Steric and electronic tuning of Michael addition reactions induced by pentacarbonyl metal fragments

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Abstract

The addition of a series of 2- and 4-substituted imidazoles to unsaturated Fischer carbene complexes of the type $(CO)_5MC[(OC_2H_5)C_2C_6H_5]$ was studied as a function of temperature and pressure. A comparison of the data for the addition of the 2- and 4-substituted imidazoles enables a discussion of steric and electronic effects that control the rate of the addition process. The reported activation parameters are used to discuss the mechanism of the addition process in comparison to related addition reactions of amines and pyrazoles reported in the literature. The data in combination with kinetic isotope effect measurements clearly reflect that the reactions proceed via a two-step process with a zwitterionic intermediate.

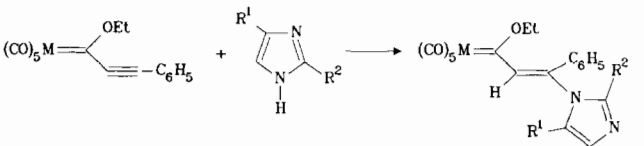
Key words: Kinetics and mechanism; Michael reactions; Metal complexes; Carbonyl complexes; Carbene complexes; Imidazole complexes

Introduction

We have in recent years developed an interest in the mechanistic details of Michael-type addition reactions of amines to α,β-unsaturated Fischer carbene complexes to form β-aminovinyl-substituted products. Such reactions are well-known [1–7] because of their role as intermediates in organic synthesis reactions via organometallics. The presence of the pentacarbonyl-carbene fragment assists the delocalization of charge density and results in a tremendous acceleration of the addition reaction. Thus the use of organometallic species has a significant advantage over the pure organic reaction. From a mechanistic point of view it is not only our goal to clarify the underlying reaction mechanism, but also to determine in what way such addition processes can be tuned via steric and electronic effects.

Earlier work from our laboratory reported on the temperature, pressure and solvent dependence of the addition of pyrrolidine to a series of α,β-unsaturated Fischer carbene complexes [8]. The basicity of the amine plays a crucial role in determining the rate of the addition process [9], as found for the addition of a series of *para*-substituted anilines. The pressure dependence of the latter reactions indicated that the faster reactions proceed via an 'early' (reactant-like) transition state, whereas the slower reactions proceed via a 'late' (product-like) transition state. The electronic tuning via the basicity of the amine can cause seven orders of magnitude increase in the rate constant for the addition process. The investigated reactions follow a two-step process in which nitrogen–carbon bond formation is followed by a rapid intramolecular proton transfer step [8, 9]. The solvent dependence [8, 10] of these reactions indicates that the transition state for the addition step is significantly more polar than the reactant state and leads to the formation of a zwitterionic intermediate.

We have now extended this work to focus in more detail on the effect of steric hindrance on the amine. We have studied the addition of a series of 2- and 4-substituted imidazoles to Fischer carbene complexes of the type $(CO)_5MC[(OC_2H_5)C_2C_6H_5]$ (M = Cr, W) according to reaction (1). It was our objective to gain insight into the intimate nature of the mechanism in comparison to the other systems mentioned above.



R^1 = H, Me, Ph: R^2 = H, Me, Et, i-Pr, Ph (1)

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Furthermore, we wanted to distinguish between basicity and steric hindrance as crucial parameters for the addition process.

Experimental

Materials

All experiments were carried out under an atmosphere of argon. Glassware was soaked in KOH-saturated i-propanol, rinsed thoroughly with distilled water, and oven dried at 100 °C. The carbene complexes were synthesized by literature procedures as described before [1, 11]. Imidazole and its derivatives were purchased in the purest grade available (Merck or Fluka). Prior to use, the imidazoles were recrystallized from water and dried over P_2O_5. Acetonitrile was dried by standard methods (molecular sieves), distilled in the usual way and then stored under an atmosphere of argon.

