

Impact of Carbon Dioxide Pressurization on Liquid Phase Organic Reactions: A Case Study on Heck and Diels–Alder Reactions

S. Fujita,^a T. Tanaka,^a Y. Akiyama,^a K. Asai,^a J. Hao,^b F. Zhao,^b and M. Arai^{a,*}

^a Division of Chemical Process Engineering, Graduate School of Engineering, Hokkaido University, Sapporo 060-8628, Japan

Fax: (+81)-(0)11-706-6594; e-mail: marai@eng.hokudai.ac.jp

^b State Key Laboratory of Electroanalytical Chemistry, Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, Changchun 130022, People's Republic of China

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Abstract: Heck coupling reactions of methyl acrylate with various aryl bromides have been investigated using a Pd/TPP catalyst in toluene under pressurized CO₂ conditions up to 13 MPa. Although CO₂ is not a reactant, the pressurization of the reaction liquid phase with CO₂ has positive and negative impacts on the rate of Heck coupling depending on the structures of the substrates examined. In the case of either 2-bromoacetophenone or 2-bromocinnamate, the conversion has a maximum at a CO₂ pressure of about 3 MPa; for the former, it is much larger by a factor of 3 compared with that under ambient pressure. For 2-bromobenzene, in contrast, the conversion is minimized at a similar CO₂ pressure, being half compared with that at ambient pressure. In the other substrates, including the other isomers of these three aryl bromides, the conversion simply decreases or does not change so much with the CO₂ pressure. To examine the factors responsible for the effects of CO₂ pressurization, the phase behavior and the mo-

lecular interactions with dense phase CO₂ have also been studied by visual observation and *in situ* high pressure FT-IR spectroscopy. In addition, impact of CO₂ pressurization was also studied for the Diels–Alder reactions of isoprene with a few dienophiles like methyl acrylate, methyl vinyl ketone, and acrolein in the same solvent, toluene, but a heterogeneous silica-alumina catalyst was used (the reaction system was liquid-solid biphasic). When the CO₂ pressure is raised, the conversion monotonously decreases for the three dienophiles; however, the product selectivity changes with the pressure, in particular for acrolein. The FT-IR spectroscopic measurements suggest that its reactivity is altered by interactions with CO₂ molecules under pressurized conditions.

Keywords: carbon dioxide; Diels–Alder reaction; expanded solvent phase; Heck reaction; multiphase reaction; pressure effect

Introduction

A CO₂-expanded organic liquid phase is an interesting medium for catalytic reactions; it is produced by increasing the volume of an organic liquid through the dissolution of a relatively large amount of CO₂ under high pressure conditions. Subramaniam and his co-workers first demonstrated the merits of using CO₂-expanded organic solvents for homogeneous catalytic oxidation reactions.^[1] The CO₂-expanded liquid phases offer several advantages like increased solubility of gaseous reactants involved, enhanced reaction rates, and decreased volume of organic solvents used. Studies have also reported on other catalytic reactions of hydrogenation^[2] and hydroformylation.^[3]

The present authors also studied the selective hydrogenation of α,β -unsaturated aldehydes of cinnamaldehyde and citral in CO₂-expanded liquid phases using soluble metal complexes and insoluble supported metal particles as catalysts.^[4] For the former, for instance, the total conversion is enhanced by the pressurization of the liquid substrate phase with CO₂ at pressures up to 16 MPa. This is the same positive effect as observed so far in other chemical reactions including gaseous reactants such as H₂, O₂, and CO, which may be similarly ascribed to the increase of the H₂ concentration in the liquid substrate phase. Furthermore, CO₂ pressurization shows another interesting feature, namely, the selective hydrogenation of the C=O bond can be promoted compared with that of the C=C bond, resulting in an increase in the selec-

tivity towards unsaturated alcohol (cinnamyl alcohol in the case of cinnamaldehyde). An important factor responsible for this promotion should be an interaction of the dissolved CO₂ molecules with the substrate, in particular with its carbonyl group, through which the reactivity of the carbonyl group may be modified. These interactions were evidenced by *in situ* high pressure FT-IR measurements.^[4b] We may expect from these results that the CO₂ pressurization has not only a physical effect of enhancing the dissolution of gaseous reactants but also a chemical effect of improving the reactivity of substrates and/or catalysts, in addition to modification of solvent properties (polarity, for example).

Thus, it is interesting to examine the effects of CO₂ pressurization on *true* liquid phase reactions that do not include any gaseous reactants. In the present work, our attention has been directed to Heck coupling using molecular homogeneous catalysts, which is one of most important carbon-carbon bond forming reactions in organic synthesis.^[5] The influence of such an elevated pressure of 100 MPa or above was previously studied on the rate of reaction and the product selectivity in several organic reactions including cross-coupling reactions. The interesting results and discussions obtained so far have been described in previous reviews.^[6] In those works chemical reactions were investigated under greatly elevated *static* pressures. In the present work, the liquid reaction mixture is pressurized by CO₂ at lower pressures, below 20 MPa, and a simple static pressure effect cannot be expected. However, the CO₂ pressurization is expected to have physical and/or chemical effects. The volume of a liquid phase may expand by dissolution of CO₂ molecules, causing a dilution of reacting species in the liquid phase. The dissolved CO₂ molecules may have interactions with substrates and/or catalysts, modifying their reactivity and activity. This work is the first case study to investigate the effects of CO₂ pressurization on liquid phase reactions. The Heck reactions of methyl acrylate with various aryl bromides were tested with a homogeneous Pd/TPP catalyst in toluene under pressurized CO₂ conditions. The effects of CO₂ pressurization will be compared and discussed with respect to the CO₂ pressure and the molecular structure of the substrates. This work shows that the rate of *liquid phase* Heck reaction is indeed enhanced by the presence of pressurized CO₂, although the rate enhancement is limited to bromoarenes of a certain structure. In addition, the impact of CO₂ pressurization was also studied for the *liquid-solid biphasic* Diels–Alder reactions of isoprene with a few carbonyl compounds using a heterogeneous silica-alumina catalyst. Unfortunately, the CO₂ pressurization was observed to merely decrease the rates of Diels–Alder reactions. Tester et al. investigated the Diels–Alder reactions of methyl vinyl ketone and penta-1, 3-diene in

