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Influence of the reaction temperature on the regioselectivity in the rhodium-catalyzed hydroformylation of vinylpyrroles

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Abstract

The influence of the temperature on the regioselectivity in the hydroformylation of the vinylpyrrole isomers and of the corresponding *N*-tosylated substrates has been investigated in the range 20–100°C, in the presence of $Rh_4(CO)_{12}$. At all the temperatures the branched aldehyde was prevailing with respect to the linear isomer for all the substrates (α-regioselectivity). With increasing temperature, an increase of the linear aldehyde was observed to a different extent in dependence on the substrate nature. ^2H NMR investigation of the crude reaction mixture recovered from deuterioformylation of 3-vinylpyrrole at partial substrate conversion points out that the observed depression of the α-regioselectivity with increasing temperature must be connected to a β-hydride elimination process occurring for the branched alkyl–rhodium intermediates but not for the linear ones. © 1997 Elsevier Science S.A.

Keywords: Hydroformylation; Deuterioformylation; Vinylpyrroles; Vinyl-1-tosylpyrroles; Rhodium; Catalysis

1. Introduction

It is well-known that the rhodium-catalyzed hydroformylation of vinylaromatics [1–7], vinylheteroaromatics [8–14] and *N*-vinylimides [15,16] gives a large prevalence of the branched aldehyde over the linear one (α-regioselectivity). Although there are several studies [1,3–7] on the influence of the reaction parameters (temperature, gas pressure, catalyst precursor) on the regioselectivity of the rhodium-catalyzed hydroformylation of styrene and substituted styrenes, no report about analogous investigations in the case of vinylpyrroles has been published until now. In a previous communication [14] we first reported that the vinylpyrroles isomers can be hydroformylated at 40°C in the presence of $Rh_4(CO)_{12}$ as catalyst precursor, with a high α-regioselectivity. In this light, it seemed interesting to study the influence of the temperature (20–100°C) on the regioselectivity in the rhodium-catalyzed hydroformylation of vinylpyrrole isomers 1-vinylpyrrole **1a**, 2-vinylpyrrole **1b**, 3-vinylpyrrole **1c**, and of their *N*-tosylated derivatives **1b′** and **1c′** (Scheme 1), with the aim to investigate the incidence on the regioselectivity of electronic and/or steric effects connected to the different vinyl group positions in the ring.

Taking into account that the formation of the rhodium–alkyl intermediates as well as of their dissociation is a crucial step for the reaction regioselectivity [1,2] and that deuterioformylation experiments are a useful probe to obtain information in this regard [5,17,18], 3-vinylpyrrole **1c** was deuterioformylated at partial substrate conversion and different temperatures and the reaction mixtures were directly analyzed by ^2H NMR spectroscopy.

2. Results

2.1. Hydroformylation experiments

Hydroformylation of vinylpyrroles **1a–c′** (Scheme 1), was carried out in benzene with complete conversion of the substrate, in a stainless steel autoclave, with $Rh_4(CO)_{12}$ as catalyst precursor, in the temperature range 20–100°C, under 120 atm total pressure (CO/H_2 = 1:1).

The composition of the reaction mixtures was evaluated by GC analysis, using *o*-xylene as internal standard.

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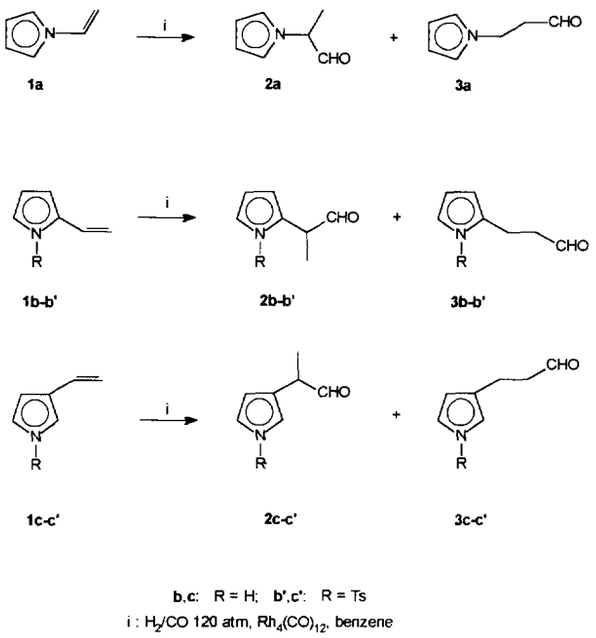


Scheme 1.

