Inorganica Chimica Acta, 18 (1976) L3 - L4
© Elsevier Sequoia S.A., Lausanne – Printed in Switzerland

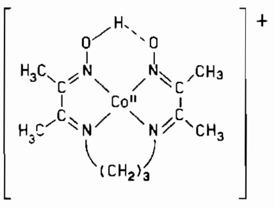
Asymmetric Homogeneous Catalytic Hydrogenation by a Macrocyclic Cobalt Catalyst

R. W. WALDRON and J. H. WEBER*

University of New Hampshire, Parsons Hall, Durham, N.H. 03824, U.S.A.

Received January 14, 1976

Asymmetric homogeneous catalytic hydrogenation, in which chiral catalysts are used to produce an excess of one enantiomer over the other, have been predominantly based on very expensive rhodium catalysts.[1] The effectiveness of asymmetric reactions is measured by the percent enantiomeric excess (*%ee*), which represents the excess of one enantiomer over the other, *e.g.*, %S–%R. Utilization of rhodium catalysts has resulted in examples of nearly 100*%ee*. Unfortunately, from a practical point of view, catalysts involving second and third transition metals are very costly. For this reason and because of a paucity of data on cobalt systems, we are studying asymmetric homogeneous catalytic hydrogenation by cobalt complexes of polydentate, strong ligands. The asymmetric hydrogenation reactions reported below, were performed using $Co^{II}(BDM1,3pn)^+$ (Struct. I) as a catalyst** in the presence of the chiral alkaloid quinine. The tetradentate diiminedioxime ligand H(BDM1,3pn) is formed by condensing 2 mol of 2,3-butanedionemonoxime with 1 mol of 1,3-diaminopropane.[2]



I

The reactions were carried out under anaerobic conditions in the following fashion. The addition of H(BDM1,3pn) to an equimolar amount of $CoCl_2 \cdot 6H_2O$ in benzene/methanol or toluene/methanol (9/1 v/v) results in the *in situ* formation of red (504 nm) $Co^{II}(BDM1,3pn)^+$. After the addition of benzylamine, quinine, and the α-diketone benzil ($C_6H_5COCOC_6H_5$) substrate, the solution is kept over 1 atm of H_2 until the reaction is complete. Further details of the catalytic hydrogenation are in Table I. The reduced substrate, the α-hydroxyketone benzoin ($C_6H_5COCHOHC_6H_5$), is isolated by a method similar to that used by Ohgo and co-workers[3] and analyzed for alcohol content to determine the percent yield.[4] Rotations are measured in acetone ($[\alpha]_D$ = +118°)[5] on a Zeiss Precision Photoelectric Polarimeter (0.005°). All the experiments result in the S-(+)-benzoin product.[6]

TABLE I. Experimental Conditions and Percent Enantiomeric Excess for the Asymmetric Homogeneous Catalytic Hydrogenation of Benzil by a Cobalt Catalyst.[a,b]

Run	Q/Co	Temp. (°C)	Time (hr)	Catalyst conc. (*M*)	*%ee*[c]
1	1	30	12	0.0080	10.2
2	2	30	11	0.0100	22.4
3	3	30	12	0.0100	39.5
4	4	30	11	0.0100	44.3
5	3	30	6	0.0080	42.5
6	3	8	12	0.0080	59.7
7	2	8	11	0.0200	35.8
8	4	8	11	0.0200	36.2
9[d]	4	–8	20	0.0100	64.8

[a] Abbreviation: Q, quinine; Co, $(Co^{II}BDM1,3pn)^+$. [b] Solvent is benzene/methanol (9/1, v/v); benzil/cobalt ratio is 20; benzylamine/cobalt ratio is 1. [c] *%ee* = %S–%R. [d] Solvent is toluene/methanol (9/1, v/v).

The sample results shown in Table I emphasize the effect of experimental variables on the *%ee*. Runs 1 to 4 demonstrate that increasing the quinine/catalyst ratio from 1 to 4, while leaving the other variables nearly constant, increases the *%ee* from 10.2% to 44.3%. Runs 5 and 6 indicate an enhanced *%ee* with a temperature decrease. The *%ee* increases from 42.5% at 30 °C to 59.7% at 8 °C. These two results are deceptive in their simplicity and they do not adequately describe a means of obtaining a maximum *%ee*.

Runs 2, 4, 7 and 8 show that one cannot change variables one at a time and obtain a pitfall-free experimental path to the goal of highest *%ee*. Runs 2 and 4 show that at a 0.0100 *M* catalyst concentration, the *%ee* approximately doubles from 22.4 to 44.3% as the quinine/cobalt ratio increases from 2 to 4. In contrast, the same increase in the quinine/cobalt ratio using a 0.0200 *M* solution of the catalyst has very little effect on the *%ee*. In fact, the 35.8 and 36.2 *%ee* values are within experimental error. For this reason we are presently designing experiments

---

*Author to whom correspondence should be addressed.

**Since the exact chemical nature of the catalytic species is generally unknown, the complex prepared *in situ* before hydrogenation will be called the catalyst.

using the 2^n factorial approach, in which all variables are experimentally set at two levels.[7] By this technique, we hope to find an experimental path to the maximum *%ee* value. Run 9 represents our presently highest *%ee* value of 64.8%. However, not only the maximum *%ee* but also the mechanism of the reactions are of interest.

