Inorg. Chem. **2003**, *42*, 7340–7341

Inorganic Chemistry

Communication

High-Pressure Combinatorial Screening of Homogeneous Catalysts: Hydrogenation of Carbon Dioxide

Chih-Cheng Tai,[†] Tangel Chang,[†] Brentin Roller,[†] and Philip G. Jessop*,[†,‡]

Departments of Chemistry, University of California, Davis, Davis California 95616, and Queen's University, Kingston, Ontario, Canada K7L 3N6

Received July 25, 2003

A simple method for high-pressure combinatorial catalyst discovery with visual (dye-based) assay is described. With this method, the first highly active catalyst, incorporating metals outside the platinum group, has been identified for CO_2 hydrogenation.

Carbon dioxide, the cheapest and most available carbon feedstock, has the potential to be transformed into a wide variety of organic products, given the identification of inexpensive and efficient catalysts. However, the range of reactions for which efficient catalysts have been identified is disappointingly small. We have developed an inexpensive method for combinatorial screening of potential catalyst precursors, and tested the method by screening for new catalysts for CO_2 hydrogenation.

Reports of homogeneous catalysts for the hydrogenation of CO_2 into formic acid (eq 1) date from Inoue's work in 1976.[1] However, active catalyst precursors have been restricted[2−4] to complexes of the "precious" or platinum-group metals Pd, Rh, Ir, and Ru, except for the mention, in Inoue's original paper,[1] of a non-platinum-group metal catalyst, Ni(dppe)$_2$, which gave only 7 turnovers (TON). In contrast, many non-platinum-group metal complexes are active for the hydrogenation of alkenes, ketones, and imines.[5,6] We therefore sought to determine, using the new screening method, whether highly active non-platinum-group metal catalyst precursors could be identified.

$$CO_2 + H_2 \xrightarrow[\text{base}]{\text{catalyst}} HCO_2H \qquad (1)$$

Figure 1. The apparatus for high-pressure catalyst screening.

Because there seem to be no commercially available vessels designed for combinatorial chemistry at high pressure, we developed an inexpensive system for performing reactions on a 6 × 6 array at pressures up to 200 bar, based upon modifications to a commercially available traditional pressure vessel (Figure 1, details in the Supporting Information).[7]

Combinatorial catalyst screening is most efficient if a method for rapid assay of the results is available.[8] Visual assay, rather than instrumental analysis, is obviously the most efficient method when possible. A report of homogeneous catalyst discovery using visual assay was described by Cooper et al.,[9] who used reactive dyes as substrates for hydrogenation reactions. However, this technique is not applicable in situations where the substrate cannot be a dye, as in the current case where CO_2 is the substrate. For reaction 1, we elected to use an acid−base indicator, bromothymol blue, to make it possible to do a visual determination of formic acid yield. So that the indicator cannot influence the reaction,

---

* Corresponding author. E-mail: jessop@chem.queensu.ca. Tel: (613) 533-3212.

[†] University of California, Davis.

[‡] Queen's University.

(1) Inoue, Y.; Izumida, H.; Sasaki, Y.; Hashimoto, H. *Chem. Lett*. **1976**, 863−864.

(2) Jessop, P. G.; Ikariya, T.; Noyori, R. *Chem. Rev*. **1995**, *95*, 259−272.

(3) Leitner, W. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2207−2221.

(4) Darensbourg and Ovalles reported the use of W and Cr carbonyl anions as catalysts for the synthesis of a related product, methyl formate, with TON up to 16. Darensbourg, D. J.; Ovalles, C. *J. Am. Chem. Soc.* **1984**, *106*, 3750−3754.

(5) James, B. R. *Homogeneous Hydrogenation*; John Wiley: New York, 1973.

(6) Chaloner, P. A.; Esteruelas, M. A.; Joó, F.; Oro, L. A. *Homogeneous Hydrogenation*; Kluwer Academic: New York, 1994.

(7) A vessel for low-pressure use has been described. Constable, G. S.; Gonzalez-Ruiz, R. A.; Kasi, R. M.; Coughlin, E. B. *Macromolecules* **2002**, *35*, 9613−9616.

(8) A variety of ingenious screen and assay methods have been reported. (a) Crabtree, R. H. *Chem. Commun.* **1999**, 1611−1616. (b) Evans, C. A.; Miller, S. J. *Curr. Opin. Chem. Biol*. **2002**, *6*, 333−338. (c) Taylor, S. J.; Morken, J. P. *Science* **1998**, *280*, 267. (d) Tian, J.; Coates, G. W. *Angew. Chem., Int. Ed*. **2000**, *39*, 3626−3629. (e) Shimizu, K. D.; Snapper, M. L.; Hoveyda, A. H. *Chem. Eur. J.* **1998**, *4*, 1885−1889.

(9) Cooper, A. C.; McAlexander, L. H.; Lee, D. H.; Torres, M. T.; Crabtree, R. H. *J. Am. Chem. Soc.* **1998**, *120*, 9971−9972.