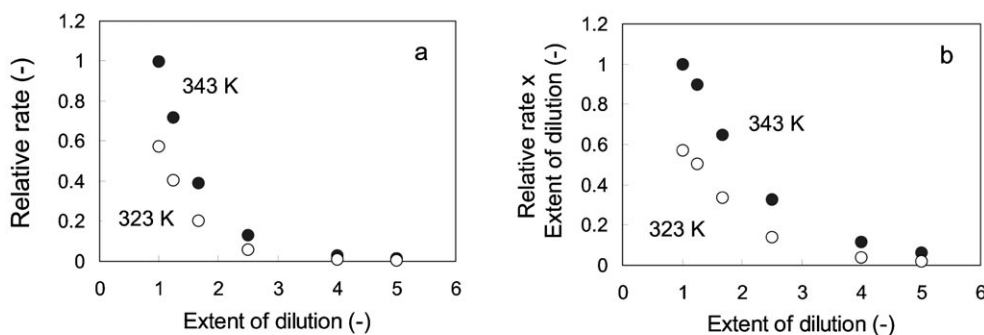
dense phase CO₂ (solvent) using an SiO₂ catalyst and showed the yield to simply decrease with the CO₂ pressure.^[7a] In our liquid-solid reactions of isoprene with a few carbonyl compounds under pressurized CO₂, however, the selectivity towards the [2] and [3] adducts can be altered by the CO₂ pressure. The results of Diels–Alder reactions at elevated static pressures are reviewed in a comprehensive book.^[7c] Elevated static pressures (100–2000 MPa used in the previous works) are expected to enhance the rate of a reaction that exhibits a large negative activation volume, such as the Diels–Alder reaction and the Heck coupling.^[6,7c] However, the present reaction systems are organic liquid phases pressurized by gaseous CO₂ at not such elevated pressures, i.e., below 20 MPa.

Results and Discussion

Heck Reactions

Previous Heck Reactions under Conventional Conditions: Influence of Dilution

As described later, the reactions were observed to occur in an expanded solvent (toluene) phase in the presence of pressurized CO₂. The volume expansion of the reaction phase causes the dilution of reacting species and this will change the rate of reaction. Since the analysis of Heck reaction kinetics is complicated, only a few workers^[8] have attempted so far to formulate the rate of reaction in spite of its importance in practical organic synthesis. Previously the authors presented an empirical rate equation for the Heck coupling of methyl acrylate and iodobenzene in NMP with the same catalyst and organic base as used in the present work.^[8a] This rate equation can be used to estimate the influence of simple dilution on the rate of Heck reaction under atmospheric pressure. This estimation will be helpful for later discussion of the Heck reactions under CO₂ pressurization, although the substrates and reaction conditions are different from those used in the present work. The rate of reaction was first calculated under such concentration conditions: methyl acrylate, iodobenzene, triethylamine 1 mmol cm⁻³ each; Pd(OAc)₂ 0.01 mmol cm⁻³; TPP 0.04 mmol cm⁻³. The rate of the reaction is further calculated for smaller concentration conditions, supposing that the reaction mixture is diluted by adding the solvent. Figure 1 gives the relative rate of the Heck reaction with respect to the one at the initial concentrations as a function of the extent of dilution (the initial concentration against the diluted concentration). As expected, the rate of reaction tends to decrease simply with the dilution (caused by the expansion of the reaction volume in the following cases



$$\text{Rate} = \frac{kAB^2CD}{(1+K_B B^2)(1+K_C C^4)(1+K_D D)^3(1+K_E E)}$$

k, K_B, K_C, K_D, K_E : constants. A, B, C, D, E : concentrations of aryl halide, vinyl compound, base, Pd, TPP.

Figure 1. Change in the rate of Heck coupling of iodobenzene and methyl acrylate with the extent of dilution of the liquid phase (NMP solvent) as estimated from an empirical rate expression obtained previously.^[8a] (a) Relative rate per unit volume with respect to that with no dilution (under initial concentration conditions) at 343 K (mole volume⁻¹ time⁻¹); (b) Relative rate produced by extent of dilution = total rate in expanded volume (mole time⁻¹). The initial concentrations of iodobenzene, methyl acrylate, triethylamine, palladium, and TPP used for this calculation are given in the text.

with CO₂ pressurization), in particular in the range of the small extent of dilution up to a factor of 2.

Heck Reactions under Pressurized CO₂ Conditions

The pressurization with CO₂ was observed to have different impacts depending on the aryl bromides used. Figure 2 shows the results of the conversion of iodobenzene and non-activated bromobenzene against CO₂ pressure. For both the substrates the con-

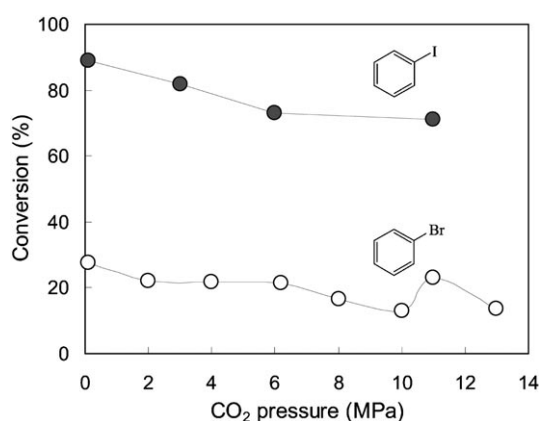


Figure 2. Influence of CO₂ pressurization on the Heck reaction of iodobenzene and bromobenzene with methyl acrylate. Reaction conditions: bromobenzene (iodobenzene) 10 mmol, methyl acrylate 10 mmol, Pd(OAc)₂ 0.1 mmol, TPP 0.4 mmol, triethylamine 10 mmol, toluene 10 cm³, temperature 393 K, time 2 h.

version tends to simply decrease with pressure; no positive effect was observed when the liquid reaction mixture was pressurized by CO₂. The results with activated bromobenzenes are given in Figure 3, which are complicated depending on the aryl bromide substrate and its structure. It is interesting to note that the conversion increases with the pressure in the range up to 3 MPa for 2-bromoacetophenone and ethyl 2-bromocinnamate. For the former substrate, the maximum conversion is larger by a factor of about 3 compared with that under ambient pressure. For the other isomers of these two substrates, the pressurization with CO₂ causes a significant or a marginal decrease in the conversion, similar to the results of the largest substrates, ethyl bromocinnamates. The conversion of 4-bromobenzaldehyde changes little with the CO₂ pressure, while that of 2-bromobenzaldehyde is minimized at around 2 MPa. These results demonstrate that the CO₂ pressurization can accelerate the conversion of the Heck reaction for a few specific substrates.