Instrumentation and characterization of the products

For a variety of substituted imidazoles, the characterization was done by *in situ* ^{1}H NMR spectroscopy and the adducts were similar to other products obtained in related studies [8, 9]. The NMR spectra were recorded on a Bruker AM 400 WB spectrometer with $CDCl_3$ as internal reference.

Synthesis of N-deuterioimidazole

Imidazole was dissolved in deuterium oxide by heating. The clear solution was refluxed and stirred for 24 h and the deuterioimidazole was obtained as a solid by cooling the solution. The solid was dried over P_2O_5, and the extent of deuteration was checked by ^{1}H NMR.

Kinetic measurements

Depending on the rate of the reaction, the overall addition process was studied at ambient pressure by using a UV–Vis spectrophotometer (Shimadzu UV-250 or Varian Cary 1) or a stopped-flow unit (Durrum D110). The progress of the reaction was usually followed by the appearance of the product MLCT band at 400 nm. The high-pressure kinetic measurements were either performed on a homemade high-pressure stopped-flow unit [12] or on a Zeiss DMR10 spectrophotometer equipped with a high-pressure cell [13]. In the latter case solutions were placed in a quartz pillbox cell [14] using a special filling technique [15]. All spectroscopic instruments were thermostated at ± 0.1 °C, and the reactions were carried out under pseudo-first-order conditions by using a large excess of the imidazoles. Reactions were followed for at least 3 half-lives, and an infinity absorbance program was employed to calculate the rate constants. Stopped-flow data acquisition and handling were performed on an on-line computer system [16]. The corresponding first-order plots were linear over the studied time range, and the estimated rate constants were reproducible to within 5%.

Results and discussion

The addition reactions outlined in eqn. (1) in general produce adducts of the type shown and are accompanied by characteristic changes in the MLCT (π–π^*) bands [17, 18] as indicated in Fig. 1. The reactions exhibit clean isosbestic points for at least three half-lives of the reaction, and kinetic measurements were performed at 400 nm. The appearance of the product MLCT bands depends slightly on the nature and the position of the substituent, whereas for the corresponding addition of substituted anilines to identical carbene complexes, larger differences in the MLCT band of the products were observed [9]. The reaction was studied for seven different imidazoles and for two different carbene complexes, and in all cases the pseudo-first-order rate constant varied linearly with the imidazole concentration over the investigated concentration range. The selection of the concentration range was limited by the experience that not all imidazoles were soluble enough in acetonitrile and by the fact that in some cases deviations from the linear concentration dependence were observed at higher concentrations. However, under the selected conditions all plots of k_{obs} versus [imidazole] were linear and exhibited no meaningful intercepts, as demonstrated in Table 1 and Fig. 2, such that k_{obs} can be expressed as indicated in eqn. (2).

$$k_{obs} = k[\text{imidazole}] \quad (2)$$

The absence of a significant intercept indicates that, under the selected conditions, no parallel concentration independent reaction occurs and that the reaction is not reversible. This result is in good agreement with the earlier investigated amine and pyrazole systems [8, 9].

The temperature and the pressure dependence of k_{obs} is also included in Table 1. The rate and activation parameters for the series of investigated imidazoles are summarized in Table 2, and for the different metals the activation parameters are reported in Table 3. Plots of $\ln k_{obs}$ versus pressure were linear (see typical example in Fig. 3) within the experimental error limits over the investigated pressure range, and ΔV^* values were calculated from the slope ($= -\Delta V^*/RT$) of such plots in the usual way [19].

