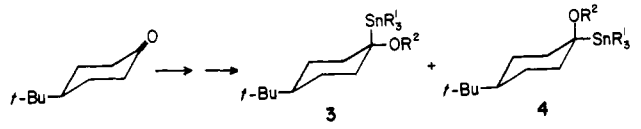


**4**, $R^1$ = *n*-Bu) could be varied from 93:7 under thermodynamic conditions (e.g., reversible stannane addition in THF at −60 °C) to 25:75 under kinetic conditions (e.g., $Et_2O$ at −100 °C). The configurations of the α-alkoxy stannanes (**3** and **4**, $R^2 = CH_2OMe$) were established by analysis of the $^{119}Sn$–$\beta^{13}C$ coupling constants in each epimer[8] and by correlation of the cyclohexyl ethers derived via protonation of the derived organolithium species with independently synthesized materials of known configuration. The reversibility of the (tri-*n*-butylstannyl)lithium addition was confirmed by subjecting the kinetic reaction mixture (**3** and **4**, $R^2$ = H) to *n*-BuLi in THF at −60 °C to afford the thermodynamic ratio of products.[9]

Axial alkoxycyclohexylstannanes (e.g., **3**) are extremely useful synthetic intermediates since carbanion generation and subsequent electrophile trapping contrasts sharply with the normal stereochemical mode of addition to cyclohexanones by carbon nucleophiles.[10] This methodology provides unique entry to highly stereoselective axial substitution of cyclohexanones by relatively hindered carbon centers. Selected alkylation sequences are presented in Table I. It should be noted that the stereochemical integrity of **5** and **6** is completely maintained throughout the sequence. Also, while (arylalkylalkoxymethyl)lithium species (e.g., **7**) underwent smooth alkylation reactions in every case examined, the less stable dialkyl alkoxylithium species appear to favor proton or hydride transfer reactions in preference to alkylation with alkyl halides. Although the reason for this behavior has yet to be defined, modification of the organometallic species in anticipation that a "softer" nucleophilic metal center might promote alkylation is currently being pursued.

**Acknowledgment** is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the National Institutes of Health (AM32453 and AI18889) for support of this research.

**Registry No. 3** ($R^1$ = *n*-Bu; $R^2$ = MOM), 89726-83-0; **4** ($R^1$ = *n*-Bu; $R^2$ = MOM), 89746-17-8; **5** (R = $CH(OH)CH_2CH_3$), 89726-84-1; **5** (R = $CA(OH)C_6H_5$), 89726-85-2; **5** (R = $C(CH_3)_2OH$), 89726-86-3; **5** (R = H), 89726-87-4; **5** (R = $CH_3$), 89726-88-5; **6** (R = $CH(OH)CH_2CH_3$, 89726-89-6; **6** (R = H), 89726-90-9; **6** (R = $CH_3$), 89726-91-0; **7** (R = $CH(OH)CH_2CH_3$), 89726-92-1; **7** (R = $CH(OH)C_6H_5$), 89726-93-2; **7** (R = $C(CH_3)_2OH$), 89726-94-3; **7** (R = $CH_3$), 24142-63-0; **7** (R = $CH_2CH{=}CH_2$), 89726-95-4; **7** (R = *n*-Bu), 89726-96-5; **8**, 89726-97-6; $Me_3SnCH(OMOM)CH(CH_3)_2$, 89726-98-7; *n*-$Bu_5$nCH(OMOM)-$CH_2CH_3$, 89726-99-8; $Me_4Sn$, 594-27-4; *n*-$BuSnMe_3$, 1527-99-7; $Me_3SnCH_2OMOM$, 89727-00-4; $Me_3SnCH(Me)OMOM$, 89727-01-5; 1-$Me_3Sn$(c-$C_6H_{10}$)OMOM, 89727-02-6; 1-(*n*-$Bu)_3Sn$(c-$C_6H_{10}$)OMOM, 89727-03-7; *n*-$Bu_3Sn$(c-$C_6H_{11}$), 40218-10-8; MeLi, 917-54-4; *n*-BuLi, 109-72-8; PhCHO, 100-52-7; MeCOMe, 67-64-1; $H^+$(MeOH), 38684-25-2; MeI, 74-88-4; $Me_2SO_4$, 77-78-1; $H_2C{=}CH\text{-}CH_2Cl$, 107-05-1; *n*-BuI, 542-69-8; *n*-$Bu_3SnLi$, 4226-01-1; propionaldehyde, 123-38-6; 4-*tert*-butylcyclohexanone, 61203-82-5.