To examine the importance of CO₂, N₂ was used at pressures up to 6 MPa instead of CO₂ for Heck reactions of a few substrates (2-bromoacetophenone, ethyl 2-bromocinnamate, and 2-bromobenzaldehyde) for which the CO₂ pressurization has significant positive or negative impacts. The pressurization of these liquid reaction mixtures with N₂ was found to have no impact on the reactions. That means, the chemical nature of CO₂, as well as high pressure, is an important factor responsible for the changes of the Heck conversion observed (Figure 3).

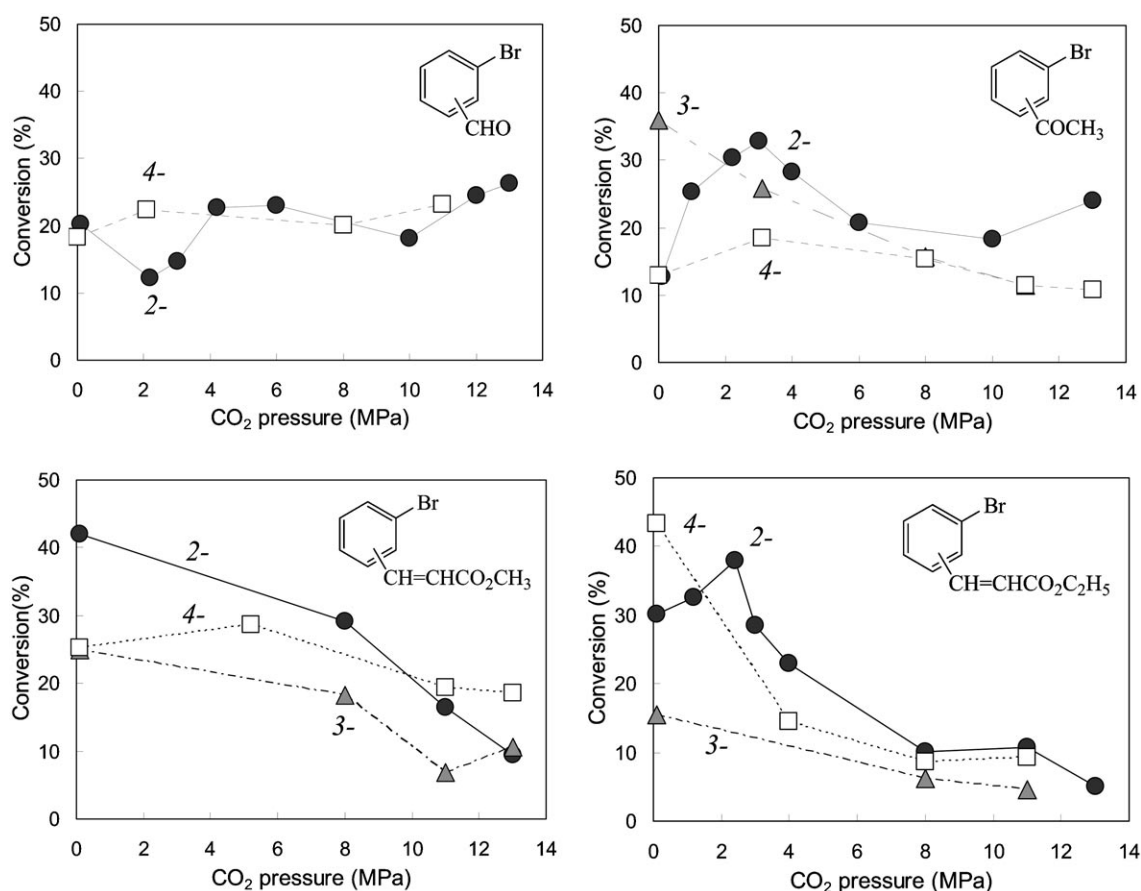


Figure 3. Influence of CO₂ pressurization on the Heck reactions of 2-, 3-, 4-isomers of bromobenzaldehydes, bromoacetophenones, methyl *trans*-bromocinnamate, and ethyl *trans*-bromocinnamate with methyl acrylate. Reaction conditions: bromoarene 10 mmol, methyl acrylate 10 mmol, Pd(OAc)₂ 0.1 mmol, TPP 0.4 mmol, triethylamine 10 mmol, toluene 10 cm³, temperature 393 K, time 2 h.

Volume Expansion of Organic Solvent Phase by CO₂ Pressurization

At high pressures a large quantity of CO₂ is dissolved into a liquid phase and this causes an expansion of the liquid phase.^[1] The volume expansion of the solvent phase by CO₂ pressurization was examined at the reaction temperature (393 K) by visual observation of pure toluene solvent at different CO₂ pressures. Figure 4 (a) shows that the volume of the toluene phase increases with pressure by dissolution of CO₂ molecules. The extent of volume expansion with respect to the initial volume at atmospheric pressure is given in Figure 4 (b). The volume expansion was also examined for toluene in the presence of substrates (methyl acrylate and 2-bromoacetophenone or 2-bromobenzaldehyde) and base (triethylamine) at similar concentrations to those used in the Heck reactions. The extent of volume expansion was not observed to change with the presence of these reacting species. In addition, no volume expansion was observed when the liquid phase was pressurized by N₂ instead of CO₂ at similar pressures.

