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REGIO- AND STEREO-SELECTIVITIES IN THE TITANIUM COMPLEX CATALYZED HYDROBORATION OF CARBON-CARBON DOUBLE BONDS IN VARIOUS UNSATURATED COMPOUNDS

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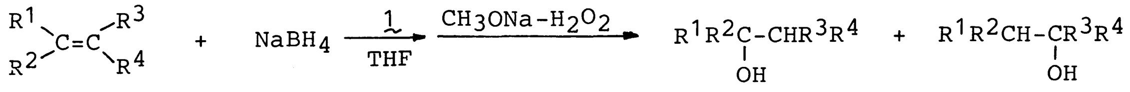
The titanium complex prepared from $TiCl_3$ and $NaBH_4$ in THF in the presence of 18-crown-6 promotes the catalytic hydroboration of carbon-carbon double bonds in alkenes, alkadienes and unsaturated ethers with $NaBH_4$, giving sodium organoborates which can be converted into alcohols by oxidation with H_2O_2/CH_3ONa. The reaction proceeds with high regio- and stereo-selectivities.

We have previously reported that the Ti complex generated from Cp_2TiCl_2 and $LiBH_4$ serves as a catalyst for hydroboration of alkenes.[1] Sodium borohydride can also be utilized as a reagent for the hydroboration if the reaction is carried out in the presence of 18-crown-6.[2] We now report that the reagent system consisting of $TiCl_3$-$NaBH_4$-18-crown-6 promotes a highly regio- and stereo-selective hydroboration of double bonds in various unsaturated compounds with $NaBH_4$ under mild conditions.

In a typical procedure, $TiCl_3$ (0.55 mmol) was added to a mixture of $NaBH_4$ (2.64 mmol) and 18-crown-6 (0.50 mmol) in THF (10 ml), and the mixture was stirred for 1 h at 30 °C under argon atmosphere. During this period, the mixture turned to dark violet. Styrene (2.52 mmol) was then added, and the mixture was stirred for 3 h at the same temperature. After adding a 3 mol dm^{-3} methanolic CH_3ONa solution (3 ml) and then 30% aqueous H_2O_2 (5 ml) at 40 °C, the resulting mixture was extracted with ether. The GLC analysis of the organic layer indicated that the reaction mixture contains 1- and 2-phenylethanols (90%) in a 80:20 ratio along with small amounts of ethylbenzene (2%) and unreacted styrene (6%).

The efficiency of the hydroboration of styrene varied with kinds of the catalysts employed. The results are given in Table 1.

$$TiCl_3 \quad + \quad NaBH_4 \xrightarrow[\text{THF}]{\text{18-crown-6}} \underset{\mathbf{1}}{\text{Ti complex}}$$



$$R^1R^2C{=}CR^3R^4 \quad + \quad NaBH_4 \xrightarrow[\text{THF}]{\mathbf{1}} \xrightarrow{CH_3ONa\text{-}H_2O_2} R^1R^2\underset{OH}{C}\text{-}CHR^3R^4 \quad + \quad R^1R^2CH\text{-}\underset{OH}{C}R^3R^4$$

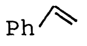
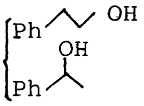
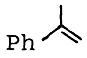
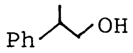
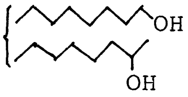
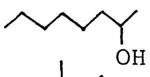
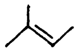
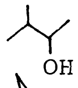
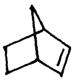
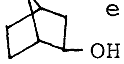
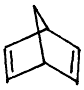
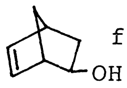
The $TiCl_3$-$NaBH_4$-18-crown-6 system was found to be especially effective for the hydroboration of alkenes under mild conditions. In a similar manner, various alkenes and alkadienes were converted into alcohols. The results are listed in Table 2.

Table 1. Effects of Catalysts on the Hydroboration-Oxidation Reaction of Styrene in THF[a)]

Catalyst	Reaction conditions temp /°C	time/h	Yield of phenyl-ethanols/%[b)]	Ratio of 1-ol/2-ol
Cp_2TiCl_2	65	5	70	69 / 31
Cp_2ZrCl_2	65	24	0	———
$TiCl_3$	30	3	90	80 / 20
$TiCl_4$	65	5	33	72 / 28

a) All the reactions were conducted by using the reagent system; styrene : $NaBH_4$: catalyst : 18-crown-6 = 5 : 5 : 1 : 1.
b) Yields were determined by GLC and based on styrene used.

Table 2. Hydroboration-Oxidation Reaction of Alkenes and Alkadienes[a)]

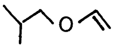
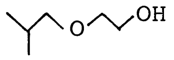
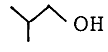
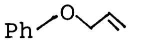
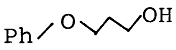
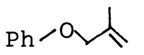
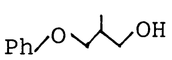
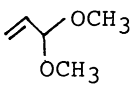
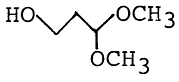
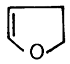
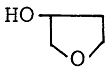
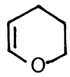
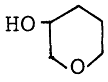
Substrate	Reaction time/h	Total yield/%[b)]	Product(s)	Ratio[c)]
	3	90		80 (69) 20 (31)
	5	84		—
	3	92		95 (94) 5 (6)
	5	84	 d)	—
	5	85		—
	20	92	 e)	—
	5	77	 f)	—
	5	79	 f)	—
	24	80	 f)	—

a) Substrate : $NaBH_4$: $TiCl_3$: 18-crown-6 = 5 : 5 : 1 : 1; at 30 °C.
b) GLC yields based on substrates used. c) The figures in parentheses refer to the ratios obtained by the hydroboration using the Cp_2TiCl_2-$NaBH_4$-18-crown-6 reagent system.[2)] d) A trace amount (<1%) of 1-octanol was detected. e) A trace amount (<1%) of the endo-isomer was detected. f) Trace amounts (<1%) of the corresponding diols were detected.

