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Chapter 11

HETEROGENEOUS REACTION MEDIA USING DENSE PHASE CARBON DIOXIDE FOR CATALYTIC SELECTIVE HYDROGENATION

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ABSTRACT

Effectiveness and potential of multiphase reaction systems using dense phase CO_2 are demonstrated for several catalytic hydrogenation reactions of α, β-unsaturated aldehydes, nitro compounds, phenol, and other substrates. The reaction rate and the product selectivity depend on several factors, including phase behavior, molecular interactions of CO_2 with reacting species, formation of CO from CO_2, and so on. The molecular interactions are evidenced by *in situ* high pressure Fourier transform infrared spectroscopy and these are an important factor responsible for the positive effects of CO_2 pressurization on the reactions. The interactions occur between CO_2 and the carbonyl group of α, β-unsaturated aldehydes, for example, and make it more reactive to hydrogenation compared with C=C group, facilitating the selective transformation to the corresponding unsaturated alcohols. In the hydrogenation of nitrobenzene, the first step of hydrogenation to nitrosobenzene is slowed down but the second hydrogenation step to *N*-phenylhydroxylamine and the third transformation step to the desired product aniline are accelerated. As a result, the 100% selective hydrogenation of nitrobenzene to aniline can be achieved at any conversion level up to 100% with conventional supported Ni catalysts in the presence of dense phase CO_2. For the hydrogenation of phenol with supported Rh catalysts under dense phase CO_2, the selectivity to cyclohexanone is

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increased and an important factor for this is the formation and adsorption of CO during the reaction. Various interesting results of selective hydrogenation reactions under dense phase CO_2 are reviewed and possible factors promoting the reaction rate and controlling the product selectivity are discussed.

INTRODUCTION

Supercritical CO_2 is an effective green medium that can replace conventional organic solvents for various chemical transformations [1-6]. Homogeneous reactions in supercritical CO_2 are advantageous in several aspects such as the absence of gas - liquid mass transfer limitations and higher rates of molecular diffusion and heat transfer. However, all reacting species of substrates and catalysts should be dissolved in the CO_2 gas phase, and this makes it difficult to apply those homogeneous reactions for practical processes. When a large volume of liquid phase (substrate or solvent) is used in the presence of dense phase CO_2, a gas - liquid biphasic reaction system is formed (Scheme 1). In some cases, a large quantity of CO_2 is soluble in the liquid phase and this causes its volume expansion. This liquid phase is often called as a CO_2 (dissolved) expanded liquid (CXL) phase and it is an interesting reaction medium as compared with homogeneous and ordinary heterogeneous media. Several previous workers show the effectiveness of CXLs for chemical reactions including gaseous reactants like H_2, O_2, and CO although CO_2 is not a reactant but a diluent [5]. The reactions in CXLs are multi-phase systems and several physical/chemical factors should influence the outcome of the reactions. One of important factors is the enhancement of dissolution of gaseous reactants into the liquid phase. That is, the dissolution of CO_2 in a liquid phase will cause the dissolution of gaseous reactants and so this will enhance the rate of reactions such as hydrogenation by H_2 and oxidation by O_2 in the liquid phase, in which homogeneous or heterogeneous catalysts are present. Such a promotional effect of CO_2 pressurization is possible to appear even at low CO_2 pressures below its subcritical/critical pressure.

The present authors also show that the use of dense phase CO_2 can enhance the rates of selective hydrogenation with H_2, Heck coupling, and Diels-Alder reaction, in which no gaseous reactants are included in the latter two reactions [1, 7]. *In situ* high pressure FTIR measurements reveal the important roles of molecular interactions of CO_2 with the reacting species for the rate enhancement observed, in addition to the above-mentioned increased dissolution of H_2 (in the hydrogenation). Those molecular interactions modify the reactivity of selected functional groups of the substrates and/or the intermediates, accelerating or retarding certain reaction steps involved. It is noteworthy that CO_2 can be a reaction promoter/controller in CXLs and in homogeneous media in a few different fashions.

This chapter will review the significance of dense phase CO_2 for the selective hydrogenation reactions of α, β-unsaturated aldehydes, nitro compounds, and other substrates. It will also discuss possible factors responsible for the enhancement of the reaction rate and the product selectivity, including above-mentioned molecular interactions, phase behavior, and others. The potential and features of dense phase CO_2 in any reaction media and multiphase reactions in CXLs will be presented for future application to other reactions.
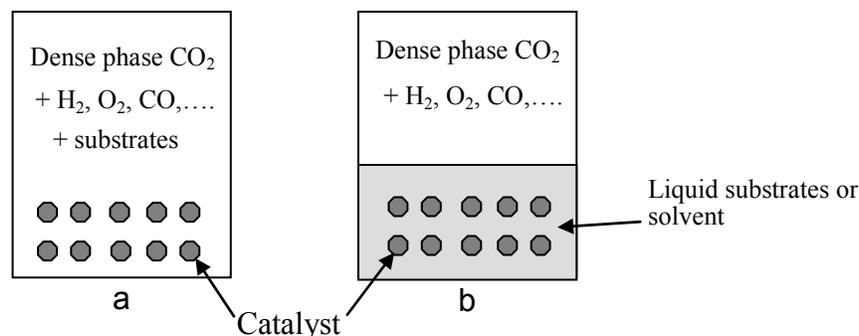
Scheme 1. Typical chemical reaction systems (a) in and (b) under dense phase CO$_2$ in the presence of homogeneous or heterogeneous catalysts for hydrogenation, oxidation, hydroformylation, C-C coupling reactions, and others. These systems are effective for enhancing the reaction rate and improving the product selectivity in not only reactions including gaseous reactants but also those in which no gaseous reactants are involved [1].
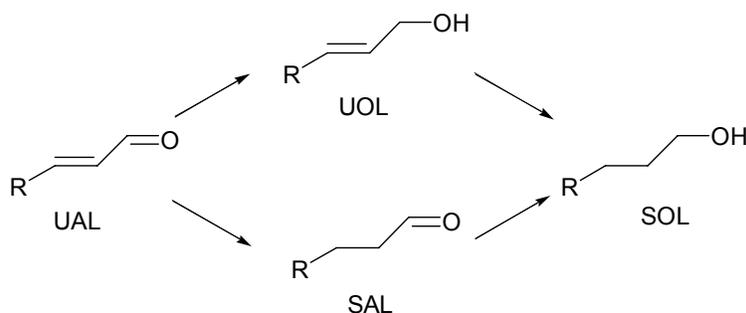
Scheme 2. Hydrogenation of α,β-unsaturated aldehyde. UAL, unsaturated aldehyde; UOL unsaturated alcohol; SAL, saturated aldehyde; SOL, saturated alcohol.

HYDROGENATION OF α, β-UNSATURATED ALDEHYDES

Selective hydrogenation of α,β-unsaturated aldehydes (UAL) to unsaturated alcohols (UOL) is an industrially important reaction in the field of fragrance and flavor chemistry. Because saturated aldehyde (SAL) and saturated alcohol (SOL) can also be formed in the course of this reaction (Scheme 2), improving the selectivity to unsaturated alcohol is required. Boron and aluminum hydrides are known as the reagents for the stoichiometric regioselective reduction of carbonyl groups; however, catalytic hydrogenation would be more preferable for large-scale reactions. The present authors investigated the influence of dense phase CO$_2$ on the hydrogenation of UAL using several catalyst systems like metal-phosphine ligand complexes, supported metal catalysts, and biphasic catalysts [8-16].