High Pressure FT-IR of Substrates in Pressurized CO₂

According to the established reaction mechanisms, the Heck reaction goes through several reaction steps.^[5] We are at present unable to explain which steps are influenced by the CO₂ molecules dissolved in the reaction solution. We tested the Heck reactions of various aryl bromides with methyl acrylate using triethylamine in toluene. The interaction of CO₂ with triethylamine is likely to be weak.^[9] High pressure FT-IR measurements were used to examine the interactions of dense phase CO₂ with a few selected aryl bromides, as well as methyl acrylate, for which significant effects of CO₂ pressurization were observed. Unfortunately it is difficult to examine the C–Br bond of aryl bromides, for which the corresponding absorption bands may appear at small wavenumbers of 600–500 cm^{−1},^[10] due to the limitation of the FT-IR apparatus used. Figure 5 shows FT-IR spectra in the range of the ν(C=O) absorption for three bromoacetophenones (see Figure 3) in dense phase CO₂. The ν(C=O) absorption peak position for 2-bromoacetophenone

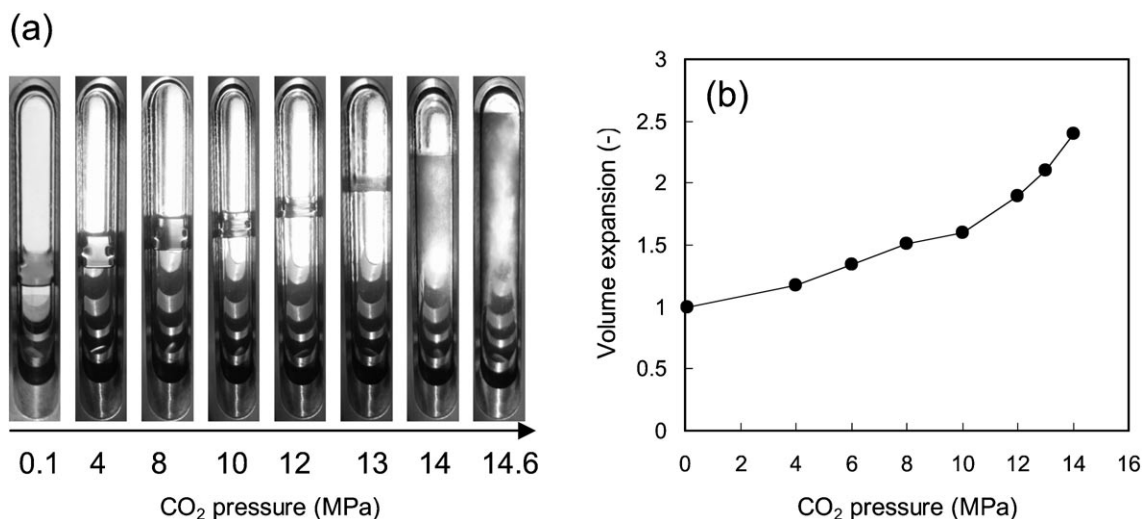


Figure 4. Volume expansion of pure toluene with pressurized CO₂ at different pressures at 393 K using an initial volume of toluene of 23.8 cm³ in a reactor volume 85 cm³.

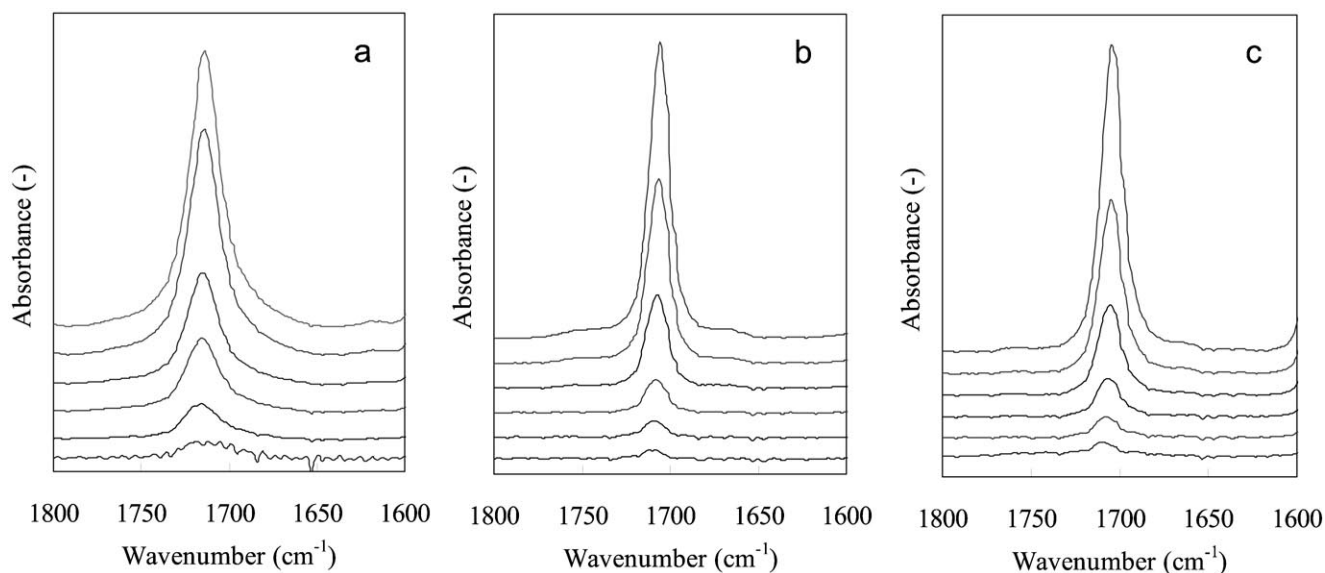


Figure 5. FT-IR spectra of 2-, 3-, 4-bromoacetophenones (**a**, **b**, **c**) dissolved in CO₂ at different pressures of 0.1, 3, 6, 8, 10, and 12 MPa (from bottom to top) and at 393 K. For **b**, the absorption at 0.1 MPa was very weak and so it is increased by three times herein.

changes with CO₂ pressure in a different manner as compared with those of 3- and 4-bromoacetophenones (Figure 6). The $\nu(\text{C}=\text{O})$ absorption band of the former substrate in dense phase CO₂ appears at larger wavenumbers by 7–10 cm⁻¹ than those of the latter two ones; the carbonyl bond of 2-bromoacetophenone is stronger compared with that of 3- or 4-bromoacetophenone. It is thus suggested that the C–Br bonds of the three substrates are modified by the presence of dense CO₂, indirectly through interactions of CO₂ with the other moieties or directly with the C–Br moiety. In addition, the modification of 2-bromoacetophenone should be different from that of 3- or 4-

bromoacetophenone. The above discussion is based on the FT-IR results of the substrates dissolved in dense CO₂ phase. However, the same discussion may be possible for the CO₂-dissolved expanded toluene phase, where the Heck reactions occurred, because the concentration of CO₂ in this phase is large.

