

The Effect of High Pressure on the Heck Reaction – A Contribution to a Deeper Understanding of the Mechanism

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The influence of high pressure on the Heck reactions of iodobenzene with methyl, ethyl and *tert*-butyl acrylate, and of both 4-nitrophenyl iodide and 4-nitrophenyl triflate with methyl acrylate, has been studied for the first time by quantitative on-line FT-IR spectroscopy. Reaction rates and activation parameters ($\Delta H^\ddagger$, $\Delta S^\ddagger$, $\Delta V^\ddagger$) were determined at temperatures between 50 and 120 °C and pressures up to 3000 bar. A clear influence on the kinetics of the reactions was observed by the nature of the leaving group and by the steric and electronic features of the acrylate. *tert*-Butyl acrylate, which is more electron-rich than methyl acrylate according to PES measurements, was found to react 1.4-times faster on average than methyl acrylate and, at elevated pressures, triflate turned out to be a better leaving group than iodide.

Thus, the observed activation volume for the reaction of iodobenzene with *tert*-butyl acrylate ($\Delta V^\ddagger = -12 \text{ cm}^3 \text{ mol}^{-1}$) is more negative than that of the reaction of iodobenzene with ethyl acrylate ($\Delta V^\ddagger = -7 \text{ cm}^3 \text{ mol}^{-1}$) or methyl acrylate ($\Delta V^\ddagger = -5 \text{ cm}^3 \text{ mol}^{-1}$). For the variation of the leaving group in 4-nitrophenyl iodide and 4-nitrophenyl triflate, the activation volumes for the reaction of each with methyl acrylate are -9 and $-37 \text{ cm}^3 \text{ mol}^{-1}$, respectively. The results suggest that the rate-determining step of the overall reaction is not the oxidative addition, but is either the alkene coordination or the subsequent carbopalladation.

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Introduction

The kinetic approach to elucidating the mechanism of a chemical reaction involves the measurement of reaction rates and the determination of rate coefficients as a function of as many chemical and physical variables as possible. High pressure has been used as an important variable within an increasing number of studies into the mechanism of organic and inorganic reactions.^[1,2] From the pressure dependence of the rate coefficients, k , the activation volume, $\Delta V^\ddagger$, is derived according to the relation: $\Delta V^\ddagger = -RT (\partial \ln k / \partial p)_T$. Under conditions of chemical reaction control, the partial molar volume of the transition structure may be estimated from $\Delta V^\ddagger$ at known partial molar volume(s) of the starting materials. If the transition structure (TS) is more compact than the sum of the reactands, the reaction is accelerated by pressure and $\Delta V^\ddagger$ is negative, whereas a reaction with a TS that is more expanded than the sum of the reactands is retarded by high pressure and $\Delta V^\ddagger$ is positive. The more-negative (positive) is $\Delta V^\ddagger$, the larger is the

acceleration (retardation) of the reaction by pressure. Partial formation of a bond en route to the TS between atoms previously not bonded to each other, and separation of electrostatic charges (as, e.g., in solvolysis), which gives rise to solvent electrostriction, lead to a negative contribution to the activation volume. Conversely, partial cleavage of a bond and dispersal of electrostatic charge en route to the transition state enhance the activation volume.

A few high-pressure studies have been reported for organometallic reactions in general,^[3–5] and for the palladium-catalyzed arylation and alkenylation of alkenes — the well-known Heck reaction^[6] — in particular.^[4,7–12] Trost et al. observed that palladium-catalyzed [3+2] cycloadditions are retarded under high pressure,^[5] whereas the rate of Heck reactions is enhanced by high pressure.^[7,9–12] Reiser et al. were the first to combine high pressure and palladium catalysis, by which they achieved an enhanced enantioselectivity,^[7] and an increase of turnover numbers.^[8] High pressure also allows alkenyl and aryl chlorides^[9] or bromides^[10] to be coupled at lower temperature and with better yields as compared to the same reactions at ambient pressure.

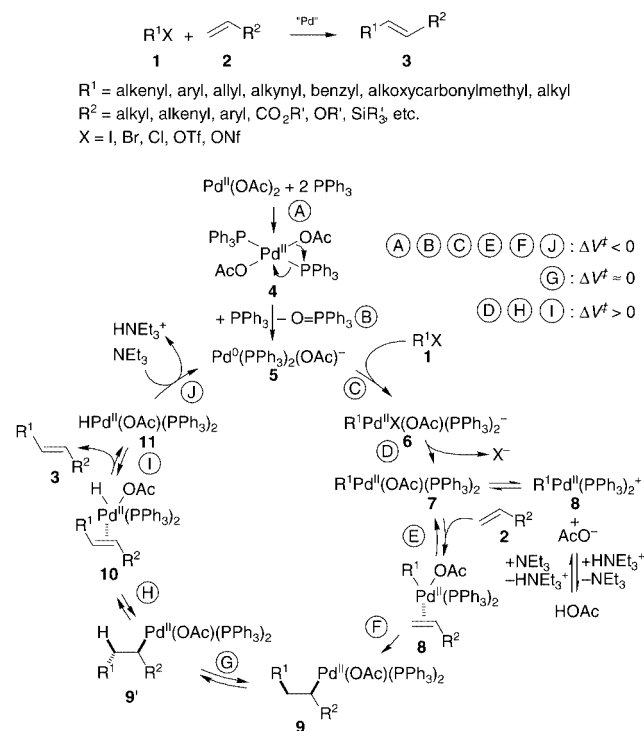
Most transition metal-catalyzed reactions do not occur in a single step, but consist of a sequence of individual steps with different types and extents of pressure dependence. It is, therefore, difficult to predict whether the overall reaction will be accelerated or retarded by high pressure. For the Heck reaction, it has been postulated that the formation of