Hydrogenation of cinnamaldehyde (CAL, R = C$_6$H$_5$ in Scheme 2) with a Ru complex with a fluorinated phosphine ligand (bis(pentafluorophosphine)phenyl phosphine/Ru = 3) was carried out in the presence of dense phase CO$_2$ by changing the amount of the CAL substrate to investigate the influence of the phase behavior [8]. For comparison, the reaction was also conducted in propanol. Table 1 shows the reaction results obtained. When the reaction was carried out in scCO$_2$ using 0.2 mmol of CAL, the reaction system was in a single system and

the selectivity to UOL was low (entry 1). The reaction runs were also conducted in two-phase systems under solvent-less conditions and in the presence of high pressure CO_2 or N_2. Under the solvent-less conditions, a high UOL selectivity was obtained (entry 2). When the CAL liquid phase was pressurized by CO_2, the CAL conversion was enhanced appreciably, UOL selectivity was also improved slightly, and the enhancement was more under CO_2 at the higher pressure (entries 3, 4). However, pressurizing the CAL phase by N_2 instead of CO_2 affected neither the conversion nor the UOL selectivity (entry 5). Hence, the influence of CO_2 on the reaction cannot be explained by simple hydrostatic pressure effect. The high UOL selectivity should partly result from the higher concentration of the CAL substrate, because a higher selectivity was also obtained by increasing the CAL concentration in an organic solvent of propanol (entries 6, 7). A similar effect of CAL concentration on the UOL selectivity was also reported for the reaction with Pt/SiO_2 in ethanol [17]. However, pressurization of the CAL phase by CO_2 improves both the total reaction rate and the UOL selectivity. Thus, the influence of phase behavior is significant and the presence of dense phase CO_2 is necessary for selective CAL hydrogenation.

Influence of dense phase CO_2 was also investigated for hydrogenation reactions of CAL and benzaldehyde (BAL) with a Pt/C catalyst [9]. Figure 1 shows the effects of CO_2 pressure on the conversion of CAL and BAL. The effects of CO_2 are markedly different between the reaction substrates used. The conversion of BAL decreased with increasing CO_2 pressure, while that of CAL showed a maximum at a CO_2 pressure around 10 MPa. The selectivity to UOL from CAL was slightly improved by the presence of dense phase CO_2. In separate runs, it was found that pressurization with N_2 had no effect on the hydrogenation reactions. By visual observations, it was found that the reaction mixture changed from gas-liquid-solid three phases to gas-solid two phases around 10 MPa irrespective of the substrate under the conditions for Figure 1. Thus, the difference in the influence of CO_2 pressure on the reaction cannot be explained by the phase behavior. It should be noted here that the maximum of the CAL conversion was observed at the CO_2 pressure where the phase change occurred, and pressurizing the CAL liquid phase with CO_2 again enhances the total reaction rate.

Table 1. CAL hydrogenation with Ru complex.

Entry	Ru (μmol)	CAL (mmol)	CO_2 (MPa)	Conversion (%)	Selectivity (%)			Phase present[a]
					UOL	SAL	SOL	
1	0.15	0.2	10	22	23	51	26	G
2	50	7.5	0	11	88	9	3	G, L
3	50	7.5	8.5	24	91	7	2	G, L
4	50	7.5	16	31	93	6	1	G, L
5	50	7.5	8.5 (N_2)[b]	12	88	10	2	G, L
6[c]	0.075	0.2	0	4	17	50	33	G, L
7[c]	50	7.5	0	40	70	18	12	G, L

The reaction was carried out in a 50 cm^3 autoclave. Reaction conditions: H_2, 4 MPa; temperature, 50°C; time, 2 h.

[a] G: CO_2-rich or H_2 gas phase; L: liquid phase.

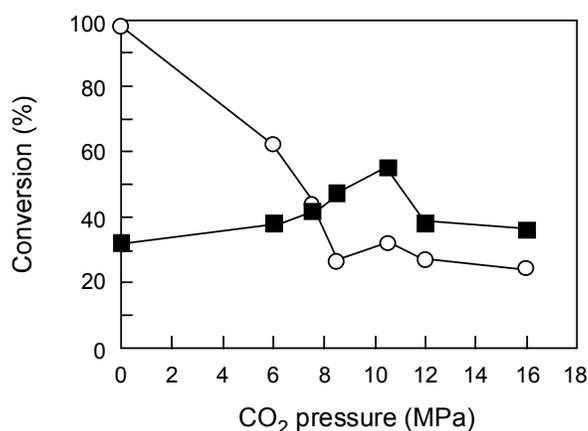[b] N_2 was used instead of CO_2.

[c] In propanol.

Figure 1. Effects of CO_2 pressure on CAL (■) and BAL (○) hydrogenation reactions with Pt/C. The reaction was carried out in a 50 cm^3 autoclave. Reaction conditions: CAL, 0.25 mmol; BAL, 5 mmol; PtC, 0.5 mg (for CAL) and 10 mg (for BAL); H_2, 4 MPa; temperature, 50°C; reaction time, 2 h.

As shown above, pressurization of CAL liquid phase with CO_2 improves the total reaction rate and the UOL selectivity of the CAL hydrogenation, while such an effect is absent for the BAL hydrogenation. The promotional effect would be caused by CO_2 dissolution into CAL liquid phase. Three factors should be taken into account to explain the difference between the CAL and BAL hydrogenation reactions: (a) Interaction between CO_2 and the substrate. (b) Expansion of liquid phase by dissolution of CO_2. (c) Enhancement of the H_2 dissolution into CO_2-dissolved liquid phase.

(a) Interaction between CO_2 and the Substrate

In a CO_2 molecule, the carbon atom is partially positive and the oxygen atoms are partially negative. So, Lewis acid-base interaction can be possible between the carbon atom of CO_2 and the oxygen atom of aldehyde C=O group. High-pressure FTIR was used to investigate the interaction between dense phase CO_2 and the aldehydes. FTIR spectra of CAL and BAL were measured in dense CO_2 at various pressures in the presence of 4 MPa H_2 [9]. For comparison, the measurements were also conducted for saturated aldehyde (hydrocinnamaldehyde, HCAL) [10]. In the spectra of CAL, ν(C=O) and ν(C=C) absorption bands were observed around 1700 and 1630 cm^{-1}, respectively. With increasing the CO_2 pressure, only the former peak is red-shifted to a smaller wave number, indicating that the interaction exists between CAL and CO_2 and it is stronger for the C=O bond than C=C bond. Similar red-shifts of ν(C=O) peak positions were observed for BAL and HCAL. As shown in Figure 2, the extent of the red-shift for CAL was the largest among the aldehydes investigated, probably due to the conjugation of C=C–C=O in CAL. The red-shift of ν(C=O) means the enhancement of the reactivity of C=O group by dense phase CO_2. The stronger interaction between CAL and CO_2 would be one of the reasons of the CO_2 promotional effect, which was observed only for the CAL hydrogenation but not for BAL. This interaction could also explain the improvement of the UOL selectivity by CO_2, because the red-shift was observed

only for the C=O bond of CAL but not for the C=C bond, suggesting that the presence of dense phase CO_2 did not alter the reactivity of the C=C bond.
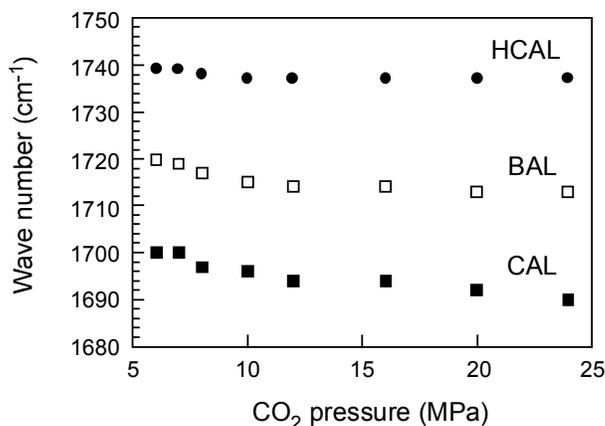

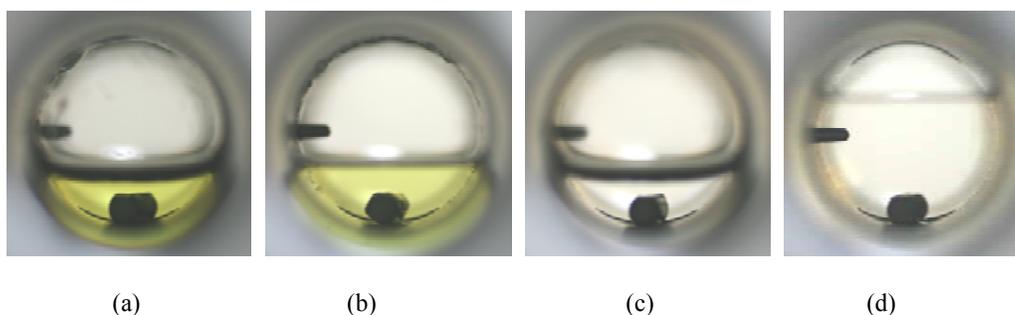Figure 2. Influence of CO_2 pressure on the peak positions of ν(C=O) of CAL, HCAL and BAL at 50°C.

| (a) | (b) | (c) | (d) |

Figure 3. Phase behavior of CAL and BAL liquid phase under pressurized CO_2 at 50°C. (a) CAL under 0.1 MPa CO_2, (b) CAL under 16 MPa CO_2, (c) BAL under 0.1 MPa CO_2 and (d) BAL under 9.5 MPa CO_2. The amounts of CAL and BAL used were 2 cm³. Note that these amounts were different from those for the reaction runs for Figure 1.