We also made similar FT-IR measurements with methyl acrylate. Unfortunately, the solubility in dense phase CO₂ was decreased with increasing CO₂ pressure, and so noisy spectra were obtained. It was thus difficult to examine the influence of dense CO₂ molecules on the strength of the bonds of this substrate. However, we may speculate that CO₂ is unlikely to

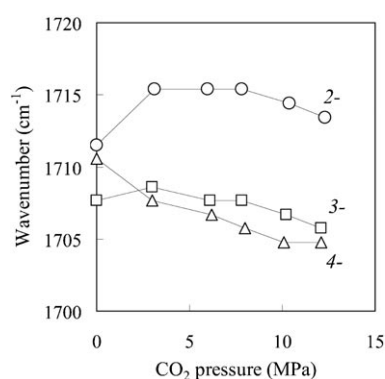


Figure 6. Dependence of $\nu(\text{C}=\text{O})$ absorption peak position on CO_2 pressure for 2-, 3-, 4-bromoacetophenones ($\circ$, $\square$, $\triangle$) based on the FT-IR results shown in Figure 5.

have a positive impact on the reactivity of methyl acrylate because of its decreasing solubility in dense phase CO_2 (decreasing attractive interactions with CO_2).

Roles of Dense CO_2 Molecules in Heck Reactions

It should be noted again that the rate of the *liquid phase* Heck reaction can be enhanced by pressurizing the reaction mixture with CO_2 at a low pressure of 2–4 MPa, although the enhancement effect is limited to a few bromoarenes of a certain structure (2-bromoacetophenone and ethyl 2-bromocinnamate). A brief discussion is given here on the role of dense phase CO_2 in this observed enhancement. The pressurization with CO_2 decreases the concentration of reacting species in the liquid reaction phase as a result of its volume expansion due to the dissolution of CO_2 at high pressures (Figure 1 and Figure 4). This is a negative impact on the rate of reaction, and so the other positive impacts involved with CO_2 should be superior to that negative impact.

Toluene is a non-polar solvent with a dielectric constant $\epsilon_r = 2.38$ and an empirical parameter of solvent polarity $E_T(30) = 33.9 \text{ kcal mol}^{-1}$ at 298 K.^[11] Dense CO_2 fluid is a non-dipolar solvent^[12] and the ϵ_r value increases with pressure, ranging from 1.020 to 1.556 at 298 K at pressures of 2–18 MPa.^[13] The $E_T(30)$ value was also estimated for dense CO_2 fluid, being 28.5 and 29.0 kcal mol^{-1} at 15 and 20 MPa, respectively, at 313 K.^[14] Then, it is assumed that the dissolution of CO_2 into the toluene phase scarcely changes its nature as a continuum of non-polar reaction medium.

Several aryl bromides and methyl acrylate were used in the present Heck reactions and the effects of CO_2 pressurization significantly depended on the structures of bromoarenes used. No effects were observed with N_2 pressurization and so the molecular features of CO_2 are important. The high pressure FT-

IR measurements indicate that dense phase CO_2 molecules interact with the aryl bromide substrates in different manners depending on their structures. It is speculated that the steps involved with a bromoarene are influenced by the CO_2 molecules dissolved in the liquid phase. The Heck reaction is such a complicated system that it goes through several steps with several reacting species (Pd/TPP catalyst and substrates),^[5] and so further discussion is not possible at present. We think that spectroscopic measurements of the reaction mixtures under the reaction conditions are also required.

Diels–Alder Reactions

The impact of CO_2 pressurization was also studied for a different reaction system, the Diels–Alder reaction with a heterogeneous $\text{SiO}_2\text{--Al}_2\text{O}_3$ catalyst, which was a liquid-solid biphasic system including no gaseous reactant. We did not use Heck reactions using heterogeneous Pd catalysts like Pd/C because the leaching of supported Pd species into the solvent would occur and the reactions would not be heterogeneous.^[5,15] The Diels–Alder reactions were also studied at such an elevated static pressure of 1000 MPa.^[7e] Such elevated pressures are expected to accelerate the rate of reaction because the Diels–Alder reaction as well as the Heck coupling may exhibit a negative activation volume. The present reactions were conducted under gaseous CO_2 atmosphere at pressures below 20 MPa.

Diels–Alder Reactions under Pressurized CO_2 conditions

Figure 7 shows the results obtained with three different dienophiles. Unfortunately, the conversion was observed to merely decrease with the CO_2 pressure. This simple decrease of the conversion should result from a simple dilution effect of CO_2 molecules into the liquid phase at high pressures. One may consider another possibility that CO_2 molecules are adsorbed on the surface of the $\text{SiO}_2\text{--Al}_2\text{O}_3$ catalyst and this may mask the catalytically active sites and decrease the total activity. A few previous authors reported detailed investigations of the adsorption of CO_2 on a similar oxide, SiO_2 and C.^[7a,16]

Table 1 summarizes the product selectivity at different CO_2 pressures in the Diels–Alder reactions of isoprene with the three dienophiles. The results show that the ratio of [3] adduct to [2] adduct can be altered by the CO_2 pressure, which changes most extensively from 47:53 to 73:27 at pressures up to 16 MPa for acrolein. The change is less significant for the other dienophiles but the ratio does also change from 63:37 to 73:27 and from 70:30 to 75:25 for methyl