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the catalytically active Pd^0 species, the oxidative addition of an alkenyl or aryl halide to the Pd^0 species, and the complexation of an alkene to the resulting Pd species are accelerated by pressure, whereas the reductive elimination and decomplexation reactions are retarded by pressure, and that the insertion, migration and deinsertion steps are not associated with significant pressure effects.^[12] According to the superb mechanistic and kinetic studies by Amatore and Jutand into palladium-catalyzed reactions,^[13] the individual steps in the catalytic cycle of the Heck reaction under high pressure conditions with $\text{Pd}(\text{OAc})_2/\text{PPh}_3/\text{NEt}_3$ as the catalyst system (Scheme 1)^[6] have been found to belong to three categories:



Scheme 1. The mechanism of the Heck reaction and the influence of high pressure on the individual steps of the reaction

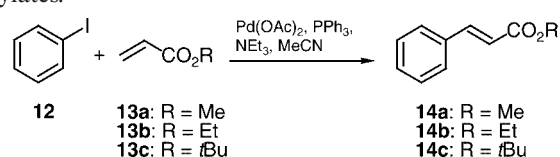
(i) The ligand association (A), intramolecular reduction (B), oxidative addition (C), coordination (E), *syn* addition (F) and reductive elimination (J) steps should be pressure-accelerated. (ii) The dissociation of X^- (D), *syn* elimination (H) and decomplexation (I) should be pressure-retarded. (iii) The internal rotation (G) with no changes in bonding or in electrostatic charges, should not be influenced by pressure.

Reiser et al. determined the activation volume for the Heck coupling of iodobenzene with 2,3-dihydrofuran, with the kinetic data being deduced from several separate runs and monitored the reaction by GC analysis.^[11] To achieve a more accurate kinetic analysis, we have applied quantitative on-line FT-IR spectroscopy for measuring concentrations in the present study into the Heck coupling under high pressure of three different acrylates to phenyl iodide and of methyl acrylate to *p*-nitrophenyl triflate. This technique has proven to be very

valuable for detailed kinetic studies of organic reactions at elevated temperatures and high pressures.^[14]

Results

First, the coupling reactions of iodobenzene **12** with different alkyl acrylates **13a,b,c** to yield the corresponding cinnamates **14a,b,c** (Scheme 2) were studied as a function of pressure, between 250 and 3000 bar, at 70 °C and as a function of temperature, between 50 and 100 °C, at 1500 bar. The concentrations of the reactants, the solvent, and the catalyst were the same in the three reaction systems. Thus, any change in the determined parameters must be related to differences in steric and/or electronic properties of the acrylates.



Scheme 2. Heck reaction of iodobenzene (**12**) with selected acrylates

The absorptions of the carbonyl stretching fundamentals of **13** and of **14** were recorded to monitor the progress of the reactions. A typical series of absorbance spectra obtained during the reaction of **12** with **13c** at 1750 bar and 70 °C over a time period of 6.5 h is shown as an example in Figure 1. The peak maxima in IR spectra of **13c** and **14c** occur at 1717 and 1704 cm^{-1} , respectively. The arrows indicate the direction of spectral changes with reaction time.

To eliminate any absorbance of the solvent, of the silicon windows, and of the walls of the internal Teflon® cell, the first spectrum recorded immediately after the system had reached constant reaction conditions, for each spectral series taken during a reaction at constant *p* and *T*, was subtracted from all subsequently measured spectra. By this procedure, the spectral sequence from Figure 1 is trans-

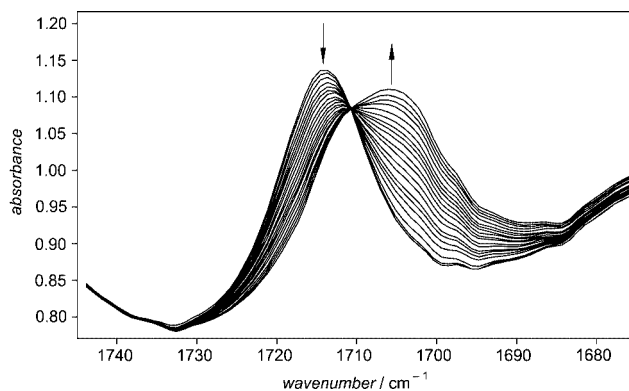


Figure 1. Series of spectra recorded during the Heck reaction of iodobenzene (**12**) with *tert*-butyl acrylate (**13c**) to form the corresponding cinnamate **14c** at 1750 bar and 70 °C (for better clarity only about one third of the ca. 60 spectra actually recorded are shown); a reaction time of nearly 6.5 h is covered, corresponding to 7.5 half-lives; the arrows indicate the direction of intensity changes with time.