**Supplementary Material Available:** Representative experimental procedure and a listing of spectral and analytical data for selected new compounds (10 pages). Ordering information is given on any current masthead page.

(8) See the following and references therein: (a) Wickham, G.; Olszowy, H. A.; Kitching, W. *J. Org. Chem.* **1982**, *47*, 3788. (b) Kitching, W.; Olszowy, H. A.; Harvey, K. A. *Ibid.* **1982**, *47*, 1893. (c) Kitching, W.; Olszowy, H. A.; Waugh, J.; Doddrelly, D. *Ibid.* **1978**, *43*, 898.

(9) The thermodynamic perference for an axial tri-*n*-butylstannyl substituent preseumably reflects the small *A* value for this group (~1.0[8b]) relative to that for the bulky, THF-complexed lithium alkoxide.

(10) (a) Rei, M.-H. *J. Org. Chem.* **1979**, *44*, 2760 and references therein. (b) Wipke, T.; Gund, P. *J. Am. Chem. Soc.* **1976**, *98*, 8107. (c) Ashby, E. C.; Laemmle, L. A. *Chem. Rev.* **1975**, *75*, 521. (d) Toromanoff, E. *Top. Stereochem.* **1967**, *2*, 157.

## Novel Kinetic Profile of Zinc Ion Catalysis in Dihydroquinoline Reduction of 2-Pyridinecarbaldehyde in Aqueous Solution

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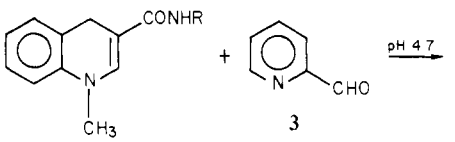
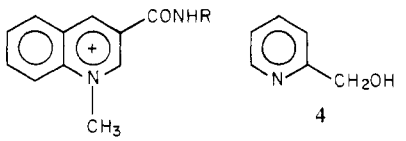
*Received November 21, 1983*

Metal ion catalysis in the reduction of carbonyl compounds with 1,4-dihydropyridines have attracted much attention;[1] since zinc ion at the active site of alcohol dehydrogenase is suggested to play an important role in the reduction.[2] However, the kinetic studies on the reduction of carbonyl compounds with 1,4-dihydropyridines or related compounds reveal that the effect of metal ion on the rate is complicated, and nature or even existence of catalysis is not clear.[3-8] We now wish to report the following new findings. (1) Zinc ion remarkably accelerates the reduction of 2-pyridinecarbaldehyde with dihydroquinoline derivatives *in aqueous solution*. (2) Kinetic complexities in catalysis disappears when the reaction is carried out under carefully deaerated, *dark* conditions. (3) A hydroxyl group on dihydroquinoline accelerates the rate appreciably.[9]

Two dihydroquinolines **2a** and **2b** were prepared.[8] The reduction of 2-pyridinecarbaldehyde **3** with **2** was carried out in a *carefully deaerated* buffer solution[10] (pH 4.7, 0.02 M AcOH–AcONa) at 50 °C under Ar *in the dark*. At appropriate time




**2a**, R = H
**b**, R = $CH_2CH_2OH$




**1**

intervals, the decrease of absorption at 350 nm characteristic to **2** was measured. After the reduction was practically over, the reaction mixture was analyzed on HPLC (cation-exchange column, Toyo-Sotatsu, iex-230/0.02 M AcOH–AcONa pH 5.0). Formation of 2-pyridylmethanol (**4**) was confirmed by IR (3200, 1590, 1640, and 1430 $cm^{-1}$), electronic spectra, TLC ($SiO_2$/AcOEt), and HPLC (cation-exchange column).[11] The yields of **4** were

(1) (a) Creighton, D. J.; Sigman, D. S. *J. Am. Chem. Soc.* **1971**, *93*, 6314. Creighton, D. J.; Hajdu, J.; Sigman, D. S. *Ibid.* **1976**, *98*, 4619. (b) Shinkai, S.; Bruice, T. C. *Ibid.* **1972**, *94*, 8258; *Biochemistry* **1973**, *12*, 1750. (c) Shirai, M.; Chishina, T.; Tanaka, M. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 1079.

(2) Branden, C. I.; Jornvall, H.; Eklund, H.; Furugen, B. *Enzymes, 3rd Ed.* **1969**, *11*.

(3) Entirely different kinetics were reported for metal ion effect; one-half-order dependence followed by inhibition,[4,5] zeroth-order dependence,[6] and inhibition.[7]

(4) Gase, R. A.; Boxhoorn, G.; Pandit, U. K. *Tetrahedron Lett.* **1976**, 2889.