The data in Table 2 clearly show a dependence of the second-order rate constant k on the nature and position of the substituent on imidazole. In total k increases *c.* 50-fold on going from 2-phenyl- to 4-methylimidazole. The introduction of a substituent

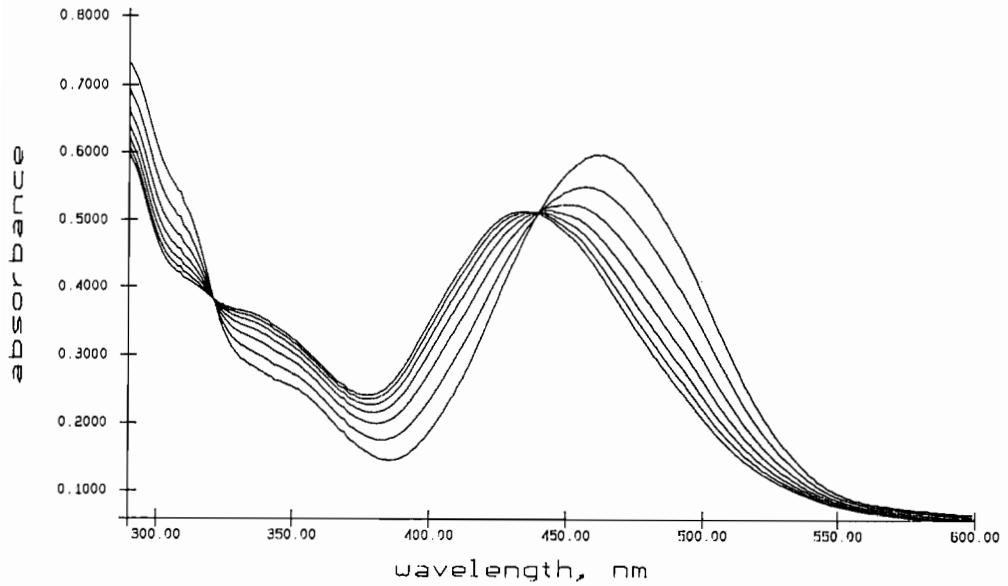


Fig. 1. Repetitive scan spectra for reaction (1) in acetonitrile at 25 °C. Experimental conditions: [W] = 1×10^{-5} M, [imidazole] = 1.1×10^{-4} M, $\Delta t = 120$ s.

in position 2 has a significant influence on the basicity of the N-donor. In the case of 2-methyl-, 2-ethyl- and 2-isopropylimidazole, electron donating properties cause an increase in basicity, which is not accompanied by the expected increase in k. The latter value is presumably strongly affected by steric hindrance at the N-donor atom caused by substitution in this position, which results in a steady decrease in k on increasing the bulkiness of the substituent. In the case of 2-phenylimidazole, electron-withdrawing properties cause a decrease in basicity on the N-donor, which is accompanied by a decrease in k. However, steric arguments could also partially account for the observed decrease in k. The introduction of substituents in the 4 position also significantly affects the basicity of the N-donor atom along the lines expected. The increase in basicity for 4-methylimidazole causes an increase in k, whereas a decrease in basicity for 4-phenylimidazole causes a significant decrease in k.

It follows from these trends that electronic and steric effects can account for the observed variation of k for substituents in the 2 and 4 position. A direct comparison of the values of k for methyl- and phenylimidazole clearly shows that the reactions are significantly faster for substitution in the 4 position as compared to the 2 position with respect to the N-donor atom.