10.1021/ic034881x CCC: $25.00

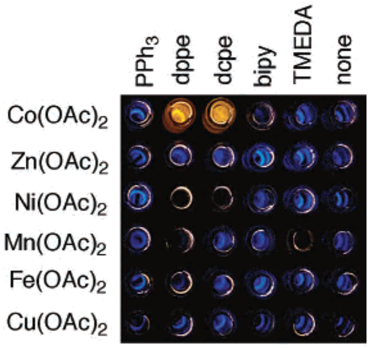

Figure 2. Results from one experiment from the first-tier screening of potential catalysts. Conditions: 3 μmol of metal salt, 9 μmol of PPh_3, or 4.5 μmol of dppe, dcpe, bipy, or TMEDA, 30 μmol of DBU in 400 μL of DMSO solution, 50 °C with 40 bar of H_2 and total 100 bar of H_2 and CO_2 mixture, reaction time 21 h.

it is only added after the reaction time is over. This indicator changes from blue to green at a formic acid:DBU ratio of 1.47 and to yellow at a ratio of 2.08, as shown by a titration of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) by formic acid in DMSO in the presence of bromothymol blue. Thus, for experiments in which the DBU to metal ratio was 10, a TON (turnover number, or formic acid:metal ratio) of 15 would be required for a color change to green and 21 for yellow. Because an acid/base indicator was used for assay, it was important not to use an alcoholic solvent which could form an alkylcarbonic acid upon exposure to CO_2 pressure, thereby giving a false positive reading. The solvent and base also had to be nonvolatile so that liquid volume losses from the vials would be negligible.

Preliminary trials were performed to test the method. Vials containing a known[10] catalyst, $RuCl(OAc)(PMe_3)_4$, were tested alongside vials without catalyst. The former turned green upon addition of the dye solution after the reaction, as expected, while the latter turned blue, showing that cross-contamination of the vials is not occurring.

First-tier screening of the metal/ligand combinations was performed with a 10:1 ratio of DBU:metal. In a series of runs, combinations of 29 metal salts with 5 ligands (or without any ligand) were tested (e.g., Figure 2). Several non-platinum-group metal salts were found to be active, including $Co(OAc)_2$, $CoCl_2$, $CrCl_3$, $FeCl_3$, $InCl_3$, $Mo_2(OAc)_4$, $MoCl_3$, $NbCl_5$, $NiCl_2$, WCl_4, WCl_6, and $W(CO)_6$ (OAc = acetate). This is a far wider range of catalytically active metals than has previously been published. Most of these were active with dcpe ($Cy_2PCH_2CH_2PCy_2$) or dppe ($Ph_2PCH_2CH_2PPh_2$). Amine ligands TMEDA (*N*,*N*,*N*′,*N*′-tetramethylethylenediamine) and bipy (2,2′-bipyridyl) were less effective, giving yellow or green only when used in combination with $MoCl_3$ or salts of platinum-group metals. Metal salts which were not active with any ligand were $Cu(OAc)_2$, $Fe(OAc)_2$, $Mn(OAc)_2$, $Ni(OAc)_2$, $Zn(OAc)_2$, and $ZnCl_2$.

Table 1. Hydrogenation Tests Assayed by NMR Spectroscopy[a]

metal salt	phosphine	formic acid:DBU mole ratio	TON	TOF,[b] h^{-1}
$FeCl_3$	PPh_3	0.09	20	2.7
$FeCl_3$	dppe	0.10	23	3.1
$FeCl_3$	dcpe	0.51	113	15.1
$MoCl_3$	PPh_3	0.10	23	3.1
$MoCl_3$	dppe	0.10	23	3.1
$MoCl_3$	dcpe	0.28	63	8.4
$NiCl_2$	PPh_3	0.00	0	0
$NiCl_2$	dppe	0.20	45	6.0
$NiCl_2$	dcpe	0.52	117	15.6

[a] Conditions: 15 μmol of metal salt, 45 μmol of PPh_3 or 22.5 μmol of dppe or dcpe, 1 mL of DMSO, and 0.5 mL (3.3 mmol) of DBU, 1 h pretreatment with 40 bar of H_2, reaction time 7.5 h at 40 bar of H_2, total pressure 100 bar, 50 °C. [b] TOF is turnover frequency.

Table 2. Reactions with the Catalyst Precursor $NiCl_2(dcpe)$[a]

catalyst, μmol	DBU, mmol	time, h	formic acid:DBU mole ratio	TON
5	60	216	0.37	4400
15	6	21	0.81	330

[a] Conditions: 1 mL of DMSO, 1 h pretreatment with 40 bar of H_2, reaction at 40 bar of H_2, total pressure 200 bar of H_2 and CO_2.

A second tier of screening experiments was performed to identify the more active metal precursors. The 12 active non-platinum-group precursors were evaluated in combinations with PPh_3, dppe, and dcpe. The DBU:metal mole ratio was increased to 50, so that a TON of ca. 75 would be required to register as a color change to green. The combinations of $MoCl_3$ or $FeCl_3$ with any of the phosphines, $NiCl_2$ with dppe or dcpe, and $W(CO)_6$ with PPh_3 showed a green color. These experiments were performed 4 times, with excellent reproducibility.

Combinations of the three phosphines with the three chloride salts were also tested on a larger scale but a shorter reaction time, and the results were quantified by ^1H NMR spectroscopy (Table 1). The results show that dcpe is the optimum ligand for all three metal salts, and that $FeCl_3$ and $NiCl_2$ are superior to $MoCl_3$.

The known complex $NiCl_2(dcpe)$ was then tested and found to be capable of catalyzing the production of formic acid in up to 4400 TON (Table 2). Although this does not approach that of the very efficient Ru catalyst precursors previously reported, the TON exceeds, by 3 orders of magnitude, that of the only previously known non-platinum-group catalyst precursor for this reaction.

Acknowledgment. We acknowledge support from the Division of Chemical Sciences, Office of Basic Energy Sciences, Office of Science, U.S. Department of Energy (Grant No. DE-FG03-99ER14986). P.G.J., Canada Research Chair in Green Chemistry, acknowledges the support of the Canada Research Chair program.

Supporting Information Available: Experimental description including the construction of the rapid-throughput high-pressure vessel. This material is available free of charge via the Internet at http://pubs.acs.org.

IC034881X

---

(10) Jessop, P. G.; Hsiao, Y.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1996**, *118*, 344−355.