(5) (a) Hughes, M.; Prince, R. H. *J. Inorg. Nucl. Chem.* **1978**, *40*. 703. (b) Hughes, M.; Prince, R. H.; Wyeth, P. *Ibid.* **1978**, *40*, 713.

(6) Ohno, A.; Yamamoto, H.; Okamoto, T.; Oka, S.; Ohnishi, Y. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2385.

(7) Shinkai, S.; Hamada, H.; Kusano, Y.; Manabe, O. *Ibid.* **1979**, *52*, 2600.

(8) Preparation of **1b** was carried out from 3-quinolinecarbonyl chloride with methyl iodide via 1-methyl-3-(chloroformyl)quinolinium iodide, followed by the treatment with ethanolamine. Reduction was performed with 1-methyl-1,4-dihydronicotinamide.

(9) Tabushi, I.; Kugimiya, S.; Mizutani, T. *J. Am. Chem. Soc.* **1983**, *105*, 1658.

(10) Buffer solutions were deaerated by freeze–pump–thaw cycles before use. Sample solutions were prepared in a vacuum box filled with Ar.

(11) The product was identical with the authentic **4** on TLC and HPLC.

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**Table I.** Second-Order Rate Constants $k_2$ for the Reduction and Yields of 2-Pyridylmethanol (**4**)[a]

| | dihydroquinoline | |
|---|---|---|
| $[ZnCl_2]$, M | **2a** (yield of **4**, %) | **2b** (yield of **4**, %) |
| 0 | <0.3 (<5)[d] | <0.3 (<5)[d] |
| | <0.3[b] | |
| 0.01 | 1.2 ± 0.1 (65)[d] | 1.7 ± 0.2 (88)[d] |
| 0.1 | 8.4 ± 0.9 (95)[d] | 13.1 ± 0.7 (93)[d] |
| | 18.7 ± 0.4[b] | |
| | 17.0 ± 1.4[c] | |
| 0.5 | 26.4 ± 1.3 | |
| 1.0 | 58.7 ± 8.3 (98)[e] | 72.1 + 11.5 (96)[e] |

[a] pH 4.7, 50 °C, $h^{-1}$ $M^{-1}$, $k_2 = (k_{obsd} - k_0)/[3]$ where $k_0$ is the spontaneous decrease of **2**. Errors are standard deviations. [b] NaCl (1 M) was added. [c] $NaClO_4$ (1 M) was added. [d] Yields after 30 h. [e] Yield after 15 h.

determined by HPLC using pyridine as an internal standard, being good to excellent depending on the $Zn^{2+}$ concentration (see Table I).

The rate constants[12] corrected for the spontaneous decrease of **2** (vide infra) and the yield of **4** are summarized in Table I (see also Figure 1). It should be reemphasized that the rates and yields were reproducible only when oxygen was carefully removed and the reaction was carried out in the dark. The amount of recovered quinolinium salt **1** after the reaction determined by HPLC was higher than 95%.

Obviously, Table I shows that the yields were much improved and the rates were remarkably accelerated by the increase of $Zn^{2+}$ concentration contrary to the previous observations.[13] Rates were further accelerated to some extent by the addition of 1 M NaCl or $NaClO_4$ (see Table I), demonstrating the existence of a moderate salt effect.

The following kinetic and spectroscopic observations were made:

(i) Plot of $k_2$ against $[Zn^{2+}]$ showed the gradual rate saturation at higher $Zn^{2+}$ concentration.

(ii) Linear correlations were observed between $1/k_{obsd}$ and $1/[Zn^{2+}]$ [**3**] (Figure 1). The equilibrium constant $K_2$ and the rate constant $k_2$ (Scheme I) estimated from the dependence of rate on the concentration of 3 and $Zn^{2+}$ were (58 ± 16) $M^{-2}$ and (1.3 ± 0.3) $h^{-1}$, respectively, at 1.0 M $ZnCl_2$.

**Scheme I**

$$3 + Zn^{2+} \underset{}{\overset{K_1}{\rightleftharpoons}} 3\cdot Zn^{2+}$$

$$2 + 3 + Zn^{2} + \overset{K_2}{\rightleftharpoons} 2\cdot 3\cdot Zn^{2+}$$

$$3\cdot Zn^{2+} + 2 \xrightarrow[\text{rds}]{k_1} 1 + 4 + Zn^{2+}$$

$$2\cdot 3\cdot Zn^{2+} \xrightarrow[\text{rds}]{k_2} 1 + 4 + Zn^{2+}$$

(iii) The maxima of fluorescence spectra of **2a** and **2b** were shifted to longer wavelength and intensities markedly decreased by the addition of $Zn^{2+}$ and **3**, but they were not shifted by the addition of **3** alone. These observations indicate ternary complex formation.