(b) Expansion of Liquid Phase by Dissolution of CO$_2$

Figure 3 compares the expansion of a CAL liquid phase by CO_2 pressurization with that of a BAL liquid phase. The expansion of the BAL liquid phase even at a lower CO_2 pressure of 9.5 MPa was much more drastic than that of the CAL phase at 16 MPa. The expansion greatly depended on the type of the substrate. The expansion of the liquid phase can have negative effect on reactions, because the concentrations of substrate and catalysts are diluted by the expansion. So, it can be concluded that such dilution effect for the BAL liquid phase is much more significant than for the CAL liquid phase.

(c) Enhancement of the H_2 Dissolution into CO_2-Dissolved Liquid Phase

When the CAL liquid phase was pressurized by CO_2 at 16 MPa in the presence of 4 MPa H_2, the expansion was slightly larger than that in the absence of H_2 [10]. However, when the CAL phase was pressurized with pure H_2 at the same pressure, no expansion was observed. These observations strongly suggest that dense phase CO_2 promotes the dissolution of H_2 into the CAL liquid phase, which was previously concluded by Devetta et al. [18] and Phiong et al. [19]. This would cause higher reaction rates of CAL hydrogenation. In contrast, when the BAL liquid phase was pressurized by CO_2 at 9.5 MPa in the presence of 4 MPa H_2, the expansion was much less than that in the absence of H_2. H_2 might retard the dissolution of CO_2 into BAL and, probably, dissolved CO_2 little promote the dissolution of H_2 into the BAL liquid phase.

Combination of these factors can explain the difference in the influence of dense phase CO_2 between the BAL and CAL hydrogenation reactions. When the CAL liquid phase is pressurized by CO_2, it expands by the dissolution of CO_2. This would lower the CAL hydrogenation rate because of the dilution effect. At the same time, however, CO_2 dissolved in the liquid phase promotes the reaction by interacting with CAL molecules and promoting the H_2 dissolution. Probably, because such promotional effects are stronger than the dilution effect, the reaction rate is enhanced by the pressurization with CO_2 (positive effect > negative effect). The decrease in the CAL conversion observed at CO_2 pressure above 12 MPa (Figure 1), where all CAL dissolved in CO_2, would result from simple dilution effect. On the other hand, when the BAL liquid phase is pressurized by CO_2, the extent of expansion is much more than CAL; however, the promotional effect on the H_2 dissolution is marginal. So, the dilution effect exceeds the promotional effect of CO_2 by the interaction with BAL, which is weaker than that with CAL. Consequently, the total reaction rate of BAL hydrogenation is lowered by pressurization with CO_2 (negative effect > positive effect), as shown in Figure 1.

Transition metal complexes prepared from Ru, Rh, Pd and Ni with triphenyl phosphine (TPP) complexes were used for the hydrogenation of citral (Scheme 3) in the presence of dense phase CO_2 [11]. Among the catalysts tested, only Ru-TPP produced unsaturated alcohols (geraniol, nerol and citronellol) in a good total yield. The yield of the partially saturated aldehyde (citronellal) was very small, and no formation of completely saturate aldehyde (dihydrocitronellal) was observed. Pd-TPP was active, but it mostly produced citronellal. Rh-TPP and Ni-TPP showed low activities and selectivities to the unsaturated alcohols. Figure 4 shows the influence of CO_2 pressure on the reaction with Ru-TPP. The conversion was maximal at around 12 MPa, and the total yield of geraniol and nerol also showed a maximum at the same CO_2 pressure. At higher CO_2 pressures, the conversion decreased. Visual observations showed that the reaction mixture was in liquid-gas two phases at lower CO_2 pressures, and it changed to a homogeneous phase at a CO_2 pressure around 12 MPa, where the maximum conversion was observed. The liquid phase contained the substrate and the catalyst, and the gas phase contained CO_2 and H_2. Some amounts of the substrate and the catalyst might also exist in the gas phase. Thus, pressurization of the substrate liquid phase with CO_2 was again found to be significant for the formation of unsaturated alcohols. However, the citral phase did not form an expanded liquid phase, which was observed in the cases of CAL hydrogenation, under dense phase CO_2. Its volume simply decreased with increasing CO_2 pressure. This is probably because citral is easily dissolved in the CO_2 phase, and such a dissolution exceeds the volume expansion by the dissolution of CO_2 and H_2.

Under the two-phase conditions, it is likely that the reaction proceeds in the liquid phase, in which the catalyst mainly exists. Although the expansion of the liquid phase was not observed, the dissolution of CO_2 into the liquid phase might occur, and this might also enhance the dissolution of H_2. As expected from the FTIR measurements of CAL and BAL, the C=O group of citral would interact with dissolved CO_2 molecules, enhancing its reactivity and hence the total conversion.
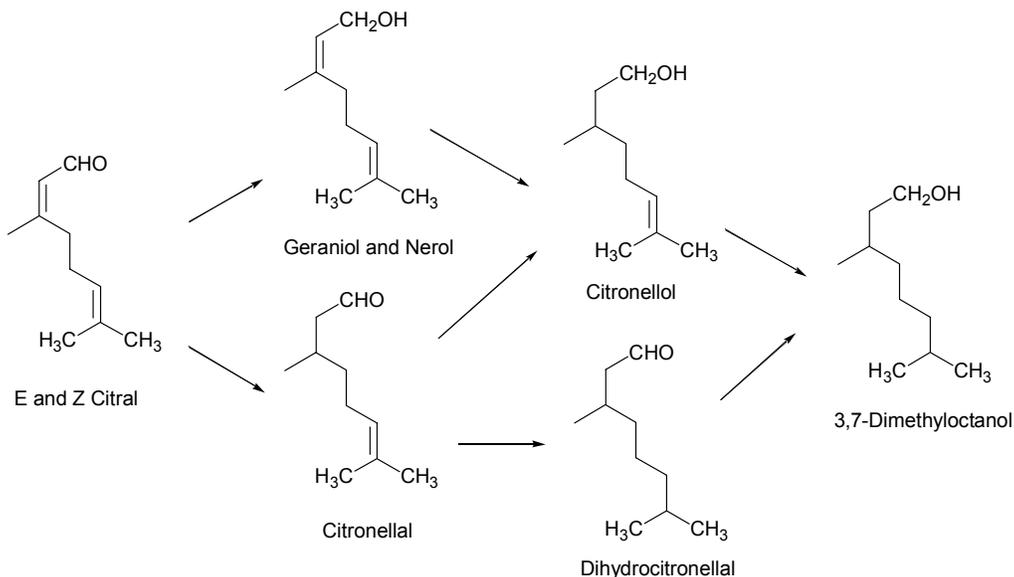
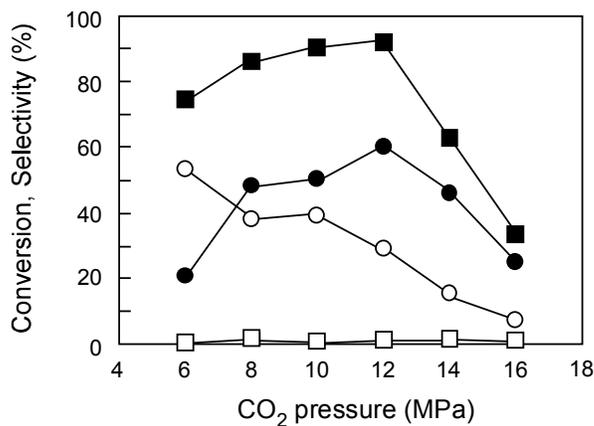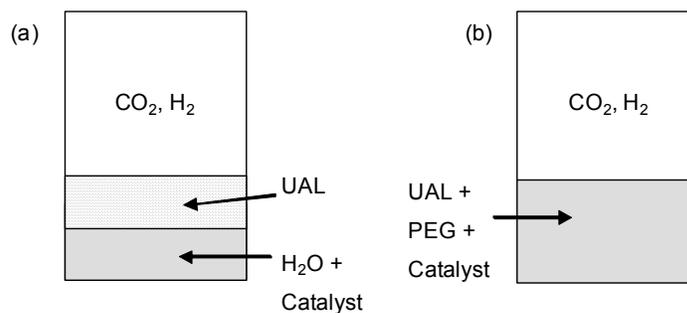