The mechanism of these cobalt catalyst reactions is very different from that of the rhodium analogs. By use of a rhodium catalyst, the hydrogen, substrate, and chiral molecule are simultaneously coordinated to the complexed metal. Despite detailed studies of the rhodium systems, the mechanisms are usually too complex to be completely clarified.[1] In the $Co^{II}(BDM1,3pn)^+$ system, the chelating ligand occupies four coordination sites in a plane, and the benzylamine undoubtedly occupies one axial site. Thus, the quinine, the substrate, and the catalyst must be intimately bound together at one coordination site. One possible mechanism involves the formation of a sigma bond between the cobalt and the relatively positive carbonyl carbon of the substrate. According to Ohgo and co-workers[8] the substrate is positioned for asymmetric reduction by a hydrogen bond between the quinine and the substrate. Then cleavage of the cobalt–carbon bond forms the reduced substrate. To date, we have not confirmed or refuted parts of Ohgo's mechanism, but we have found strong evidence for a cobalt–carbon bond.

It is well known that $Co^I(BDM1,3pn)$ reacts with alkyl halides such as CH_3I to form cobalt–carbon bonds (Eqn. 1).[2]

$$Co^I(BDM1,3pn) + CH_3I \rightarrow CH_3Co(BDM1,3pn)^+ + I^- \qquad (1)$$

To test for $Co^I(BDM1,3pn)$, we added excess CH_3I to a typical reaction solution in the absence of H_2. After a five hour period, we spectrophotometrically measured exactly one-half the theoretical amount of $CH_3Co(BDM1,3pn)^+$ (λ = 460 nm, ϵ = 2120 M^{-1} cm^{-1}). We attribute this behavior to the disproportionation of $Co^{II}(BDM1,3pn)^{2+}$ (Eqn. 2) followed by the rapid reaction of the cobalt(I) complex with CH_3I (Eqn. 1).

$$2Co^{II}(BDM1,3pn)^+ \rightleftharpoons Co^I(BDM1,3pn) + Co^{III}(BDM1,3pn)^{2+} \qquad (2)$$

The alkylation reaction is slow because of the low equilibrium concentration of $Co^I(BDM1,3pn)$ in the slightly basic reaction medium.

The addition of excess CH_3I to an approximately 50% completed asymmetric hydrogenation reaction rapidly stops the reaction. The theoretical amount of $CH_3Co(BDM1,3pn)^+$, not 50% of it, is obtained. We attribute this to the H_2 reduction of the cobalt(II) complex to the cobalt(I) analog, which rapidly forms $CH_3Co(BDM1,3pn)^+$ as shown in Eqn. 1.

Because of the hydridocobalt(III)–cobalt(I) equilibrium (Eqn. 3)

$$Co^I(BDM1,3pn) + H^+ \rightleftharpoons HCo^{III}(BDM1,3pn)^+ \qquad (3)$$

we have not positively demonstrated whether the cobalt(I) complex, the cobalt(III) hydride, or both are the active catalytic species. However, we have determined an approximate pK_a value of 3 for the cobalt(III) hydride in the presence of $P(C_6H_5)_3$.* Thus, the equilibrium of Eqn. 3 for our slightly basic reaction conditions must lie far to the left, and the very nucleophilic cobalt(I) species probably is the active catalyst.

References

1 J. D. Morrison, W. F. Masler, and M. K. Neuberg, "Advances in Catalysis and Related Subjects", vol. 25, Academic Press, New York, 1976 (to be published).
2 V. E. Magnuson and J. H. Weber, *J. Organometal. Chem., 74,* 135 (1974).
3 Y. Ohgo, S. Takeuchi, and J. Yoshimura, *Bull. Chem. Soc. Japan, 44,* 583 (1971).
4 S. Siggia, "Quantitative Organic Analysis", 3rd Edit., Wiley, New York, 1962, p. 12.
5 I. V. Hopper and F. J. Wilson, *J. Chem. Soc.,* 2483 (1928).
6 W. Klyne and J. Buckingham, "Atlas of Stereochemistry", Oxford University Press, New York, 1974, p. 27.
7 (a) W. J. Youden, "Statistical Methods for Chemists", Wiley, New York, 1951. (b) W. G. Cochran and G. M. Cox, "Experimental Designs", 2nd Edit., Wiley, New York, 1957, Chap. 5, 6A. (c) O. Kempthorse, "Design and Analysis of Experiments", Wiley, New York, 1952, Chap. 13, 20.
8 Y. Ohgo, Y. Natori, S. Takeuchi, and J. Yoshimura, *Chem. Lett.,* 1327 (1974).
9 G. N. Schrauzer and R. J. Holland, *J. Am. Chem. Soc., 93,* 1505 (1971).
10 J. H. Weber and G. N. Schrauzer, *J. Am. Chem. Soc., 92,* 726 (1970).

---

*This value compares with $pK_a \simeq 10.5$ and $\simeq 10$ for $HCo(DMG)_2(P(n\text{-}Bu)_3)$[9] and $HRh(DMG)_2(P(C_6H_5)_3)$,[10] respectively.