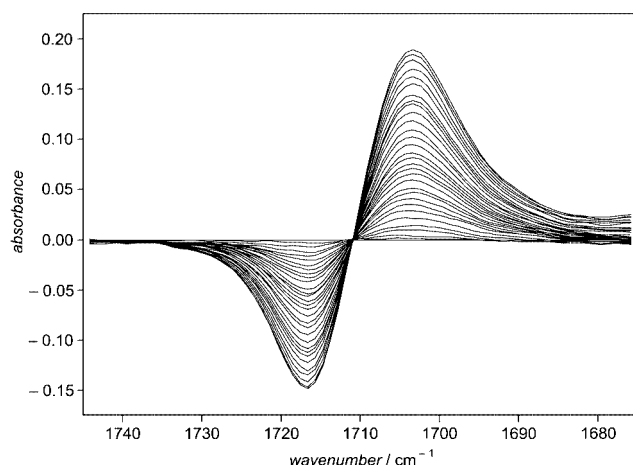


Figure 2. Series of difference spectra recorded during the Heck reaction of iodobenzene (**12**) with *tert*-butyl acrylate (**13c**) to form the corresponding cinnamate **14c** at 1750 bar and 70 °C (for better clarity only about one third of the actually recorded spectra is shown)

ferred into the series shown in Figure 2. Positive absorbance indicates dominant product absorption, whereas negative absorbance refers to dominant absorption of starting material.

In dilute solutions at constant temperature and pressure, the Lambert–Beer law holds for the C=O stretching modes in Figure 1 and Figure 2. The changes in integrated absorbance of these vibrations are proportional to changes in concentration of the associated reactant or product species. To achieve a reliable quantitative analysis, the areas between the curves in Figure 2 and the horizontal line through zero absorbance (difference) were determined by integration over the high-wavenumber band (for analysis of **13c** within the limits from 1711.5 to 1726.4 cm⁻¹) and over the low-wavenumber band (for analysis of **14c** within the limits from 1691.5 to 1711.5 cm⁻¹).

With the concentration of the aryl iodide and the aryl triflate, respectively, by far exceeding the concentration of the acrylate (by a factor of 30), the coupling reaction may be treated by first-order kinetics with respect to the acrylate concentration.^[15] Fitting the data of the integrated absorbance vs. time to a first-order rate expression, by means of a least-squares procedure using the Levenberg–Marquardt algorithm,^[16] yields the first-order rate coefficients, k .^[17] The plot of integrated absorbance vs. time, which relates to the primary spectroscopic data of the experiment in Figure 1 and Figure 2, is presented in Figure 3. The time required for reaching constant p and T conditions was typically about ten minutes. This time span is seen as the plateau region at the onset of the plot.

Table 1 summarizes the pseudo-first-order rate coefficients k for the Heck reaction of iodobenzene and methyl acrylate that were obtained from the spectra.^[18] The slight deviation of the rate coefficients derived from the analysis of the cinnamate **14c** absorbance band from those derived from the acrylate **13c** absorbance band are caused by the influence of a time-dependent growth of additional absorbances in the region from ca. 1690 cm⁻¹ down to lower

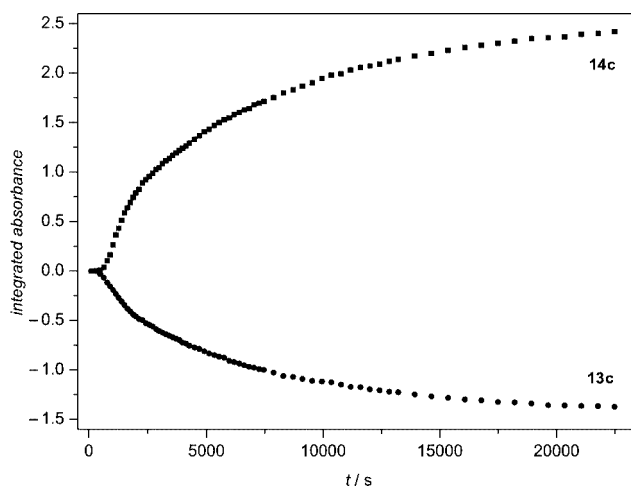


Figure 3. Plot of integrated absorbance vs. reaction time for the Heck reaction of iodobenzene (**12**) with *tert*-butyl acrylate (**13c**) to the corresponding cinnamate **14c** at 1750 bar and 70 °C