Scheme 3. Hydrogenation of citral.

Figure 4. Effects of CO_2 pressure on hydrogenation of citral with Ru-TPP. The reaction was carried out in a 50 cm^3 autoclave. Conversion (■), and selectivities to citronellol (○), geraniol and nerol (●), and citronellal (□). Reaction conditions: citral, 5 mmol; RuCl$_3$, 0.05 mmol; TPP, 0.15 mmol; H$_2$, 5 MPa; temperature, 60°C; reaction time, 2 h.

Scheme 4. Biphasic catalysis for hydrogenation of α,β-unsaturated aldehyde (UAL) in the presence of dense phase CO_2.

Other several supported metal catalysts were employed for the hydrogenation of UAL in the presence of dense phase CO_2 [12-15]. CAL hydrogenation was carried out with several Pt/SiO_2 catalysts prepared at various reduction conditions, and the surface state of Pt was measured by XPS [12]. It was revealed that metallic surface was more selective for the UOL formation than cationic surface. This was explained by the difference in the polarity between C=O and C=C bonds. It was also found that the catalyst with higher Pt dispersion was more selective for the UOL formation. This was ascribed to the favorable adsorption of C=O group at the interface between Pt and the support. Chatterjee et al. employed bimetallic Pt-Ru/MCM-48 and monometallic Pt/MCM-48 catalysts for the hydrogenation of citral in the presence of CO_2. Similar to the reaction with Ru-TPP described above, a maximum of the conversion was observed over both the catalysts at the CO_2 pressure where the reaction mixture changed from gas (CO_2, H_2) - liquid (substrate) - solid (catalyst) three phases to gas (CO_2, H_2, substarte) - solid (catalyst) two phases. The reaction selectivity was greatly different depending on the catalysts used. The monometallic Pt/MCM-48 catalyst selectively produced unsaturated alcohols (geraniol, nerol and citronellol), while the bimetallic Pt-Ru/MCM-48 catalyst selectively produced the partly saturated aldehyde (citronellal). Interestingly, the same bimetallic catalyst was selective for the CAL hydrogenation to unsaturated alcohol. The reason for this difference in the product selectivity was unknown. Pd/C was also found to be selective for the formations of saturated aldehydes from CAL and crotonaldehyde (R = CH_3 in Scheme 1) [15]. Similar to this, micelle-hosted Pd and Ru nanoparticles were selective for the formation of partly saturated aldehyde (citronellal) from citral in the presence of dense phase CO_2 [20].

Biphasic reactions are attractive in view of catalyst recycling, clean product separation, and applicability to continuous operations. For the hydrogenation of UAL in water/organic biphasic systems using water-soluble metal complexes, the interface between water and organic liquid (pure substrate or its solution in less-polar solvent) is a locus for hydrogenation. Polar C=O bond of an UAL molecule is oriented to the catalyst-containing water phase and it is more easily hydrogenated than the less-polar C=C bond existing away from the water phase in the organic phase. So, the selective hydrogenation of UAL to UOL can be easily achieved. Other polar solvents like ethylene glycol and poly(ethylene glycol) (PEG) are also usable for the biphasic catalysis. Influence of dense phase CO_2 was studied for the hydrogenation of UAL with biphasic catalysts using Ru complexes (Scheme 4) [10, 16]. Figure 5 represents the

reaction results of CAL hydrogenation obtained with a Ru-TPPTS (tris(m-sulfophenyl)-phosphine trisodium salt) dissolved in water [10]. The selectivity was not influenced by CO_2 pressure, while the conversion decreased above 11 MPa. At this CO_2 pressure, the reaction mixture changed from gas (CO_2, H_2) - liquid (substrate) - liquid (water, Ru-TPPTS) three phases to gas (CO_2, H_2, substrate) - liquid (water, Ru-TPPTS) two phases. The decrease of conversion at higher CO_2 pressures could be ascribed to simple dilution effect. The pressurization with CO_2 is not effective for this reaction system.

A biphasic catalyst system consisting of $H_2Ru(TPP)_4$ and PEG was used for the hydrogenation of citral [16]. Figure 6 shows the influence of CO_2 pressure on the reaction. The conversion was enhanced with increasing CO_2 pressure, while the selectivity to geraniol and nerol was always very high irrespective of the CO_2 pressure. The citral substrate was found to be well dissolved in both PEG and dense phase CO_2. So, the citral rich liquid phase was hardly formed under the reaction conditions. On the other hand, the Ru catalyst remained in the PEG liquid phase under the reaction conditions. So, the reaction mostly proceeded in the PEG liquid phase. The PEG phase was observed to expand by CO_2 dissolution. This is known to drop the viscosity of PEG drastically [21] and can enhance the solubility of H_2 in the PEG phase. Probably, the rate of mass transfer and the solubility of H_2 in PEG were enlarged by CO_2 dissolution, resulting in the higher conversion at elevated CO_2 pressures. The high selectivity to geraniol and nerol arose from the specific nature of the Ru complex catalyst, because very high selectivity was obtained in homogeneous reaction systems with conventional organic solvents and $scCO_2$. It was also found that, after the reaction, the product could be separated by $scCO_2$ extraction and the catalyst remained in the PEG was recyclable with a little deactivation. The high selectivity was unchanged after the catalyst was recycled several times [16]. As described above, pressurization with CO_2 was not effective for the biphasic reaction using H_2O. The difference between PEG and H_2O as the reaction medium would result from the lower solubility of CO_2 in H_2O.
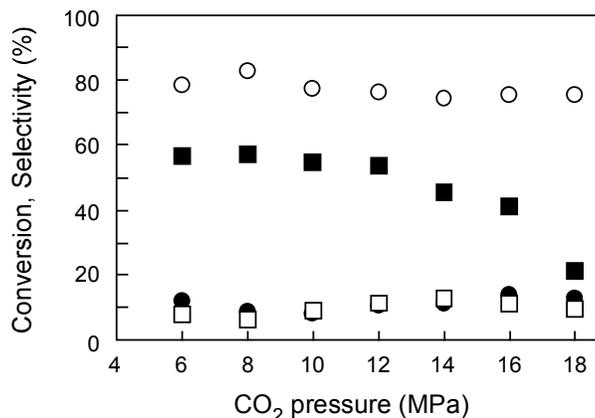