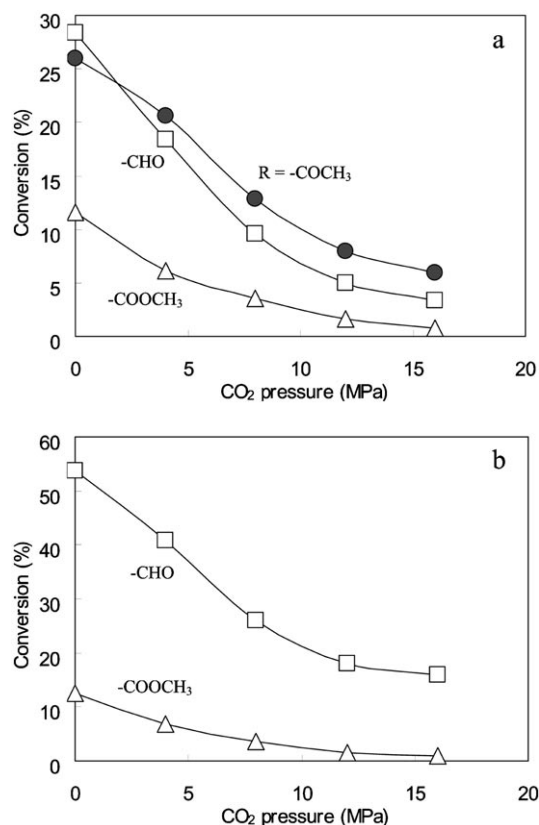


Figure 7. Influence of CO₂ pressurization on the Diels-Alder reactions of isoprene with CH₂=CH-R in toluene (a) and ethanol (b). Reaction conditions: SiO₂·Al₂O₃ 0.2 g, isoprene 20 mmol, CH₂=CH-R 10 mmol, solvent 4 cm³, temperature 353 K, time 2 h (4 h for methyl acrylate).

vinyl ketone and methyl acrylate, respectively, in the same pressure range. In other words, the ratio of **3** to **2** and the effect of CO₂ pressure on this ratio are larger in the order of acrolein > methyl vinyl ketone > methyl acrylate. At a high pressure of 16 MPa, very similar **3** to **2** ratios are seen for the three dienophiles, which are similar to those with Diels-Alder reactions of cyclopentadiene with methyl vinyl ketone and methyl acrylate in dense phase CO₂ reported by Tester et al.^[7a] They reported that the product selectivity was not affected by CO₂ pressure. It should be noted again that the selectivity of liquid phase Diels-Alder reactions may be changed with CO₂ pressure when these are conducted under pressurized CO₂ (in CO₂-dissolved expanded solvent phase). The Diels-Alder reactions in dense phase CO₂ were previously investigated by several workers and the effects of CO₂ pressure on the total conversion and the product selectivity were observed for some reactions, as described in review articles.^[7b-d] As discussed above for Heck reactions, the pressurization and dissolution of CO₂ in the toluene phase will scarcely change its features as a continuum of solvent for the Diels-Alder reactions as well. The CO₂ molecules dissolved in tol-

Table 1. Influence of CO₂ pressure on the selectivity of liquid-solid biphasic Diels-Alder reactions of isoprene with methyl acrylate, methyl vinyl ketone, and acrolein.^[a]

CO ₂ pressure [MPa]	Product selectivity (3 : 2 ratio)		
	Methyl acrylate	Methyl vinyl ketone	Acrolein
0.1	70:30 (71:29) ^[b]	63:37	47:53 (68:32) ^[b]
4	70:30 (71:29) ^[b]	66:34	55:45 (69:31) ^[b]
8	70:30 (71:29) ^[b]	69:31	69:31 (83:17) ^[b]
12	76:24 (74:26) ^[b]	70:30	70:30 (83:17) ^[b]
16	75:25 (76:24) ^[b]	73:27	73:27 (83:17) ^[b]

^[a] Reaction conditions: SiO₂·Al₂O₃ catalyst 0.2 g, isoprene 20 mmol, CH₂=CH-R 10 mmol, toluene 4 cm³, temperature 353 K, time 2 h (4 h for methyl acrylate).

^[b] Data collected with ethanol instead of toluene.

uene would affect the reactivity of substrates; they surround the substrate molecules inducing interactions between the substrate and CO₂ molecules in the liquid phase. As the pressure is raised, the state of such a clump of substrate-CO₂ molecules in an organic solvent of toluene may become similar to that in a dense phase CO₂ medium. Then, the product selectivity obtained under highly pressurized CO₂ should be similar to that in the CO₂ medium. It is known that the selectivity of Diels-Alder reactions is different in a bulk organic phase and in organic droplets (dispersed in water), in which water-insoluble reactants are clumped together, increasing the *endo* selectivity in the reaction of cyclopentadiene and methyl vinyl ketone.^[17]

The reaction runs were also conducted with methyl acrylate or acrolein in ethanol instead of toluene (Figure 7, Table 1). Although toluene and ethanol are different in solvent properties,^[11] the results of Diels-Alder reactions in these organic solvents are similar for the ester methyl acrylate. For the aldehyde acrolein, however, the conversion in ethanol and the **3** to **2** ratio are larger as compared with those in toluene. The enhancement of Diels-Alder reactions by solvent effects in hydrogen-bonded donor (HBD) solvents is known with carbonyl-containing reactants and the hydrogen bonding between the substrate and the solvent, -C=O···H-O-R, is significant in accelerating

the reactions.^[11] Such a hydrogen bond may also cause the increase of the **3** to **2** ratio in ethanol. The **3** to **2** ratio is increased with increasing CO₂ pressure in either ethanol or toluene and the extent of change is large at around the critical pressure of pure CO₂. The CO₂ molecules dissolved in the solvents should play important roles for determining the product selectivity as well as the total conversion. The product selectivity may be altered by interactions of the carbonyl group with the HBD solvent (ethanol in the present case) or the dense phase CO₂ molecules (*vide infra*).

High Pressure FT-IR of Substrates in Pressurized CO₂

In situ high pressure FT-IR was used to examine molecular interactions of CO₂ with the substrates. The FT-IR measurement was made for a single substrate dissolved in dense phase CO₂ at different pressures of 0.1–20 MPa. The diene, isoprene, was observed to give several FT-IR absorption bands assignable to $\nu(\text{C}=\text{C})$ at 1600 cm⁻¹ and $\delta(\text{CH})$ at 900–1000 cm⁻¹. These absorption bands were not strong but the spectra did not seem to change with CO₂ pressure. Figure 8 presents FT-IR spectra in the range of 1800–1600 cm⁻¹, where the absorption bands of $\nu(\text{C}=\text{O})$ and $\nu(\text{C}=\text{C})$ appeared,^[10] for the three dienophiles in dense phase CO₂ at a reaction temperature of 353 K. The FT-IR absorption also occurred in different ranges of wavenumber but the absorption bands were weak and these were not used for the present purpose