This reagent system was also successfully applied to the hydroboration of oxygen-containing unsaturated compounds.$^{3)}$ The results are listed in Table 3.

The above catalytic reactions have several characteristic features: (1) The reagent system $TiCl_3$-$NaBH_4$-18-crown-6 efficiently promotes the catalytic hydroboration of carbon-carbon double bonds in a variety of unsaturated organic compounds. It is worth noting here that when the Cp_2TiCl_2-$NaBH_4$-18-crown-6 reagent system is applied to vinyl and allyl ethers, the reductive C-O bond cleavage reaction occurs in preference to the hydroboration of the double bonds: indeed, isobutyl alcohol and phenol were obtained, respectively, as predominant products by the reaction of isobutyl vinyl ether and allyl phenyl ether with the Cp_2TiCl_2-$NaBH_4$-18-crown-6 reagent system. Allyl ethers also undergo the reductive C-O bond cleavage upon treating with the Cp_2TiCl_2-$LiAlH_4$ reagent system.$^{4)}$ (2) The regioselectivity in the above hydroboration-oxidation reaction is relatively high. For mono-, di-, and tri-substituted alkenes, the hydroboration occurred preferentially in an anti-Markownikoff fashion. For isolated dienes, the monohydroboration on a specific double bond predominated at 30 °C even in the presence of excess $NaBH_4$. This is in sharp contrast to the fact that the hydroboration of dienes such as 1,5-hexadiene and 1,7-octadiene with diborane gives mainly dihydroborated products.$^{5,6)}$ The preferential anti-Markownikoff-type addition of $NaBH_4$ was also observed for oxygen-containing unsaturated compounds. The regioselectivity in the hydroboration reported in this paper is higher than that in the hydroboration with diborane and also with the Cp_2TiCl_2-$NaBH_4$-18-crown-6 reagent system.

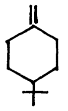
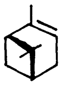
Table 3. Hydroboration-Oxidation Reaction of Unsaturated Ethers$^{a)}$

Substrate	Time/h	Product (yield/%$^{b)}$)		By-product (yield/%$^{b)}$)	
	5		(51)		(45)
	5		(77)	Ph-OH	(23)
	20		(90)	Ph-OH	(6)
	5		(79)$^{c)}$		
	20		(42)		
	20		(56)		

a) All the reactions were conducted at 25 °C by using the reagent system; substrate : $NaBH_4$: $TiCl_3$: 18-crown-6 = 5 : 5 : 1 : 1. b) GLC yields based on substrates used. c) The acid hydrolysis of the reaction mixture gave 3-hydroxypropanal.

In order to examine the stereochemical feature of the reaction, the hydroboration of some representative cyclic alkenes was studied. In these cases, the hydroborates produced by the hydroboration were converted into the corresponding alkanes by treating with acetic acid. The results are listed in Table 4. These results can be explained by assuming that in the Ti complex catalyzed hydroboration, $NaBH_4$ adds to the double bond preferentially from the opposite side to the Ti complex which coordinates with the double bond of cyclic alkenes from a less hindered side. The stereochemistry of the products obtained from this Ti complex catalyzed hydroboration differs from that of those obtained by the hydroboration with diborane,$^{7,8)}$ in which the B-H function adds to the double bond preferentially from a less hindered side.

Table 4. Stereochemistry of the Products Obtained by the Hydroboration-Protonation of Cyclic Alkenes

		Ratio of *trans* / *cis* isomers[a)]		
Substrate	Products	$TiCl_3$ [b)] $NaBH_4$ 18-crown-6	Cp_2TiCl_2 [c)] $NaBH_4$ 18-crown-6	$BF_3 \cdot OEt_2$ [d)] $NaBH_4$
	*trans*- and *cis*-4-t-butyl-1-methyl cyclohexanes	60/40 (96%)	70/30 (57%)	36/64 (93%)
	*trans*- and *cis*-pinanes	62/38 (88%)	74/26 (59%)	5/95 (95%)
	*trans*- and *cis*-pinanes	58/42 (60%)	64/36 (26%)	5/95 (90%)

a) The figures in parentheses indicate the total yields of the products.
b) Substrate : $NaBH_4$: $TiCl_3$: 18-crown-6 = 5 : 5 : 1 : 1; at 25 °C.
c) Substrate : $NaBH_4$: Cp_2TiCl_2 : 18-crown-6 = 5 : 5 : 1 : 1; at 65 °C.
d) Substrate : $NaBH_4$: $BF_3 \cdot OEt_2$ = 12 : 3 : 4; at 25 °C. The reactive species in this reaction is diborane.$^{9)}$

References

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