Figure 5. Effects of CO_2 pressure on hydrogenation of CAL with Ru-TPPTS biphasic catalyst. Conversion (■), and selectivities to UOL (○), SAL (□) and SOL (●). The reaction was carried out in a 50 cm^3 autoclave. Reaction conditions: CAL, 1 mmol; water, 2 cm^3; RuCl$_3$, 0.09 mmol; TPPTS, 0.36 mmol; H_2, 2 MPa; temperature, 70°C; reaction time, 2 h.
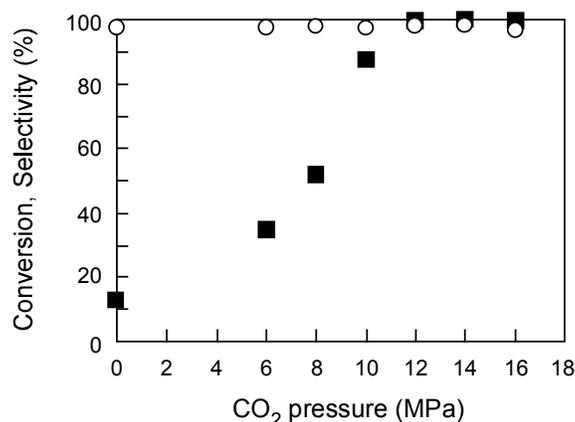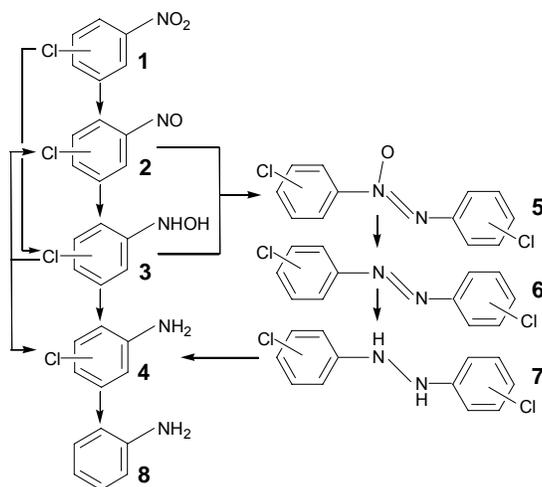
Figure 6. Effects of CO_2 pressure on hydrogenation of CAL with $H_2Ru(TPP)_4$ biphasic catalyst. Conversion (■), and total selectivity to geraniol and nerol (○). The reaction was carried out in a 50 cm^3 autoclave. Reaction conditions: CAL, 1 mmol; PEG-1000, 2 g; $H_2Ru(TPP)_4$, 0.01 mmol; H_2, 4 MPa; temperature, 65°C; reaction time, 1 h.

Scheme 5. Possible reaction pathways for the hydrogenation of chloronitrobenzene, as an example to show the complex reaction network for the hydrogenation of aromatic nitro compounds. 1: Chloronitrobenzene, 2: chloronitrosobenzene, 3: chlorophenylhydroxylamine, 4: chloroaniline, 5: dichloroazoxybenzene, 6: dichloroazobenzene, 7: dichlorohydrazobenzene, 8: aniline.

HYDROGENATION OF NITRO COMPOUNDS

The catalytic hydrogenation of aromatic nitro compounds is commonly used to manufacture aromatic amines, which are important intermediates for polyurethanes, dyes, pharmaceuticals, explosives, and agricultural products. The nitro compounds change to the desired aniline products via several reactive intermediates (Scheme 5) [22-24] and efforts have been made to achieve highly selective hydrogenation of aromatic nitro compounds in organic solvents and in the gas phase [25, 26]. It should be noted that the use of volatile

organic solvents is usually necessary for the gas phase hydrogenation of solid substrates such as chloronitrobenzene [27, 28]. Herein, we will review recent advances in the hydrogenation of aromatic nitro compounds in dense phase CO_2, a green reaction medium. Dense phase CO_2 has the ability to dissolve several aromatic nitro compounds such as nitrobenzene, chloronitrobenzene, nitroanisole, nitrotoluene, dinitrobenzene, and dinitrotoluene. The hydrogenation of these compounds has been performed in dense phase CO_2 and the role of CO_2 has recently been explored in more detail.

The hydrogenation of nitrobenzene in $scCO_2$ was investigated with several supported transition metal catalysts. The first related patent appeared in 1999 using a catalyst of Pd on polyolefinfiber. At 20 bar H_2 and 180 bar CO_2, aniline was formed with a selectivity > 90% at 40°C in 30 min [29]. Zhao et al. studied the hydrogenation of nitrobenzene at 35°C in $scCO_2$ and in ethanol with noble metal catalysts including Pd, Pt, Ru, and Rh supported on C, SiO_2, and Al_2O_3 [30]. In these media, the catalytic activity followed the order of Pt/C > Pd/C > Ru/C, Rh/C. The supports used influenced the activity of both Pd and Pt catalysts in $scCO_2$, and C was more effective than SiO_2 and Al_2O_3. The selectivity to aniline is higher in $scCO_2$ than that in ethanol for all the catalysts used. In ethanol, harmful by-products such as nitrosobenzene, azoxybenzene, and azobenzene (Scheme 5) were produced over all the Pt and Pd catalysts (supported on C, SiO_2, and Al_2O_3); in $scCO_2$, the selectivity to aniline increased somewhat for Pt catalysts and was almost 100% for Pd catalysts. Aniline could be formed in 100% yield over Pt/C and Pd/C in $scCO_2$ in a longer reaction time. The above results indicate that $scCO_2$ is a suitable replacement for organic solvents in the hydrogenation of nitrobenzene; however, the use of non-noble metal catalysts is more desirable for large-scale production due to their cost merits.

Recently, the selective hydrogenation of nitrobenzene was investigated with Ni/γ-Al_2O_3 using different media of dense phase CO_2, ethanol, and n-hexane at 35 and 50°C. In ethanol, several undesired toxic intermediates including nitrosobenzene, N-phenylhydroxylamine, azoxybenzene, and azobenzene were formed during the course of reaction [31]. Accumulation of these intermediates should be avoided for clean production processes. The use of additives might be effective to suppress the formation of those undesired intermediates; however, for Ni catalysts used in alcohols, the selection of such promoters is difficult because they cause some deactivation of the Ni catalysts [32]. It was shown that the total rate of nitrobenzene hydrogenation with Ni/γ-Al_2O_3 in dense phase CO_2 was larger than that in organic solvents under similar reaction conditions; the selectivity to aniline was almost 100% over the whole conversion range up to 100%. Thus, the reduction of intermediates can be accomplished along with an increase in the reaction rate in the presence of dense phase CO_2 [31]. Although the turnover frequency of Ni/γ-Al_2O_3 is much smaller than that of Pt/C, the selectivity to aniline is 100% for the former catalyst and so it is more attractive from the viewpoints of atom economy and unnecessary energy-consuming post-treatments (separation). In addition, the ferromagnetic properties of supported Ni catalysts may be usable for separating them by magnetic field. Thus, the combination of $scCO_2$ and Ni/Al_2O_3 is better than that of $scCO_2$ and Pt/C.

The hydrogenation of nitrobenzene was reported to be structure sensitive or structure insensitive, depending on the catalyst, experimental conditions, and medium used [33-35]. For instance, on Pd/C (activated carbon powder, Pd dispersion: 0.09–0.42), the reaction in methanol was structure sensitive at 50°C and at 5 bar H_2 [34]; however, on Pt/C (activated carbon cloth, Pt dispersion <0.2), it was a structure insensitive reaction in ethanol at 0°C and

at atmospheric H_2 pressure [35]. Zhao et al. also studied the influence of metal particle size on the hydrogenation of nitrobenzene in $scCO_2$ and in ethanol [30, 33]. The catalysts they used were commercially available Pd/C, Pd/Al_2O_3, Pt/C, and Pt/Al_2O_3 (Wako) and silica-supported Pd and Pt prepared by ion-exchange method. The dispersion of metal was changed from ca. 0.03 to 0.6. The hydrogenation over all Pd and a few selected Pt catalysts is structure sensitive in both ethanol and $scCO_2$ [30]. An exception was the reaction on Pt/C with Pt dispersion ranging from 0.04 to 0.13; the hydrogenation in ethanol was structure sensitive, TOF decreasing with an increase in Pt dispersion; in contrast, the reaction was structure insensitive in $scCO_2$ (Figure 7). The product selectivity in $scCO_2$ did not change with the size of supported Pt particles so much, while in ethanol the selectivity to either aniline or azobenzene slightly changed with the particle size [33].