Table 1. Experimental pseudo-first-order rate coefficients k , for the Heck reaction of iodobenzene (**12**) with *tert*-butyl acrylate (**13c**) to form the cinnamate **14c**, derived from the analysis of the decreasing IR absorbance band of **13c** and the increasing band of **14c**

p [bar]	$T = 70\text{ °C}$ k [10^{-4} s^{-1}]		T [°C]	$p = 1500\text{ bar}$ k [10^{-4} s^{-1}]	
	from 13c	from 14c		from 13c	from 14c
250	—	—	50	0.49	0.43
500	1.67	1.46	60	1.08	1.05
750	1.76	1.59	70	2.26	1.91
1000	1.94	1.71	80	4.50	3.28
1250	2.14	1.87	90	7.87	6.59
1500	2.26	1.91	100	12.3	11.5
1750	2.43	2.12			
2000	2.41	2.33			
2250	2.71	2.31			
2500	2.86	2.42			
2750	2.93	2.59			
3000	3.07	2.67			

wavenumbers, which could not yet be assigned unequivocally. The results obtained from the analysis of the acrylate absorbances are representative for the Heck reaction and serve as the basis for the following discussion. For each experiment the k values derived from the decreasing reactant and from the increasing product absorbance match within experimental uncertainty.^[18] A full report on the experimental data (k values for Heck reactions of iodobenzene with methyl and ethyl acrylate) is provided in the Supporting Information (see also footnote on the first page of this article).

Activation enthalpies $\Delta H^\ddagger$ were derived from the Arrhenius plot ($\ln k$ vs. T^{-1}) [Equation (1)], and activation entropies $\Delta S^\ddagger$ were calculated according to Equation (2).

$$\Delta H^\ddagger = -R (\ln k/dT - 1)_p - RT \quad (1)$$

$$\Delta S^\ddagger = R [A - \ln (k_B T/h) - 1] \quad (2)$$

where R is the gas constant, A is the natural logarithm of the pre-exponential factor in the Arrhenius expression, k_B is the Boltzmann constant, and h is the Planck constant.

Table 2. Activation parameters and experimental rate coefficients k at 70 °C and 1.5 kbar for the Heck reaction of the acrylates **13a,b,c** with iodobenzene (**12**) to form the corresponding cinnamates **14a,b,c**

Derived from	$\Delta H^\ddagger$ ^[a] [kJ·mol ⁻¹]	$\Delta S^\ddagger$ ^[a] [J·mol ⁻¹ ·K ⁻¹]	$\Delta V_0^\ddagger$ [cm ³ ·mol ⁻¹]
13a	62 ± 6 ^[b]	-(171 ± 16)	-(5 ± 1)
14a	54 ± 4	-(195 ± 12)	-(4 ± 1)
13b	54 ± 3	-(194 ± 9)	-(7 ± 1)
14b	53 ± 5	-(196 ± 15)	-(7 ± 1)
13c	63 ± 2	-(167 ± 6)	-(12 ± 2)
14c	62 ± 2	-(171 ± 5)	-(11 ± 2)

^[a] 1500 bar. ^[b] The reported uncertainties in $\Delta H^\ddagger$, $\Delta S^\ddagger$ and $\Delta V_0^\ddagger$ refer to standard deviations.

Table 2 summarizes the values of $\Delta H^\ddagger$ and $\Delta S^\ddagger$ for the Heck reactions of **12** with **13a,b,c** at a constant pressure of 1500 bar and their corresponding values of $\Delta V_0^\ddagger$ at ambient pressure, which are each derived from the analysis of both the corresponding acrylate absorbances and the cinnamate absorbances. The reported uncertainties in $\Delta H^\ddagger$, $\Delta S^\ddagger$ and $\Delta V_0^\ddagger$ refer to standard deviations.

The relationships between $\ln k$ and p are not perfectly linear. Thus, activation volumes $\Delta V_0^\ddagger$ were determined from the slope of the curves of $\ln k$ vs. p at ambient pressure. The data in the curves of $\ln k$ vs. p were smoothed according to the procedures described by Asano et al. [Equation (3) and Equation (5)].^[7] The activation volumes extrapolated to ambient pressure, $\Delta V_0^\ddagger$, are found from Equation (4) and Equation (6), respectively. The value of k_0 , which refers to the rate coefficient at ambient pressure, was derived from a parabolic fit of the data in the curves of $\ln k$ vs. p .

$$\ln(k/k_0) = a_1 p + [b_1 p / (1 + c_1 p)] \quad (3)$$

$$\Delta V_0^\ddagger = -(a_1 + b_1) RT \quad (4)$$

$$\ln(k/k_0) = a_2 p + b_2 \ln(1 + c_2 p) \quad (5)$$

$$\Delta V_0^\ddagger = -(a_2 + b_2 c_2) RT \quad (6)$$

The pressure and temperature dependences of the rate coefficients are plotted in Figure 4 and Figure 5, respectively. The rate coefficients for methyl acrylate (**13a**) are smaller than for ethyl acrylate (**13b**) over the entire experimental pressure range. The highest rates were measured with *tert*-butyl acrylate (**13c**). The activation volumes, derived according to Equations (3) to (6), follow the order

$\Delta V_0^\ddagger$ (**13c**) < $\Delta V_0^\ddagger$ (**13b**) < $\Delta V_0^\ddagger$ (**13a**); i.e., the largest negative value of $\Delta V_0^\ddagger$ is observed for *tert*-butyl acrylate (**13c**).