The amount of the aldehydes **2** and **3** was high (> 90%) at all the investigated temperatures (Tables 1 and 2), the hydrogenation products **4**, arising from H_2 addition to the exocyclic double bond, being the only by-product observed.

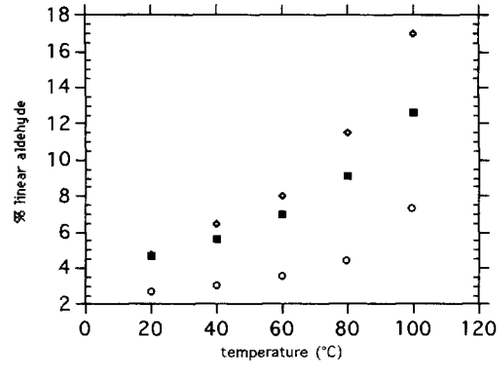


Fig. 1. Hydroformylation (total pressure 100 atm, $CO/H_2 = 1:1$) of the 1-vinylpyrrole (**1a**) (○), 2-vinylpyrrole (**1b**) (■) and 3-vinylpyrrole (**1c**) (◇) at complete conversion. Influence of the reaction temperature on the regioselectivity.

The composition of the reaction mixtures is reported in Tables 1 and 2 and the variation of the linear aldehyde with reaction temperature is shown in Fig. 1 for unprotected substrates **1a**, **1b**, **1c** and in Fig. 2 for the *N*-tosylated ones **1b'** and **1c'**.

When the reaction is carried out on **1a–c** at room temperature the amount of the linear aldehyde **3** is very

Table 1
Hydroformylation of the *N*-unsubstituted vinylpyrroles **1a, 1b** and **1c** at complete substrate conversion in the presence of $Rh_4(CO)_{12}$ as catalytic precursor: influence of the temperature on the products distribution[a]

T (°C)	1-vinylpyrrole (**1a**)			2-vinylpyrrole (**1b**)			3-vinylpyrrole (**1c**)		
	Reaction time (h)	Aldehydes[b] (%)	**2a/3a**[b]	Reaction time (h)	Aldehydes[b] (%)	**2b/3b**[b]	Reaction time (h)	Aldehydes[b] (%)	**2c/3c**[b]
20	52	100	97/3	70	99	95/5	60	98	95/5
40	22	100	97/3	44	98	94/6	24	98	94/6
60	20	99	96/4	24	96	93/7	10	96	92/8
80	13	98	96/4	10	96	91/9	5	91	88/12
100	4	97	93/7	4	92	87/13	3	90	83/17

[a]Determined via GLC using *o*-xylene as internal standard; ±1% accuracy; reaction conditions: 1 g of vinylpyrrole, 5 g of benzene, 40 mg of $Rh_4(CO)_{12}$; autoclave volume 25 ml; 120 atm total pressure, CO/H_2 (1:1).
[b]**(2 + 3)/((2 + 3) + 4)**.
2 = 2-pyrrolylpropanal; **3** = 3-pyrrolylpropanal; **4** = ethylpyrrole.