The CO_2 pressure has significant effects on the total conversion of nitrobenzene over Pt, Pd, and Ni catalysts [30, 31, 33]. Generally, at CO_2 pressures > 6 MPa, the conversion increases first and then decreases on further introduction of CO_2; the conversion is maximal at a pressure near the phase transition point. For example, Meng et al. investigated the influence of CO_2 pressure on the conversion with Ni/Al_2O_3 at 35 and 50°C. The maximum conversion appeared at ca. 9 MPa at 35°C and ca. 12 MPa at 50°C, which were similar to the cloud points (9.2 and 12.6 MPa) observed at these temperatures (Figure 8). The phase behavior is an important factor in determining the rate of the hydrogenation of nitrobenzene in the presence of dense phase CO_2 [31]. The selectivity to aniline changed slightly with CO_2 pressure for Pd/C and Pt/C [30, 33]; in contrast, the perfect selectivity (~100%) to aniline remained unchanged for Ni/Al_2O_3 even when the reaction mixture changed from the gas–liquid–solid system to the gas–solid one [31]. The functions of dense phase CO_2 in the hydrogenation of nitrobenzene will be discussed later in more detail.

Hao et al. investigated the hydrogenation of nitrobenzene over Pd/C in CO_2-expanded cyclohexane [36]. At 50°C, cyclohexane (10 cm^3 in an 85 cm^3 reactor) expanded 3-fold at 7 MPa CO_2, above which the volume considerably increased and the liquid phase disappeared at above 8 MPa. Under 4–8 MPa CO_2, the conversion of nitrobenzene (> 90%) was larger than that in the neat cyclohexane (~70%); the selectivity to aniline was a little improved in CO_2-expanded cyclohexane but slightly lower than that in $scCO_2$.
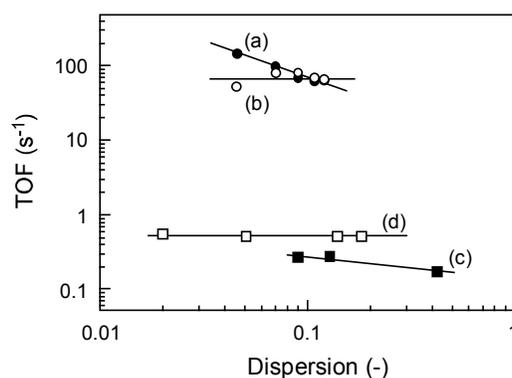

Figure 7. Plots of TOF against the degree of metal dispersion for liquid phase hydrogenation of nitrobenzene using different catalysts and reaction conditions. (a, b) 5 wt%Pt/C, solvent: (○) $scCO_2$ (14MPa), (●) ethanol. (c) (■) 3 wt% Pd/C, H_2 0.5 MPa, reaction temperature 50°C, methanol. (d) (□) Pt/C catalysts, atmospheric H_2 pressure, reaction temperature 0°C, ethanol.
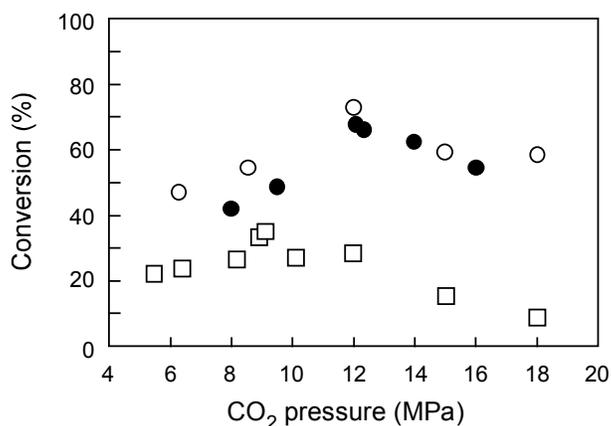
Figure 8. Influence of CO_2 pressure on the conversion of nitrobenzene in dense phase CO_2 over IM-Ni/Al$_2$O$_3$ and CP-Ni/Al$_2$O$_3$ catalysts. (○) IM-Ni/Al$_2$O$_3$ 0.3 g, 50°C; (●) CP-Ni/Al$_2$O$_3$ 0.1 g, 50°C; and (□) CP-Ni/Al$_2$O$_3$ 0.075 g, 35°C. (H$_2$ 4 MPa, 50 min.)

For the hydrogenation of halogenated aromatic nitro compounds, the suppression of dehalogenation is a challenging task. Moreover, nitro compounds with electron-withdrawing substituents, e.g., sulfonamide or halogen, will yield undesired arylhydroxylamines, colored azoxy, and azo products in large amounts during their hydrogenation reactions [37, 38]. The presence of dense phase CO_2 is helpful to improve the selectivity to the desired haloanilines during the hydrogenation of halogenated aromatic nitro compounds with several supported metal catalysts. A related patent was filed in 2004, using noble metal catalysts for hydrogenation at 0.1–30 MPa CO_2. It was reported that the hydrogenation of 2-chloronitrobenzene (0.79 g) with 1 wt% Pt/C (0.002 g) gave 2-chloroaniline (99.7 mol%) and aniline (0.3 mol%) in 150 min at 40°C and at 9.8 MPa CO_2 [39]. Ichikawa et al. examined the hydrogenation of 2-chloronitrobenzene over 1 wt% Pt/C in the presence and absence of 10 MPa CO_2 at 40 and 90°C [40]. The use of scCO$_2$ enhanced the reaction rate and strongly suppressed the dechlorination, resulting in a marked improvement in the selectivity to 2-chloroaniline compared with the neat reaction. The reaction system is also effective for the selective hydrogenation of other isomers and nitro compounds such as 3-chloronitrobenzene, 4-chloronitrobenzene, and 2,5-dichloronitrobenzene. These authors have suggested that CO_2 acts as a modifier blocking the active sites of the Pt catalyst for dechlorination. For the hydrogenation of 2-chloronitrobenzene in scCO$_2$, the catalytic activity followed the order of Pt/C > Pd/C > Ir/C > Rh/C, Ru/C, and the performance of Pt/C was better than Pt/Al$_2$O$_3$ and Pt/SiO$_2$ [40]. This trend is similar to that reported for the hydrogenation of nitrobenzene [30]. The undesired dechlorination could be almost completely suppressed for Pt/C, Ir/C, Pt/Al$_2$O$_3$, and Pt/SiO$_2$ in scCO$_2$, but not for Pd/C [40]. Xi et al. investigated the influence of CO_2 pressures on the hydrogenation of 2-chloronitrobenzene with Pd/C at 35°C. They reported that the dechlorination occurred to a less extent and the selectivity to 2-chloroaniline (ca. 90%) was higher at 8–12 MPa CO_2 than that (ca. 80%) obtained at CO_2 pressures < 6 MPa [41]. Recently, chemoselective hydrogenation of halogenated aromatic nitro compounds was achieved with supported Ni catalysts like Ni/TiO$_2$ in dense phase CO_2 at 35°C. Either the dechlorination or the accumulation of intermediates was successfully suppressed and the selectivity to the desired chloroaniline reached to ca. 99% [42].

The hydrogenation of 4-chloronitrobenzene with a Ni–B nanocatalyst was examined in CO_2-expanded methanol at 70–90°C over a total pressure range of 3.5–7.1 MPa. The conversion of 4-chloronitrobenzene in CO_2-expanded methanol was higher than that in unexpanded methanol. The enhancement in conversion was attributed to the increase in hydrogen solubility and mass transfer rate [43].