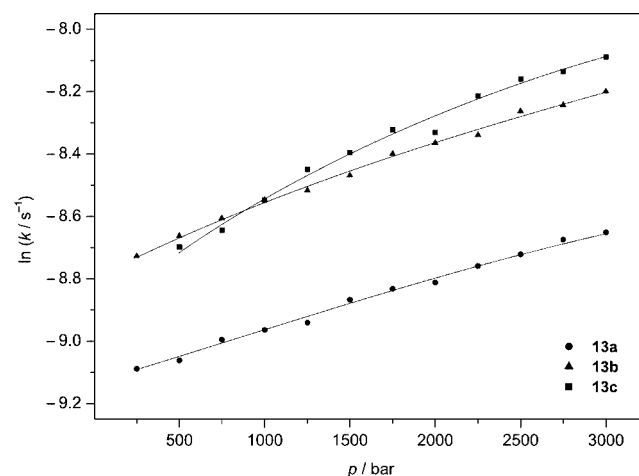


Figure 4. Pressure dependence of the experimental rate coefficients k for the Heck reaction of iodobenzene (**12**) with the acrylates **13a,b,c** to form the corresponding cinnamates **14a,b,c** at 70 °C. Only the rate coefficients of the reactand are shown

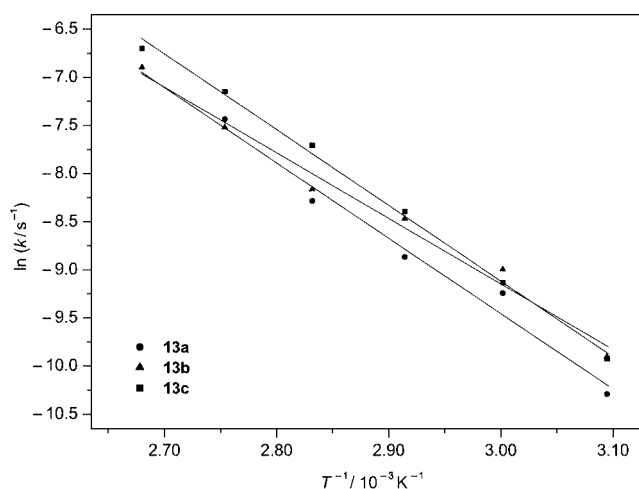
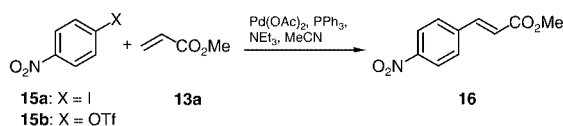


Figure 5. Temperature dependence of the experimental rate coefficients k for the Heck reaction of iodobenzene (**12**) with the acrylates **13a,b,c** to form the corresponding cinnamates **14a,b,c** at 1.5 kbar. Only the rate coefficients of the reactand are shown

To investigate the effect of the leaving group on the kinetics of the Heck reaction in the condensed phase, we studied the kinetics of the reactions of aryl iodide **15a** and aryl triflate **15b** with methyl acrylate (**13a**), to yield the cinnamate **16** (Scheme 3), in the pressure range from 250 to 3000 bar at 100 °C, and in the temperature range from 80 to 120 °C at 1500 bar. The concentrations of reactands, the solvent and the catalyst system were identical for the three reaction systems. Thus, any changes in the determined rate parameters must be due to differences in the type of leaving group. Unfortunately, because of insufficient reactivity of the aryl bromide, monitoring the Heck reaction of *p*-nitrophenyl bromide with methyl acrylate with the classical catalyst system did not give satisfactory kinetic data in the same

range of pressure and temperature as was used for the iodides and the triflate.



Scheme 3. Variation of the leaving group in the Heck reaction of aryl derivatives with methyl acrylate (13a).

The experimental pseudo-first-order rate coefficients k of the Heck reactions in Scheme 3 were obtained by the method described above. A full report on the experimental data (values of k for the Heck reactions of methyl acrylate with *p*-nitrophenyl iodide and triflate) is provided in the Supporting Information.

Rate coefficients, measured as a function of pressure, are plotted in Figure 6.