On the basis of these observations a conclusion is drawn that the reduction of **3** with **2** proceeds mainly through a ternary complex, $2\cdot 3\cdot Zn^{2+}$.

By comparison of the rate of **2a** with **2b** (Table I), introduction of a hydroxyl group in dihydroquinoline appreciably accelerates the rates[9] in the presence of $Zn^{2+}$ (0.01 to ~ 1.0 M). The acceleration suggests the enhanced interaction promoted by additional coordination between OH and $Zn^{2+}$.

Reduction of **3** with **2** was remarkably affected by $O_2$ and light,[14] and both reactions were independently affected by $Zn^{2+}$,

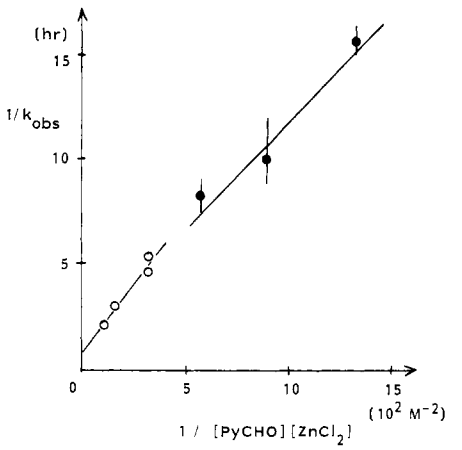


**Figure 1.** Plot of $k_{obsd}$ vs. $1/[3][ZnCl_2]$. Two lines drawn are the least-mean-square fit for each set of different ionic strength: $[ZnCl_2]$, 1.0 M (○); $[ZnCl_2]$, 0.1 M (●).

making the kinetic situation very complicated. Dioxygen lead to nonproductive consumption of **2** (oxidation to **1** by $O_2$) and irradiation with Xe lamp (>390 nm, 500 W) or even room light accelerated the rate of decrease of **2** considerably. The photochemistry will be discussed in detail in a forthcoming article.

**Registry No. 2a**, 20224-92-4; **2b**, 84811-86-9; **3**, 1121-60-4; $ZnCl_2$, 7646-85-7.

(12) Rates of spontaneous decrease is from 2% to 10% of $k_{obsd}$.

(13) Inhibition by metal ions was reported in a similar system,[7] without mentioning the effect of $O_2$ and light. The previous work[7] may not pay satisfactory attention to these.

(14) For the effect of light, see; Fukuzumi, S.; Hironaka, K.; Tanaka, T. *J. Am. Chem. Soc.* **1983**, *105*, 4722 and references therein. However, for carbonyl reduction, a sole example is known for intramoleculr reaction: Sammes, J. D.; Widdowson, D. A. *J. Chem. Soc., Chem. Commun.* **1972**, 1023.

## Vibrational Circular Dichroism of α-Phenylethylamine

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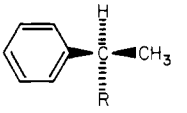
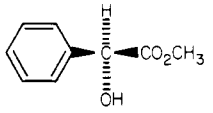
*Received October 27, 1983*

α-Phenylethylamine (**1**) has drawn considerable attention in the relatively new area of vibrational optical activity (VOA),[1,2]




(*R*)-**1**, R = $NH_2$
(*R*)-**2**, R = OH
(*R*)-**3**, R = N=C=O




(*S*)-**4**

due, in part, to the possible role of the methyl group as a probe for the assignment of absolute configuration. The infrared vibrational circular dichroism (VCD) spectrum in the 3500–2700-$cm^{-1}$ region[3] and in the 1480–1400-$cm^{-1}$ region[4] has been reported. Now we report the mid-infrared VCD spectrum in the 1625–900-$cm^{-1}$ range with three objectives: first, to report an unusual pattern of VCD features, second, to show that the VCD associated with C*–H and the phenyl ring vibrational modes appear to be significant in understanding the relation of VCD

(1) Hug, W.; Kint, S.; Bailey, G. F.; Scherer, J. R. *J. Am. Chem. Soc.* **1975**, *97*, 5589–5590.

(2) Barron, D. *Nature (London)* **1975**, *255*, 458–460.

(3) Nafie, L. A.; Keiderling, T. A.; Stephens, P. J. *J. Am. Chem. Soc.* **1976**, *98*, 2715–2723.

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