for qualitative discussion of interactions with CO₂ molecules. The strength of the absorption bands was not observed to increase monotonously with CO₂ pressure, and an important factor for this should be a change of absorption coefficient with the pressure.^[18b] Our attention will herein be given to the absorption peak positions and so the spectra of Figure 8 are given at appropriate different absorption scales. For acrolein, the spectra at 0.1 MPa and 4 MPa are different but the absorption occurs in the same wavenumber range. A weak band of $\nu(\text{C}=\text{C})$ is seen at around 1650 cm⁻¹ and the $\nu(\text{C}=\text{O})$ absorption is split into two bands, of which a stronger band is located at 1715 cm⁻¹ and a weaker band at around 1740 cm⁻¹. The absorption band splitting was previously reported for a few carbonyl compounds.^[18] The weaker band seems to make a blue-shift with increasing CO₂ pressure, while the stronger band does not shift. For methyl vinyl ketone, $\nu(\text{C}=\text{O})$ and $\nu(\text{C}=\text{C})$ absorption bands appear at 1725 cm⁻¹ and 1690 cm⁻¹, respectively, which are not seen to shift with CO₂ pressure. For methyl acrylate, the $\nu(\text{C}=\text{O})$ absorption band can be seen at around 1740 cm⁻¹ with a very weak $\nu(\text{C}=\text{C})$ absorption at 1670 cm⁻¹. One may see a red-shift of the $\nu(\text{C}=\text{O})$ absorption peak with CO₂ pressure but not so significantly. From these FT-IR results it is impossible to consider the electron negative or positive features of the C-1 and C-2 carbon atoms of the three dienophiles; however, interactions of dense phase CO₂ with the carbonyl group may be stronger for acrolein compared with the other two carbonyl compounds, as estimated from the peak shift of $\nu(\text{C}=\text{O})$

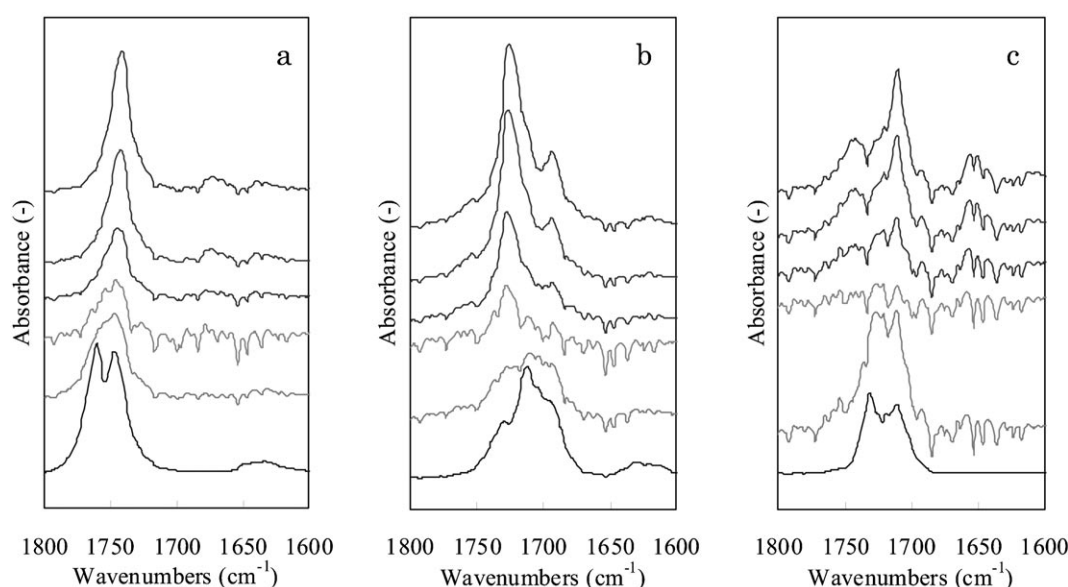
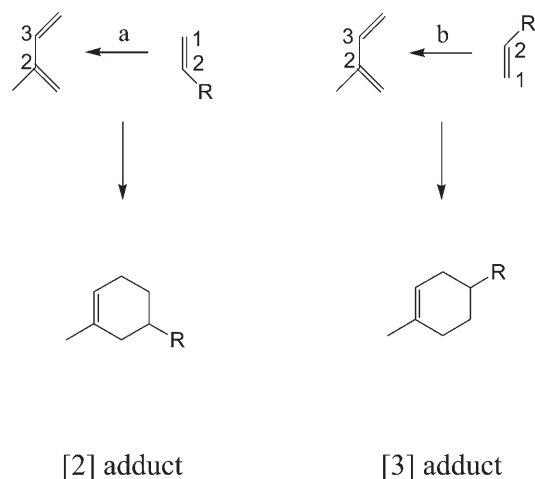


Figure 8. FT-IR spectra of methyl acrylate (**a**), methyl vinyl ketone (**b**), and acrolein (**c**) dissolved in CO₂ at different pressures of 0.1, 4, 6, 8, 12, 16, 20 MPa (from bottom to top) and at 353 K. For **a** and **b**, the absorption at 8 MPa was weak and it is increased by three and two times, respectively, herein.



Scheme 1. Two approaches, a and b, yielding [2] adduct and [3] adduct.

absorption band at a larger wavenumber with increasing CO_2 pressure. The change in the product selectivity of the Diels–Alder reaction is most significant for acrolein. Thus, CO_2 –carbonyl group molecular interactions would play a role in the alternation of the product selectivity with increasing CO_2 pressure (Table 1).

As described above, the CO_2 molecules dissolved in the liquid phases should have significant effects on the reactions. One is a simple dilution effect whereby the concentrations of the reacting species are reduced by the dissolution of CO_2 and the rate of reaction becomes decreased at increasing CO_2 pressure (Figure 7). The change of the **3** to **2** ratio with CO_2 pressure may be ascribable to another effect of modification of reactivity of reacting species through interactions of CO_2 molecules in the liquid phases. The authors speculate that CO_2 molecules interact with the carbonyl group of a dienophile and this makes its C-1 carbon more positive compared to the C-2 carbon. As a result, the approach b of Scheme 1 may be more favorable to occur than that between the dienophile and isoprene in which C-3 may be more positive than C-2 owing to the electron-withdrawing nature of the methyl group attached to C-2. Thus, the **3** to **2** ratio may be increasing with the CO_2 pressure. As another possibility it may also be suggested that the interactions of CO_2 molecules with the carbonyl group cause steric effects on the product selectivity. We envisage that a large clump of the carbonyl group surrounded by CO_2 molecules is formed through the interactions. This may make the approach b of Scheme 1 more likely to occur compared with approach a, resulting in the increase of the **3** to **2** ratio with the CO_2 pressure. These effects should be most significant for acrolein, of which the carbonyl group could have most significant interactions with CO_2 , compared with methyl vinyl ketone and methyl acrylate. The differences in

the **3** to **2** ratios among the three dienophiles may result from steric effects because the **3** to **2** ratio is in the opposite order to the electron withdrawing nature $-\text{CHO} > -\text{COCH}_3 > -\text{COOCH}_3$.