Zhao et al. [44] examined the solubility of several substituted nitro compounds such as 2-, 3-, 4-nitroanisole isomers, 2-, 3-, 4-nitrotoluene isomers, 1,3-dinitrobenzene and 2,4-dinitrotoluene (Scheme 6) in $scCO_2$ in the presence and absence of hydrogen. The structure and position of functional groups have significant impacts on the solubility in $scCO_2$. For example, the solubility of these compounds at 50°C followed the order of nitrotoluene > nitroanisole > 2,4-dinitrotoluene > 2,4-dinitrobenzene; the solubility of nitrotulene isomers was in the order of 2-nitrotoluene, 3-nitrotoluene > 4-nitrotoluene. The presence of hydrogen has a negative effect on the solubility of all these nitro compounds. These authors also made a comparative study on the hydrogenation of these compounds in $scCO_2$ and ethanol with 5 wt% Pt/C at 50°C. Under the same concentrations of nitro substrate and catalyst, the conversion in $scCO_2$ was comparable with that in ethanol; however, the selectivity to the amino products was larger in $scCO_2$ than that in ethanol.
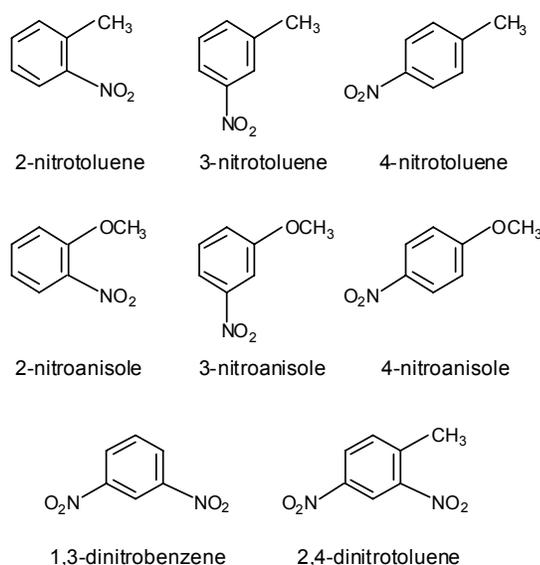
Scheme 6. Nitro compounds used for solubility measurements in $scCO_2$ and hydrogenation runs.

The role of dense phase CO_2 is a question of common interest. The properties and applications of CO_2-expanded liquids are discussed in a recent comprehensive review [45]. Dense phase CO_2 may enhance the solubility of reagent gases, increase the rate of transport, lower the melting point of substrates, generate *in situ* acidic species, and provide some environmental and safe benefits. Herein, discussion will be given to the interactions of CO_2 with the catalyst surface and reacting species that are significant for the selective hydrogenation of aromatic nitro compounds to amines.

(a) Interaction with the Catalyst Surface

Baiker and co-workers showed that CO formation via the reverse water-gas shift reaction from $scCO_2$ and H_2 ($H_2 + CO_2 \rightarrow CO + H_2O$) was a general feature of the commonly used Pt-group metal catalysts (Pt, Pd, Ru, and Rh) [46, 47]. Ichikawa et al. proposed that the dechlorination of chloroaniline with H_2 on the Pt surface was a structure-sensitive reaction and it was strongly suppressed in $scCO_2$. They also reported FTIR spectra of CO generated and adsorbed on the Pt surface during CO_2 hydrogenation. It was suggested that the *in situ* formed CO may be adsorbed preferentially on the kink or step sites of the Pt surface that are active for the dechlorination [40]. Thus, CO_2 may be a source of surface modifier (CO) for Pt/C in the hydrogenation of chloronitrobenzenes.

Additionally, interactions of $scCO_2$ with catalyst were suggested to be responsible for the highly selective Ni(II)-catalyzed hydrogenation of citral into the corresponding unsaturated alcohol in $scCO_2$ [48]. It was also demonstrated that the chemisorption of CO_2 on nickel surface results in electronic charge transfer from the metal to CO_2 as well as a change of the work function of the Ni(110) surface [49, 50]. However, it is still unclear whether the adsorption of CO_2 would have effects on the selective hydrogenation of aromatic nitro compounds with supported metal catalysts.

(b) Molecular Interactions of CO_2 with Reacting Species

The selectivity to the desired amine can be improved over various metal catalysts such as Ni, Pt, Pd, and Ir when the hydrogenation of aromatic nitro compounds is performed in/under dense phase CO_2 [30, 31, 33, 36, 40-42]. Meng et al. made *in situ* high-pressure FTIR measurements to study the roles of molecular interactions of CO_2 in the hydrogenation of nitrobenzene for such reactant and reaction intermediates: nitrobenzene, nitrosobenzene, and *N*-phenylhydroxylamine. Their FTIR results show that dense phase CO_2 strongly interacts with these compounds and modifies the reactivity of each species. For nitrobenzene, the bands of the symmetric and asymmetric stretching vibrations of the nitro group were blue shifted with CO_2 pressure up to ca. 6 MPa. At 6–20 MPa CO_2, these peaks were slightly red shifted but were located at larger wavenumbers than those in the ambient gas state and in the liquid state. The IR spectra of nitrosobenzene showed that it dominantly interacted by its oxygen atom to the carbon of CO_2 and this type of interaction weakened the N=O bond of nitrosobenzene with the increase in CO_2 pressure. Interactions also occurred between *N*-phenylhydroxylamine and dense phase CO_2 molecules. In a word, the reactivity of nitrobenzene is decreased but that of nitrosobenzene is increased and the transformation of *N*-phenylhydroxylamine to aniline is likely promoted. The interactions of CO_2 with the reacting species are an important factor responsible for the improved selectivity to aniline. These authors also proposed reaction pathways for the hydrogenation of nitrobenzene in dense phase CO_2 over Ni/γ-Al_2O_3. The hydrogenation mainly occurs through the consecutive route, i.e., nitrobenzene $\rightarrow$ nitrosobenzene $\rightarrow$ *N*-phenylhydroxylamine $\rightarrow$ aniline. The transformation of nitrobenzene to nitrosobenzene might be the rate-determining step [31]. The molecular interactions of CO_2 with reactants and/or intermediates would also be important for the selective hydrogenation of other nitro compounds to amines in dense phase CO_2.

HYDROGENATION OF OTHER SUBSTRATES

The above sections deal with hydrogenation reactions of aldehydes and nitro compounds in the presence of dense phase CO_2. The use of dense phase CO_2 is also advantageous to hydrogenation reactions of other various substrates using different types of catalysts and co-solvents. Recent interesting results will be described in this section, which further extend the scope of chemical transformations in/under dense phase CO_2.

Wang et al. conducted the hydrogenation of phenol (Scheme 7) in dense phase CO_2 using Rh nanoparticles supported on a carbon nanofiber [51]. The catalyst shows a high activity even at a low temperature of 50°C. It is important to note that dense phase CO_2 can retard the hydrogenation of cyclohexanone to cyclohexanol, resulting in an improved selectivity to cyclohexanone. Such a positive effect on the product selectivity was not observed in the presence of compressed N_2 instead of CO_2. Therefore, hydrostatic pressure is unimportant but chemical features of CO_2 molecules dissolved in the liquid phase (initially phenol) should be important. Those authors compared the activity of their Rh/carbon nanofiber catalyst with those of other heterogeneous catalysts reported in the literature [52]. Their catalyst is a better one for the selective hydrogenation of phenol to cyclohexanone. Further physicochemical works are needed to clarify reasons for the effectiveness of dense phase CO_2 and carbon nanofiber supported Rh nanoparticles for this selective hydrogenation.

Scheme 7. Hydrogenation of phenol.

Scheme 8. Hydrogenation of 2-butyne-1,4-diol to butane-1,4-diol.

Scheme 9. Hydrogenation of 4-*tert*-butylphenol to 4-butylhexanol.

Zhao et al. studied hydrogenation of 2-butyne-1,4-diol (Scheme 8) in dense phase CO_2 [53, 54], for which stainless steel reactor wall acted as an active catalyst. A high selectivity of 84% to butane-1,4-diol can be achieved at 100% total conversion and at a low temperature of 50°C. These authors claim an important point that the first step hydrogenation of butynediol (C≡C) to butenediol (C=C) is slower but the second step hydrogenation of butenediol to butanediol (C-C) is faster in dense phase CO_2 than in a conventional solvent ethanol. Butane-1,4-diol is one of useful intermediates in the manufacture of fine chemicals. This reaction system with dense phase CO_2 may have several advantages including cost and green processing benefits, compared with conventional reaction processes using noble metal catalysts and organic solvents.