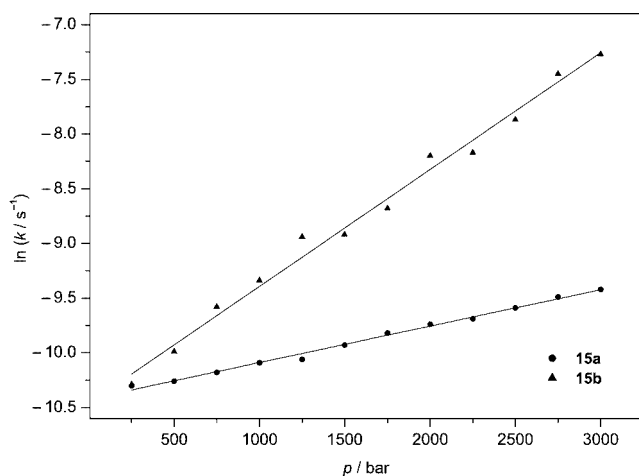


Figure 6. Pressure dependence of the experimental rate coefficients k for the Heck reaction of the aryl iodide 15a and triflate 15b with methyl acrylate (13a) to the corresponding cinnamate 16 at 100 °C. Only the rate coefficients of the reactant are shown

At 250 bar, the triflate 15b reacts at the same rate as the iodide 15a, but above 500 bar the aryl triflate 15b is the faster-reacting substrate.

The activation volumes were derived according to Equations (3)–(6) and follow the order $\Delta V^\ddagger$ (15b) < $\Delta V^\ddagger$ (15a), i.e., the largest negative value of $\Delta V^\ddagger$ is derived from the triflate 15b.

The temperature dependence of the experimental rate coefficients at 1500 bar is plotted in Figure 7. The slowest-reacting substrate is the iodide 15a.

The activation enthalpies and entropies, derived according to Equations (1) and (2), as well as the activation volumes, derived according to Equations (3) to (6), are compiled in Table 3.

Discussion

When focussing on the steric requirements of the respective alkyl acrylate and their effect on the rate coefficients

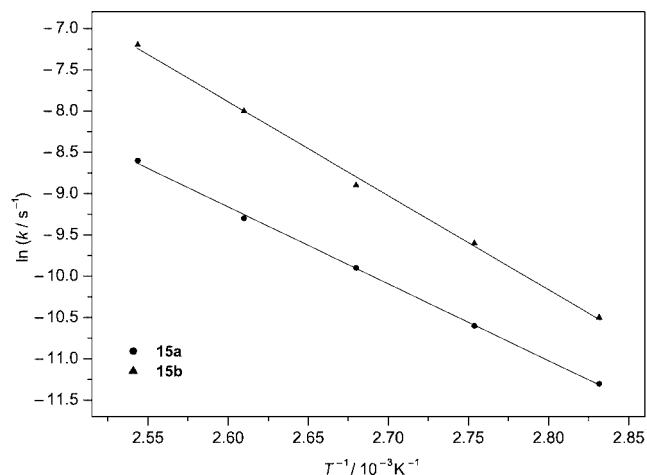


Figure 7. Temperature dependence of the experimental rate coefficients k for the Heck reaction at 1.5 kbar of the aryl iodide 15a and triflate 15b with methyl acrylate (13a) to form the corresponding cinnamate 16. Only the rate coefficients of the reactant are shown

Table 3. Activation parameters and experimental rate coefficients k at 100 °C and 1.5 kbar for the Heck reaction of the aryl iodide 15a and the triflate 15b with methyl acrylate (13a) to form the corresponding cinnamate 16

derived from	$\Delta H^\ddagger$ [a] [kJ·mol ⁻¹]	$\Delta S^\ddagger$ [a] [J·mol ⁻¹ ·K ⁻¹]	$\Delta V^\ddagger$ [cm ³ ·mol ⁻¹]
15a/13a	74 ± 2 ^[b]	$-(168 \pm 4)$	$-(9 \pm 1)$
16	75 ± 1	$-(164 \pm 2)$	$-(10 \pm 2)$
15b/13a	91 ± 3	$-(111 \pm 7)$	$-(37 \pm 6)$
16	54 ± 4	$-(208 \pm 12)$	$-(32 \pm 5)$

[a] 1500 bar. [b] The reported uncertainties in $\Delta H^\ddagger$, $\Delta S^\ddagger$ and $\Delta V^\ddagger$ refer to standard deviations.

and activation parameters, it was surprising to find that the pressure- and temperature-dependent rate coefficients for the coupling of the acrylates 13a,b,c with iodobenzene (12) to the corresponding cinnamates 14a,b,c (Scheme 2) follow the order *tert*-butyl (13c) > ethyl (13b) > methyl acrylate (13a). On average, in the Heck reaction with iodobenzene, *tert*-butyl acrylate reacts 1.4-times faster than methyl acrylate and 1.3-times faster than ethyl acrylate. Apparently, an electronic effect must override a potential retarding effect of the larger steric bulk of the alkyl acrylate. Qualitatively, the electronic difference of the three acrylates must stem from the difference in the σ -electron-donating ability of a methyl, an ethyl and a *tert*-butyl group in the ester moiety. In fact, the HOMO of an alkyl acrylate is influenced by the nature of the alkyl group, as is shown by computations^[20] at the B3LYP/6-31+G(d,p) level of theory for the optimization of geometries and at the MP2/aug-cc-pvdz level of theory for the energy single points and photoelectron spectroscopic (PES) measurements of the lowest ionization energies (IE) for the three acrylates 13a,b,c: $IE(13a)_{\text{calcd.}} = -10.73 \text{ eV}$ ($IE_{\text{exp.}} = -10.72$,^[9] -10.77 eV ^[10]), $IE(13b)_{\text{calcd.}} = -10.68 \text{ eV}$ ($IE_{\text{exp.}} = -10.66 \text{ eV}$ ^[22]), and $IE(13c)_{\text{calcd.}} = -10.59 \text{ eV}$. On the basis

of Koopmans' theorem, these decreasing values of IE correspond to an increase of the HOMO energies, and thus the reaction rates of the acrylates **13a,b,c** correlate with their increasing HOMO energies.