Similar explanations would be possible for the solvent effects of ethanol and toluene on the product selectivity (Table 1). The former HBD solvent can interact with the carbonyl group through hydrogen bonding and affect the product selectivity, similar to the impact of the interaction with dense phase CO_2 molecules as discussed above. The use of ethanol increased the rate of Diels–Alder reaction (Figure 7) compared with toluene. However, the pressurization with CO_2 caused the dilution of the reacting species, in addition to the CO_2 –carbonyl interactions, and so it simply resulted in a decrease of the reaction rate.

Conclusions

In the present work we have investigated the Heck reactions of methyl acrylate with various bromoarenes in *n*-hexane pressurized by CO_2 at pressures up to 14 MPa. The following conclusions are drawn with respect to the impacts of the CO_2 pressurization on the *true* liquid phase reactions. Indeed, the conversion is influenced by the CO_2 pressurization although the reaction mixture does not include any gaseous reactants. The effects of dense phase CO_2 strongly depend on the structures of bromoarenes used. The conversion increases with CO_2 pressure for either 2-bromoacetophenone or 2-bromocinnamate and it has a maximum at a medium pressure of 2–4 MPa. However, such promotion does not occur with the other 3- and 4-isomers of these substrates. The CO_2 pressurization increases the volume of the liquid reaction phase due to the dissolution of CO_2 molecules, which causes a decrease in the concentration of the reacting species. This negative effect on the rate of Heck reaction may be overthrown by a positive effect with CO_2 dissolved in the liquid reaction phase for these two bromoarenes. The high pressure FT-IR results suggest interactions of the bromoarenes with the CO_2 molecules, which might play a role for the rate enhancement observed. Unfortunately, such an enhancement does not appear with the other substrates such as bromobenzaldehydes and methyl *trans*-bromocinnamates. No promotion effect of CO_2 pressurization was observed for liquid-solid Diels–Alder reactions of isoprene with methyl acrylate, methyl vinyl ketone, and acrolein using a heterogeneous $\text{SiO}_2\cdot\text{Al}_2\text{O}_3$ catalyst in toluene and ethanol. It should be noted, however, that the [3] and [2] adduct ratio does change with the CO_2 pressure. The most significant change occurs for acrolein and the FT-IR spectroscopy measurements suggest that its reactivity is altered through interactions with CO_2 molecules under pressurized conditions.

Experimental Section

Heck and Diels–Alder Reactions

A stainless steel autoclave reactor (50 cm³) was used to run Heck reactions in an organic solvent (toluene) pressurized with CO₂ at different pressures up to 13 MPa. Typical reaction conditions were: palladium acetate (Wako) 0.1 mmol, triphenylphosphine (Wako) 0.4 mmol, methyl acrylate (Aldrich) 10 mmol, aryl halide 10 mmol, triethylamine (Wako) 10 mmol, toluene (Wako) 10 cm³. All the chemicals were used as received. The reactor was charged with these quantities of substrates, base, catalyst, and toluene and purged with CO₂ three times. The reactor was then heated in an oil bath while mixing the reaction mixture by a Teflon-coated magnetic stirrer. When the reactor temperature reached to the desired value of 393 K, CO₂ was introduced to the desired pressure by a backpressure regulator (JASCO SCF-Bpg) and the reaction time was measured. Then, the reactor was cooled down to room temperature and depressurized carefully. The reaction products were analyzed by gas chromatography (GL Science GC-390B) using iodobenzene as an internal standard and gas chromatography-mass spectrometry (Shimadzu GC-MS QP5050 A). The conversions were determined from the amounts of aryl halides reacted. The same high pressure reaction system was also used to run Diels–Alder reactions of isoprene with the different dienophiles methyl acrylate, methyl vinyl ketone, and acrolein. The reaction procedures were the same as used for the Heck coupling runs and for the GC analysis, decane was used as an internal standard. A heterogeneous silica-alumina, JRC-SAH-1 supplied by Catalysis Society of Japan, was used as a catalyst. Under the experimental conditions used, the total conversion and the product yield were reproducible in relative errors of within $\pm 5\%$.

Phase Behavior and FT-IR Measurements

The phase behavior was examined by visual observation using an autoclave with a transparent glass window. A desired volume of a toluene phase was added to the autoclave with the volume ratio of toluene/autoclave similar to that used in Heck reaction runs. An atmospheric pressure of CO₂ was introduced and the autoclave was closed and heated to the desired reaction temperature of 393 K. While keeping the autoclave at this temperature, more CO₂ was introduced up to higher pressures. The phase behavior was visually examined at different CO₂ pressures.

The FT-IR spectra of selected substrates in dense phase CO₂ were measured with an *in situ* high pressure FT-IR spectrometer, JASCO FTIR-620, equipped with a 1.5 cm³ high pressure cell using crystalline ZnS windows with an optical path length of 4 mm.^[4] The FT-IR measurements were made at 393 K and at CO₂ pressures up to 12 MPa. A small volume (about 0.01 cm³) of a sample carbonyl compound was introduced into the cell and it was purged with CO₂ three times. The cell was heated up to a temperature of 393 K by the circulation of preheated oil around it (JULABO F25-HP). Then, the pressure was increased slowly by introduction of liquid CO₂ by a pressure pump while stirring by a Teflon coated magnetic stirrer. When the pressure reached a certain value, the stirring was continued for 2 min and stopped. The FT-IR spectra were measured

with a triglycine sulfate (TGS) detector at a wavenumber resolution of 2 cm⁻¹ by using the absorption spectrum of pure CO₂ at the same pressure as background.

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