Hydrogenation of naphthalene was studied by Hiyoshi et al. [55] in dense phase CO_2 and *n*-heptane. These authors used Rh/C catalysts different in the degree of metal dispersion in the range of 10% - 30% and investigated the influence of metal dispersion on the specific activity (turnover frequency, TOF). They observed that the TOF increased with decreasing Rh dispersion in dense phase CO_2, while it did not change so much in *n*-heptane. That is, the structure sensitivity of naphthalene hydrogenation with Rh/C depends on the reaction media used. Zhao et al. previously investigated the structure sensitivity for hydrogenation of nitrobenzene with C, SiO_2, and Al_2O_3-supported Pt and Pd catalysts, in which the metal dispersion ranged in 4% - 60% [30]. They showed that the TOF of either Pt or Pd decreased with the metal dispersion in both dense phase CO_2 and ethanol. Those results indicate that the tuning of metal dispersion (metal particle size) is important for controlling chemical reactions using supported metal catalysts in dense phase CO_2 as well. It should be noted, however, that the structure sensitivity in dense phase CO_2 would be different from that in conventional organic solvents and we should consider interactions of CO_2 molecules with reacting species including reactants, intermediates, products [56], and/or metal particles [57].

Hiyoshi et al. studied stereoselective hydrogenation of *tert*-butylphenols to corresponding butylhexanols with a Rh/C catalyst in dense phase CO_2 [58]. They observed, in hydrogenation of 4-*tert*-bytylphenol, that the selectivity to cis-*tert*-butylcyclohexanol was higher than those in organic solvents of 2-propanol and cyclohexane (Scheme 9). The ratio of cis-product against the total cis- and trans-products was around 0.8, which did not significantly change with CO_2 pressure at 5 - 25 MPa. These authors proposed reaction mechanisms including effects of dense phase CO_2 on events of an intermediate of 4-*tert*-butylcyclohexene-1-ol on the surface of supported Rh particles and the solubility of this enol species in the CO_2 phase. For such a relatively large substrate as 4-*tert*-butylphenol, it is interesting to study the structure sensitivity with Rh/C and other supported metal catalysts in dense phase CO_2 and organic solvents.

In the above-mentioned hydrogenation reactions there exist two or three phases such as solid catalyst phase, CO_2 + H_2 gas phase, and/or an organic liquid phase depending on reaction conditions. The addition of other phases is effective to exploit greener reaction processing and easier catalyst separation and recycling, including water, poly(ethylene glycol), ionic liquids, and fluorous solvents [1]. Some selected examples are described in the following.

It is difficult to separate polar organic compounds like biologically active ones from an aqueous catalyst solution. An effective approach is the use of a dense phase CO_2 - water system in which the former is a stationary catalyst phase and the latter is a continuous phase dissolving polar substrates. Leitner et al. exploited a continuous reaction system for

enantioselective hydrogenation of methyl-2-acetamidacrylate using CO_2-philic rhodium metal complex catalyst [59, 60]. Such a CO_2 - water system makes it easy to separate the products from the catalyst and dispose the water layer after reactions. Jessop et al. used a supercritical ethane - water system for hydrogenation of arenes with free colloidal Rh particles [61]. They showed that the hydrogenation occurred effectively in this system but not in a dense phase CO_2 -water system, probably due to pH problems. This indicates, however, that acid catalyzed reactions are possible in the absence of harmful inorganic acid catalysts under adjusted conditions (temperature, CO_2 pressure) [62, 63].
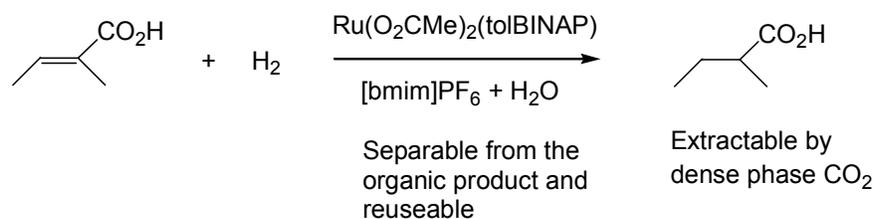
Scheme 10. Hydrogenation of tiglic acid and separation of the product.

Poly(ethylene glycol) (PEG) is one of useful green media for chemical transformations, which are less costly and toxic compared with ionic liquids and fluorous liquids [64]. While PEG is negligibly soluble in dense phase CO_2, it can dissolve organic compounds, metal phosphine complex catalysts, and CO_2. Interesting reaction and separation systems may be designed by combining these features of PEG and dense phase CO_2. Heldebrant and Jessop applied a PEG - CO_2 system for hydrogenation of styrene to ethyl benzene with a $RhCl(TPP)_3$ catalyst [65]. In this reaction system, the product can be extracted with flowing dense phase CO_2 and the catalyst-containing phase is recyclable. The loss of the active Rh species by leaching from the PEG phase into the product phase on the CO_2 extraction is negligible. The chain length of PEG is an important factor, as well as temperature and pressure, changing the features of the PEG - CO_2 reaction system. Jessop et al. made a comparative study on the effectiveness of different CO_2 - liquid polymer systems including poly(propylene glycol), poly(tetrahydrofuran), poly(dimethylsiloxane), and poly(methylphenylsiloxane) for hydrogenation reactions of arenes [66]. An additional interesting merit of using PEG is that air-sensitive catalysts could be encapsulated and protected by PEG (frozen) after reaction and depressurization.

Recently Liu et al. also showed an effective reaction and separation system using PEG and dense phase CO_2 for selective hydrogenation of α,β-unsaturated aldehydes to corresponding unsaturated alcohols with a $H_2Ru(TPP)_4$ catalyst [16]. For citral hydrogenation (Scheme 3), for example, a high selectivity of 98% to unsaturated alcohols (gerabiol and nerol) is achieved at a total conversion of 98% under H_2 4 MPa and CO_2 12 MPa conditions. The products can be extracted by compressed CO_2 stream after reaction and the PEG catalyst phase can be recycled without any post-treatment.

Moreover, it is interesting to combine dense phase CO_2 with ionic liquids (ILs) or fluorous liquids for chemical reaction and separation systems, which are both attracting much attention due to their unique solvent properties and/or catalytic actions. For those systems we should consider the solubility of organic substrates, gaseous species (H_2, CO_2), and/or catalyst components into ILs and fluorous liquids. For example, Brown et al. reported asymmetric

hydrogenation of tiglic acid in wet IL ([bmim]PF_6 and water) to 2-methylbutanoic acid with high enantioselectivity and conversion (Scheme 10) [67]. The product is separable with dense phase CO_2 after reaction and the catalyst-containing IL phase is recyclable without significant loss of the catalyst performance. West et al. used dense phase CO_2 as a switch tuning the phase behavior of organic and fluorous liquids [68]. An initial reaction mixture includes organic substrates, catalyst-containing fluorous liquid like C_6F_{14}, and H_2 (for hydrogenation), in which the organic and fluorous liquids are immiscible. When dense phase CO_2 is introduced into this mixture, the two liquid phases become miscible into a single phase and the hydrogenation takes place therein. On release of CO_2 pressure after reaction, the organic product phase and the catalyst-dissolved fluorous liquid phase are separated and the latter phase is recyclable. An important point is that dense phase CO_2 can act as phase behavior switch even at ambient temperature. We should further compare the physical and chemical properties among the above-mentioned ILs, fluorous liquids, and PEG and consider cost and environmental benefits when they are used for chemical reactions.

CONCLUSIONS

The significant features of heterogeneous reaction systems under dense phase CO_2 are demonstrated for selective hydrogenation reactions of α, β-unsaturated aldehydes, nitro compounds, phenol, and other substrates. The pressurization of the reaction liquid phases with CO_2 is effective for enhancing the rate of reaction and controlling the product selectivity. Those promotional effects may depend on several factors, as discussed above, and one of important factors is molecular interactions of CO_2 with reacting species (substrates, intermediates, and/or catalysts) in the liquid phases. Those interactions would produce unexpected positive outcome in other reactions in the presence and absence of gaseous reactants. Various types of catalysts are applicable and additional harmful organic solvents are not necessary as far as circumstances permit. The phase behavior may change depending on reaction conditions (temperature and pressure) and this may be useful for easy separation of catalysts and products after reaction. The multiphase reaction systems in/under dense phase CO_2 have several significant potentialities and may contribute to the design of effective green chemical reaction and separation processes.

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