Under high pressure, a reaction via a dipolar transition structure is more accelerated than a reaction proceeding via an apolar transition structure because of the so-called electrostriction effect.^[2] Thus, a reaction of a positively charged palladium species that certainly would prefer an electron-rich alkene (with a high HOMO) should be enhanced by high pressure more than a reaction of a neutral palladium complex that would prefer a less-electron-rich double bond.^[6f] Thus, the observed pressure dependence of the rate coefficients for the coupling reactions of the three acrylates **13a,b,c** indicates that the coordination and insertion steps (steps E and F in Scheme 1) under high-pressure conditions take place more favorably via an $[R^1Pd^{II}(PPh_3)_2]^+$ complex (**8**) than via an $[R^1Pd^{II}(OAc)(PPh_3)_2]$ complex (**7**) as described for such reactions at ambient pressure.^[13]

The changes in the experimental first-order rate coefficients for the variation of the leaving group in the arenes **15a** and **15b** under pressures above 500 bar follow the order iodide **15a** < triflate **15b**. This result is a surprising one, because it is generally assumed that the rate-determining step in the catalytic cycle of the Heck reaction is usually the oxidative addition and, therefore, one would predict the opposite order of reaction rates. Thus, the rate-determining step under high-pressure conditions cannot be the oxidative addition as has already been pointed out by Reiser et al.^[11] More recently, Amatore and Jutand,^[13] as well as de Vries and van Leeuwen et al.,^[23] have presented experimental evidence that, even at ambient pressure, the oxidative addition does not need to be the rate-determining step in the overall catalytic cycle of the Heck reaction.

The immediately ensuing question then would be: Which of the steps is the rate determining one? As already pointed out, the equilibrium between $[R^1Pd^{II}(OAc)(PPh_3)_2]$ (**7**) and $[R^1Pd^{II}(PPh_3)_2]^+$ (**8**) (Scheme 1) is shifted towards **8** under high pressure. Here, the effect of the counterion has to be taken into account. As Amatore and Jutand have demonstrated, the catalytic action cannot be affected by $R^1Pd^{II}X(PPh_3)_2$ (with $X = I$ or Br), but the only catalytically active species in such systems must be $[R^1Pd^{II}(OAc)(PPh_3)_2]$ (**7**).^[13] Thus, the reaction producing iodide ions must be more disfavored under high pressure, which enhances the formation of catalytically inactive $R^1Pd^{II}I(PPh_3)_2$. The higher rate coefficients for **15b** with the triflate leaving group are due to the fact that triflates always react via the cationic palladium species $[R^1Pd^{II}(PPh_3)_2]^+$ (**8**).^[13] These experimental results suggest that the rate-determining step in the catalytic cycle of the Heck reaction is connected with the equilibrium between $[R^1Pd^{II}(OAc)(PPh_3)_2]$ (**7**) and $[R^1Pd^{II}(PPh_3)_2]^+$ (**8**) and should be the coordination (Scheme 1, step E) or insertion of the acrylate (Scheme 1, step F), respectively, as is corroborated by the results obtained with the variation of the acrylates.

The changes in the activation volumes with the variation of the acrylates **13a,b,c** (from -5 and -7 to

-12 $cm^3 \cdot mol^{-1}$, respectively) and with the variation of the leaving groups in **15a** and **15b** (from -9 to -37 $cm^3 \cdot mol^{-1}$) follow the same trend as previously observed for other reactions under high pressure.^[1,24] The more sterically congested a reacting system is, the higher is the rate-accelerating influence of high pressure going along with a more negative activation volume.^[2a,2b] The difference between *tert*-butyl acrylate (**13c**) and ethyl acrylate (**13b**) ($\Delta\Delta V^\ddagger = 5$ $cm^3 \cdot mol^{-1}$) is larger than that between methyl acrylate (**13a**) and ethyl acrylate (**13b**) ($\Delta\Delta V^\ddagger = 2$ $cm^3 \cdot mol^{-1}$) because of the significantly larger increase in bulk on going from an ethyl to a *tert*-butyl group. The same effect is found for the leaving group variation, where **15b**, with the eight-atom triflate leaving group, yields the more negative activation volume than the iodide **15a** ($\Delta\Delta V^\ddagger = 28$ $cm^3 \cdot mol^{-1}$), which correlates with the steric bulk. The activation volume for the Heck reaction of iodobenzene and 2,3-dihydrofuran with $Pd(OAc)_2/PPh_3$ as catalyst system and under pressures up to 8000 bar and at a constant temperature of 30 °C was determined by Reiser et al. to be $\Delta V^\ddagger = -12 \pm 2$ $cm^3 \cdot mol^{-1}$.^[11] This value fits well into the order of magnitude of the activation volumes found in this study for the reactions of iodobenzene with three different alkyl acrylates.