Table 2
Hydroformylation of the vinyl-1-tosylpyrroles **1b'** and **1c'** at complete substrate conversion, in the presence of $Rh_4(CO)_{12}$ as catalytic precursor: influence of the temperature on the products distribution[a]

T (°C)	2-vinyl-1-tosylpyrrole (**1b'**)			3-vinyl-1-tosylpyrrole (**1c'**)		
	Reaction time (h)	Aldehydes[b] (%)	**2b'/3b'**[b]	Reaction time (h)	Aldehydes[b]	**2c'/3c'**[b]
20	24	92	95/5	24	92	96/4
40	21	92	94/6	24	92	96/4
60	20	92	93/7	18	92	94/6
80	16	92	84/16	17	92	92/8
90	9	91	72/28	15	91	91/9
100	6	91	64/36	11	91	90/10

[a]Determined via GLC using *o*-xylene as internal standard; ±1% accuracy; reaction conditions: 1 g of vinyl-1-tosylpyrrole, 5 g of benzene, 40 mg of $Rh_4(CO)_{12}$; autoclave volume 25 ml; 120 atm total pressure, CO/H_2 (1:1).
[b]**(2 + 3)/((2 + 3) + 4)**.
2 = 2-(1-tosylpyrrolyl)propanal; **3** = 3-(1-tosylpyrrolyl)propanal; **4** = ethyl-1-tosylpyrrole.

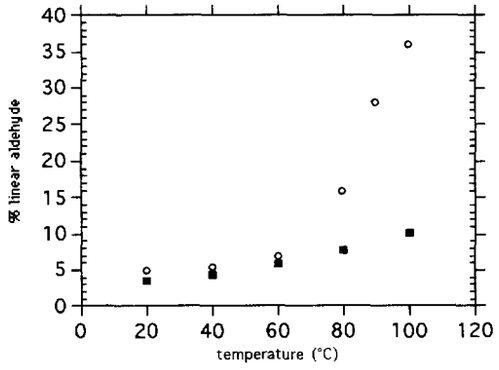


Fig. 2. Hydroformylation (total pressure 100 atm, $CO/H_2 = 1:1$) of the 2-vinyl-1-tosylpyrrole (**1b'**) (○) and 3-vinyl-1-tosylpyrrole (**1c'**) (■) at complete conversion. Influence of the reaction temperature on the regioselectivity.

low for all the substrates (3 to 5%). By increasing the reaction temperature an increase in the amount of **3** has been observed in all the cases. As shown in Fig. 1 the highest increase in the amount of **3** occurs for **1c**, the lowest for **1a**, while **1b** shows an intermediate behaviour, the regioselectivity being in favour of the branched isomer **2** at all the temperatures (Table 1).

As far as the *N*-tosylated substrates **1b'** and **1c'** are concerned, at room temperature the regioselectivity (Table 2) is similar to that observed for the corresponding unsubstituted substrates **1b** and **1c**. Also in these cases, an increase of reaction temperature produces a decrease of the α-regioselectivity. This effect is much higher for 2-vinyl-1-tosylpyrrole **1b'** (the linear aldehyde ranging from 5% at 20°C to 36% at 100°C) with respect to 3-vinyl-1-tosylpyrrole **1c'** (the linear aldehyde ranging from 4% at 20°C to 10% at 100°C).

1b' shows the highest decrease of α-regioselectivity among all the examined substrates.

2.2. *Deuterioformylation experiments*

Deuterioformylation experiments were carried out on 3-vinylpyrrole **1c,** at partial substrate conversion, at 20°C and 100°C, under the same experimental conditions employed for the hydroformylation experiments. Reactions were stopped after approximately the same drop of gas pressure corresponding to a 30% substrate conversion into aldehydes. The composition of the reaction mixtures was evaluated by GC analysis, using *o*-xylene as internal standard. The values of aldehyde yield and of regioselectivity were very similar to those observed in the hydroformylation experiments.The crude reaction mixtures were analyzed by ^2H NMR spectroscopy in order to identify all the deuterated species present in solution. Moreover MS analyses were carried out on the residual reaction gases, following the same procedure as for the deuterioformylation of styrene [5].