The relatively low $\Delta H^{\neq}$ and significantly negative $\Delta S^{\neq}$ values indicate that the rate-determining step of the reaction is an addition process that involves carbon–nitrogen bond formation between the carbene complex and the imidazole ligands. The $\Delta V^{\neq}$ values are also significantly negative and support substantial bond formation and a highly structured transition state. The reported activation parameters in Tables 2 and 3 are all in good agreement with the earlier investigated aniline and pyrrolidine systems [8, 9]. The studied reactions are significantly slower than for pyrrolidine, which is most probably related to the higher basicity in the latter case. This is also reflected in lower $\Delta H^{\neq}$ and more negative $\Delta V^{\neq}$ values for the reactions with pyrrolidine. The imidazole reactions exhibit higher $\Delta H^{\neq}$ and more positive $\Delta V^{\neq}$ values. On the basis of the observed differences in $\Delta V^{\neq}$ for these ligands, it is understandable that rather similar $\Delta V^{\neq}$ values are found for the series of reactions in Table 2 where only a moderate variation in k exists. The $\Delta V^{\neq}$ values obtained in this study are all in an absolute way significantly smaller than those reported before for the addition of a series of p-substituted anilines [9]. For a reaction with a rate constant similar to that reported in Table 2, viz. the addition of p-methylaniline, the reported $\Delta V^{\neq}$ value is -21.1 ± 1.0 cm^3 mol^{-1} as compared to an average value of -12.4 cm^3 mol^{-1} in Table 2. This difference is most probably related to the polar nature of the transition state, since the π system in the imidazoles can distribute the charge density more evenly over the heteroatomic ring, including the N-donor atom, than in the case of the p-substituted anilines. This will cause a smaller electrostriction effect, and therefore a less negative $\Delta V^{\neq}$ value [19]. A similar effect was observed for the addition of pyrazole [10] and pyrrolidine [8], where the dipole moment of the transition state is significantly smaller for the pyrazole than for the pyrrolidine reaction [10].

The data in Table 3 clearly demonstrate that the reactivity of the carbene complexes increases on going

TABLE 1. Kinetic data for the reaction of pentacarbonyl[ethoxy(phenylethynyl)carbene]tungsten(0) with imidazoles in acetonitrile as solvent

Imidazole	[Imidazole] (M)	Temp. (°C)	P (MPa)	$10^2 \times k_{obs}$ (s^{-1})
2-H	0.02	19.9	0.1	5.02 ± 0.04
		25.0		6.06 ± 0.13
		30.2		7.16 ± 0.07
		34.9		8.44 ± 0.09
		39.9		11.1 ± 0.09
		25.0	10	7.18 ± 0.28
			50	8.44 ± 0.15
			100	12.3 ± 0.3
			150	14.2 ± 0.4
2-Me	0.025	25.0	0.1	7.80 ± 0.01
	0.05			15.7 ± 0.1
	0.075			22.7 ± 0.2
	0.10			29.4 ± 0.2
	0.075	15.9		18.3 ± 0.2
		20.3		20.4 ± 0.1
		25.6		25.4 ± 0.4
		30.2		30.1 ± 0.4
		34.8		36.6 ± 0.9
	0.05	25.0	10	15.6 ± 0.7
			50	20.4 ± 0.9
			100	29.2 ± 0.9
			150	40.1 ± 0.9
2-Et	0.01	25.0	0.1	2.04 ± 0.06
	0.02			4.06 ± 0.03
	0.04			8.53 ± 0.07
	0.06			12.0 ± 0.2
	0.08			16.9 ± 0.2
	0.10			19.8 ± 0.2
	0.04	20.2		6.98 ± 0.10
		25.0		8.53 ± 0.07
		30.0		9.85 ± 0.05
		35.0		11.2 ± 0.2
		39.9		13.4 ± 0.3
	0.06	25.0	10	12.4 ± 0.9
			50	16.9 ± 0.4
			100	19.9 ± 1.2
			150	24.3 ± 0.5
2-i-Pr	0.01	25.1	0.1	1.21 ± 0.04
	0.02			2.43 ± 0.03
	0.04			4.72 ± 0.03
	0.06			7.14 ± 0.01
	0.10			12.0 ± 0.1
	0.06	15.1		5.25 ± 0.04
		20.1		6.16 ± 0.07
		25.1		7.14 ± 0.01
		30.6		8.45 ± 0.04
		35.2		9.55 ± 0.02
	0.05	25.0	10	5.68 ± 0.13
			25	6.14 ± 0.06
			50	6.85 ± 0.05
			75	7.63 ± 0.28
			100	8.88 ± 0.11
2-Ph	0.01	25.1	0.1	0.120 ± 0.005
	0.02			0.274 ± 0.007
	0.04			0.518 ± 0.003
	0.05			0.573 ± 0.001
	0.06			0.659 ± 0.004
	0.08			0.851 ± 0.006
	0.10			1.03 ± 0.01
	0.06	20.0		0.485 ± 0.002
		25.1		0.659 ± 0.004
		30.1		0.848 ± 0.007
		35.0		1.15 ± 0.01
		40.1		1.61 ± 0.03
	0.01	10.0	5	0.0567 ± 0.0010
			25	0.0641 ± 0.0008
			50	0.0711 ± 0.0007
			100	0.0866 ± 0.0020
4-Me	0.025	25.1	0.1	11.8 ± 0.1
	0.05			21.6 ± 0.1
	0.1			38.3 ± 0.3
	0.025	15.0		6.77 ± 0.05
		20.4		8.96 ± 0.05
		25.1		11.8 ± 0.1
		30.1		14.1 ± 0.1
		35.1		18.0 ± 0.1
	0.05	25.0	10	19.4 ± 0.4
			50	22.5 ± 0.4
			100	28.7 ± 0.2
			150	34.2 ± 1.1
4-Ph	0.005	25.0	0.1	0.197 ± 0.001
	0.01			0.374 ± 0.001
	0.02			0.765 ± 0.004
	0.035			1.21 ± 0.01
	0.05			1.63 ± 0.01
	0.02	15.0		0.397 ± 0.002
		20.0		0.540 ± 0.002
		25.0		0.765 ± 0.004
		30.0		0.992 ± 0.002
		35.0		1.38 ± 0.04
	0.02	35.0	10	1.53 ± 0.04
			50	1.93 ± 0.09
			100	2.51 ± 0.02
			150	3.31 ± 0.03