It is noteworthy that the activation volumes were found in a different order and to be much more negative when the palladacycle introduced by Hermann and Beller et al.^[25] was used instead of the classical catalyst system. The observed activation volumes for the coupling of iodobenzene (**12**) and bromobenzene with methyl acrylate (**13a**) were $\Delta V^\ddagger = -(21 \pm 3)$ and $-(27 \pm 4)$ $cm^3 \cdot mol^{-1}$, respectively, while the reaction rates did not differ very much for both catalyst systems in the pressure range from 500 to 3000 bar.^[26] The significantly different values of the activation volume demonstrate that the rates of reaction of bromobenzene depend more strongly on pressure than do those of iodobenzene (**12**) and, hence, bromobenzene can be made to react more efficiently by increasing pressure.^[6a]

No significant trend is observed for the activation enthalpies and entropies ($\Delta H^\ddagger$, $\Delta S^\ddagger$), neither upon variation of the alkyl acrylate nor of the leaving group in the aryl derivative; in fact, the values are nearly the same within experimental uncertainty. This finding confirms the expectation that these activation parameters should depend mainly on the catalyst system used for these reactions, rather than on the substrates. Amatore and Jutand found values in the same order of magnitude for the catalyst system $Pd(OAc)_2/PPh_3$, namely $\Delta H^\ddagger = 65$ $kJ \cdot mol^{-1}$ and $\Delta S^\ddagger = -94$ $J \cdot mol^{-1} \cdot K^{-1}$.^[27]

Conclusion

This study on the influence of high pressure on the Heck reaction, by applying on-line FT-IR spectroscopy, revealed that the activation volumes $\Delta V^\ddagger$ correlate with the degrees of steric congestion for the variation of the alkyl group in the acrylates **13a,b,c** and of the leaving groups in the aryl

derivative **15a,b**, i.e., the more highly congested systems give values that are more negative, while activation enthalpies and entropies $\Delta H^\ddagger$ and $\Delta S^\ddagger$ are virtually independent of the reactands.

The rate coefficients for the coupling of methyl acrylate (**13a**), ethyl acrylate (**13b**) and *tert*-butyl acrylate (**13c**) with iodobenzene (**12**) to form the corresponding cinnamates **14a,b,c** (Scheme 2) follow the order $k(\mathbf{13c}) > k(\mathbf{13b}) > k(\mathbf{13a})$, while those for the coupling of the *p*-nitrophenyl iodide (**15a**) and *p*-nitrophenyl triflate (**15b**) with methyl acrylate (**13a**) to the corresponding *p*-nitrocinnamate (**16**) (Scheme 3) follow the order $k(\mathbf{15b}) > k(\mathbf{15a})$. These orders are consistent with the notion that the coordination and insertion steps of the acrylate (Scheme 1, steps E and F) are rate determining. Thus, under high-pressure conditions, the rate-determining step of the overall catalytic cycle of the Heck reaction is not the oxidative addition, which is generally assumed to be the rate-determining step for such reactions at ambient pressure.

Experimental Section

Materials: Solvents were dried and distilled prior to use and degassed by applying several freeze-pump and thaw cycles. TLC was performed on precoated silica gel SIL G/UV₂₅₄ plates (Macherey–Nagel & Co.), and silica gel (0.066–0.200 mm, 70–230 mesh ASTM) (Merck) was used for column chromatography.

Pd(OAc)₂, PPh₃, NEt₃, iodobenzene (**12**), methyl acrylate (**13a**), ethyl acrylate (**13b**), *tert*-butyl acrylate (**13c**), and 4-nitrophenyl iodide (**15a**) are commercially available (Aldrich and Fluka).

4-Nitrophenyl trifluoromethanesulfonate (**15b**) was prepared according to a published procedure.^[28]

Instrumentation: The reactions were performed in an optical high-pressure cell equipped with windows made from polycrystalline silicon. The samples of the reaction mixture, which were all prepared at the same time and subsequently deep-frozen in liquid nitrogen prior to use, were contained in sealed thin-walled Teflon® bags as internal cells, one of which was positioned at each time between the windows of the high-pressure cell. The optical cell, the other high-pressure equipment, the procedures of preparing, filling and sealing the internal cells, and the data treatment have been described in detail elsewhere.^[14] The spectra were recorded with a Fourier-transform IR spectrometer (BRUKER IFS 66 and IFS 88). The decadic absorbance should not exceed $A = 1.8$ to stay within the linear range of the DTGS detector used in the spectrometer. This limitation must be taken into account to ensure reliable quantitative spectroscopic analysis. Pressures were determined to be within ± 10 bar. The uncertainties in temperature measurements were within ± 0.5 K.

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