Fig. 3 shows the ^2H NMR spectrum of the reaction mixture obtained from the deuterioformylation of **1c** at 20°C. The signals for the expected branched aldehyde 1,3-d_2-**2c** (at 9.48 ppm for CDO and at 1.24 ppm for CH_2D) and the linear one 1,3-d_2-**3c** (at 9.36 ppm for CDO and at 2.64 ppm for CHD β to the carbonyl group) (Table 3) are present. The ^2H NMR spectrum of the crude reaction mixture obtained at 100°C (Fig. 4) shows, in addition to the aldehyde signals, two resonances at 5.05 and 5.55 ppm. These signals can be ascribed to the two geometrical isomers (*Z*)-2-deutero-1-(pyrrol-3-yl)ethene (*Z*-2-d_1-**1c**) and (*E*)-2-deutero-1-(pyrrol-3-yl)ethene (*E*-2-d_1-**1c**) arising from the pres-

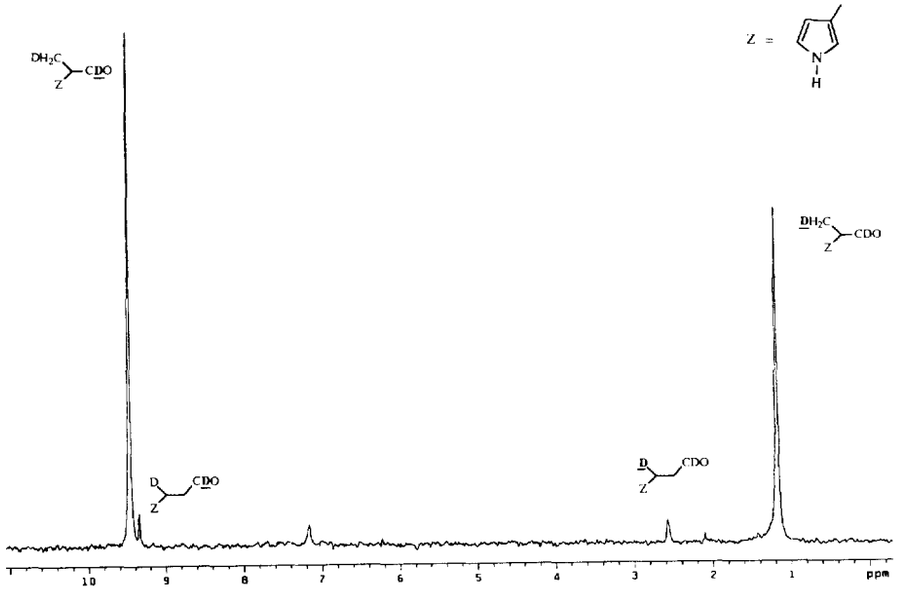


Fig. 3. ^2H NMR spectrum (46 MHz, 25°C, C_6D_6 as external standard) of the crude reaction mixture in benzene, obtained by deuterioformylation of the 3-vinylpyrrole (**1c**) at 20°C.

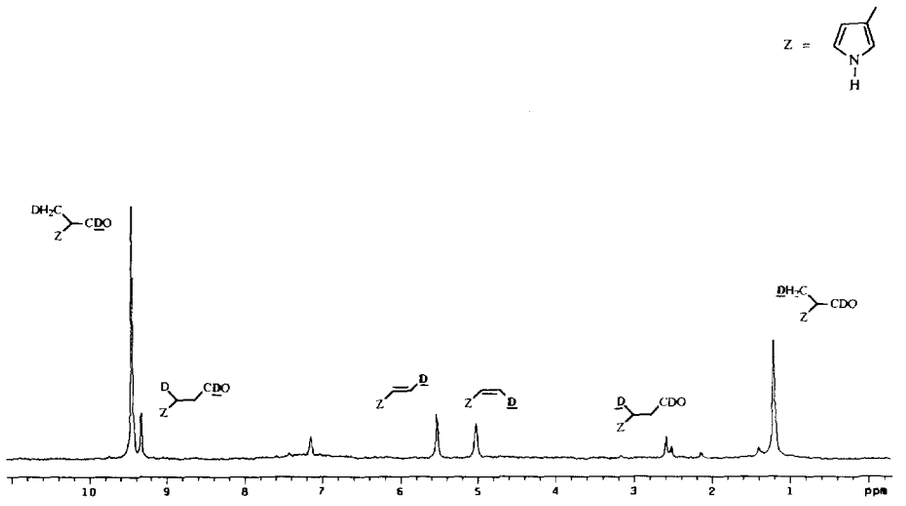


Fig. 4. ^{2}H NMR spectrum (46 MHz, 25°C, C_6D_6 as external standard) of the crude reaction mixture in benzene, obtained by deuterioformylation of the 3-vinylpyrrole (**1c**) at 100°C.

ence of deuterium in the position 2 (Pyr-CH=CHD species) of the exocyclic double bond. No resonances corresponding to a deuterium atom in the position 1 of the double bond of the unconverted olefin is detected (Table 3).

