS spectrum.
9. Authentic samples of CB, $BH_3{\cdot}THF$, $HB(O\textit{i}Pr)_2$, $(C_6H_4O_2)B(C_7H_{13})$, and $(C_6H_4O_2)B(OC_7H_{13})$ were prepared or purchased.
10. All ^{11}B NMR spectral data is referenced to $BF_3{\cdot}OEt_2$, see: Nöth, H.; Wrackmeyer, B. *Nuclear Magnetic Resonance Spectroscopy of Boron Compounds. Vol 14. NMR Basic Principles and Progress;* Springer-Verlag: New York, 1978.
11. Borgias, B. A.; Cooper, S. R.; Koh, Y. B.; Raymond, K. N. *Inorg. Chem.* **1984**, *23*, 1009-1016.
12. James, B. D.; Wallbridge, M. G. H. *J. Inorg. Nucl. Chem.* **1966**, *28*, 2456-2457.
13. Camphor and norcamphor were reduced using $BH_3{\cdot}THF$ under several conditions with the view of using endo/exo ratios as a mechanistic probe, but the selectivity varied too little. For example, norcamphor gave 84:16$\leq$ endo/exo $\leq$ 95:5 having varied addition order and stoichiometry of reagents.
14. (a) Schlesinger, H. I.; Brown, H.C.; Hoekstra, H. R.; Rapp, L. R. *J. Am. Chem. Soc.* **1953**, *75*, 199-204. (b) Rickborn, B.; Wuesthoff, M. T. *J. Am. Chem. Soc.* **1970**, *92*, 6894-6904.
15. Other than indirect ^{11}B NMR data, we have no information about titanium species generated.
16. For an overview of this work, see: Seebach, D.; Plattner, D. A.; Beck, A. K.; Wang, Y. M.; Hunziker, D.; Petter, W. *Helv. Chim. Acta* **1992**, *75*, 2171-2209.
17. Farina, M.; Bressan, G. *Chem. Abstr.* **1962**, *56*, 5621a.
18. Enantioselectivities determined by optical rotation.
19. Uncatalyzed alkene hydroboration by CB requires days at elevated temperature, but with the addition $Ti(O\textit{i}Pr)_4$ the reaction takes overnight at 20 °C.

(Received in USA 3 *May* 1994; *accepted* 19 *May* 1994)