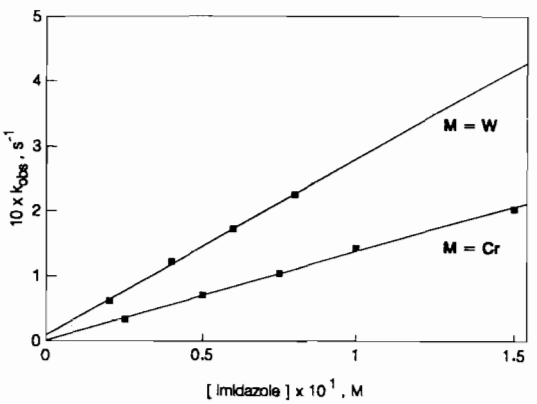


Fig. 2. Plots of k_{obs} vs. [imidazole] for reaction (1) in acetonitrile at 25 °C.

TABLE 2. Rate and activation parameters for the addition of 2- and 4-substituted imidazoles to $(CO_5)WC[(OC_2H_5)(C_2C_6H_5)]$ in acetonitrile as outlined in reaction (1)

Imidazole	pK_a[a]	k_{298} (M^{-1} s^{-1})	$\Delta H^{\neq}$ (kJ mol^{-1})	$\Delta S^{\neq}$ (J mol^{-1} K^{-1})	$\Delta V^{\neq}$ (cm^3 mol^{-1})
2-H	6.95	2.72 ± 0.04	27 ± 2	-146 ± 7	-12.5 ± 0.8
2-Me	7.86	2.88 ± 0.07	25 ± 2	-151 ± 5	-16.8 ± 0.3
2-Et	8.00	2.01 ± 0.06	23 ± 1	-166 ± 4	-10.8 ± 0.9
2-i-Pr		1.20 ± 0.01	19 ± 1	-178 ± 1	-12.0 ± 0.5
2-Ph	6.39	0.098 ± 0.004	43 ± 2	-121 ± 5	-10.2 ± 0.7[c]
4-Me	7.52	4.7 ± 0.3	33 ± 1	-121 ± 4	-10.3 ± 0.5
4-Ph	6.00	0.35 ± 0.01	43 ± 1	-108 ± 3	-14.1 ± 0.2[b]

[a]Ref. 20. [b]Determined at 308.16 K. [c]Determined at 283.16 K.

TABLE 3. Rate and activation parameters for the reaction of $(CO_5)MC[(OC_2H_5)(C_2C_6H_5)]$ with imidazole

Metal	k_{298} (M^{-1} s^{-1})	$\Delta H^{\neq}$ (kJ mol^{-1})	$\Delta S^{\neq}$ (J mol^{-1} K^{-1})	$\Delta V^{\neq}$ (cm^3 mol^{-1})
Cr	1.37 ± 0.04	31 ± 1	-140 ± 3	-14.7 ± 0.8[a]
W	2.72 ± 0.04	27 ± 2	-146 ± 7	-12.5 ± 0.8

[a]Determined at 317.16 K.

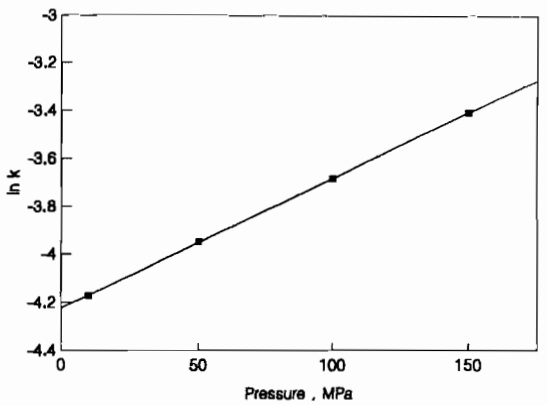
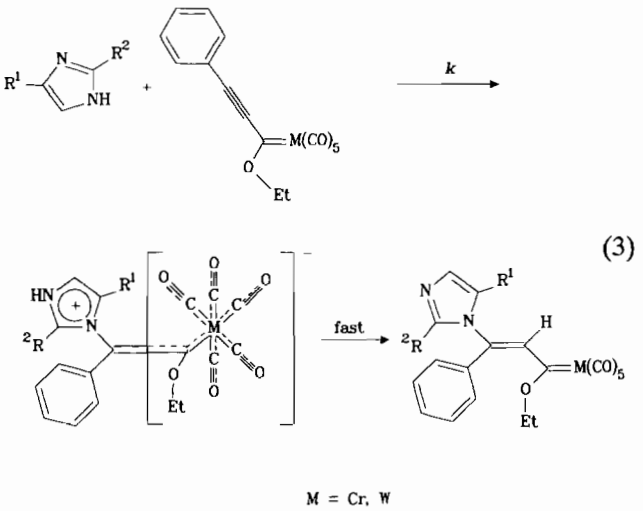


Fig. 3. Effect of pressure on k_{obs} for reaction (1) in acetonitrile at 35 °C. Experimental conditions: $[W] = 1.1 \times 10^{-4}$ M; [4-phenylimidazole] = 0.02 M.

from chromium to tungsten. This effect of the metal on the reactivity is also known from all other investigated addition reactions with amines and pyrazoles [8, 9], and furthermore established for [2+2] cycloaddition studies on such α,β-acetylene carbene complexes [21].

We conclude that the addition reactions of imidazoles to α,β-unsaturated Fischer carbene complexes also occur according to the previously established two-step mechanism [8, 9]. Significant bond formation takes place in the polar transition state, which is passed through in the rate-determining step to produce an unstable zwitterionic intermediate, which then rapidly leads to the final product as shown in eqn. (3).



(3)

Beside the reported activation parameters, the mechanism is supported by the absence of a significant isotope effect in the case of deuterioimidazole, viz. $k_D:k_H = 1.00:1.10$. The observed effect is of secondary nature and underlines the operation of a two-step mechanism in which nitrogen–carbon bond formation is followed by a rapid intramolecular proton transfer from the imidazole nitrogen to the C2 carbon atom of the carbene complex in the final product. Steric effects of substituents close to the N-donor atom cause an overlap with electronic (mesomeric) effects in terms of tuning the rate of the addition process. A comparison of the data for substituents at different sites to the donor atom allows us to distinguish between basicity and steric hindrance as controlling parameter.

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