MS analysis of the residual deuterioformylation gases showed the presence of HD and H_2 only in the experiments carried out at high temperature (100°C).

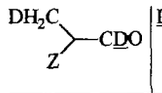
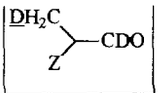
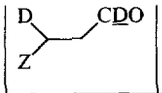
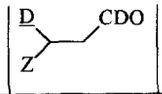
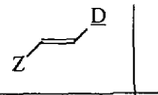
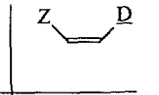
3. Discussion and conclusion

The results obtained in the hydroformylation of the vinylpyrroles **1a–c′** in the temperature range 20–100°C can be summarized as follows: (i) At room temperature the α-regioselectivity is very high for all the substrates (**2/3** = 95/5–97/3); (ii) in all the cases, the α-regioselectivity decreases with increasing temperature, this effect being maximum for 2-vinyl-1-tosylpyrrole **1b′** and minimum for 1-vinylpyrrole **1a**; (iii) in all the cases, but in particular for 3-vinylpyrrole **1c**, the trend of the α-regioselectivity with temperature is similar to that shown by styrene [3–7]; (iv) for the *N*-tosylated substrate **2b′** the decrease of α-regioselectivity with the temperature is higher than for the *N*-unsubstituted one **2b**. The opposite occurs for the substrates **2c′** and **2c**.

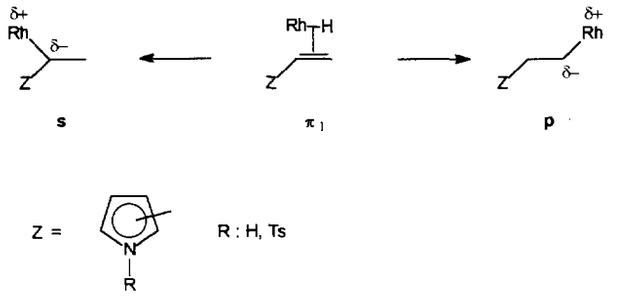
The large prevalence of the branched isomer observed at room temperature for all the substrates must be related to the preferential formation of the branched alkyl–metal intermediates with respect to the linear ones. Indeed, as previously reported for styrene [4] and substituted styrenes [18], the presence of a heteroaromatic polarizable group directly bonded to the carbon linked to the rhodium atom makes the branched alkyl **s** strongly favoured with respect to the linear one **p** (Scheme 2).

The decrease of the branched aldehyde with increasing reaction temperature must be connected to the different behaviours of the metal–alkyl intermediates **s** and **p** under hydroformylation conditions. Deuterioformylation runs carried out on **1c** at partial substrate conversion and investigated by ^{2}H NMR analysis of the reaction mixture gave experimental evidences to this regard. Indeed when the deuterioformylation reaction is carried out at 100°C, no 3-vinylpyrrole deuterated in position 1 of the double bond is detected but only olefin deuterated at position 2 (Scheme 3). This fact can be explained in terms of a reversible α-Rh addition to the

Table 3
^{2}H NMR chemical shifts (δ, ppm)[a] of mono- and dideuterated substrates arising from the deuterioformylation of 3-vinylpyrrole (**1c**) in the presence of $Rh_4(CO)_{12}$

					
9.48	1.24	9.36	2.64	5.55	5.05

[a]Referred to C_6D_6 as external standard; 46 MHz, C_6H_6, 25°C.



Scheme 2.

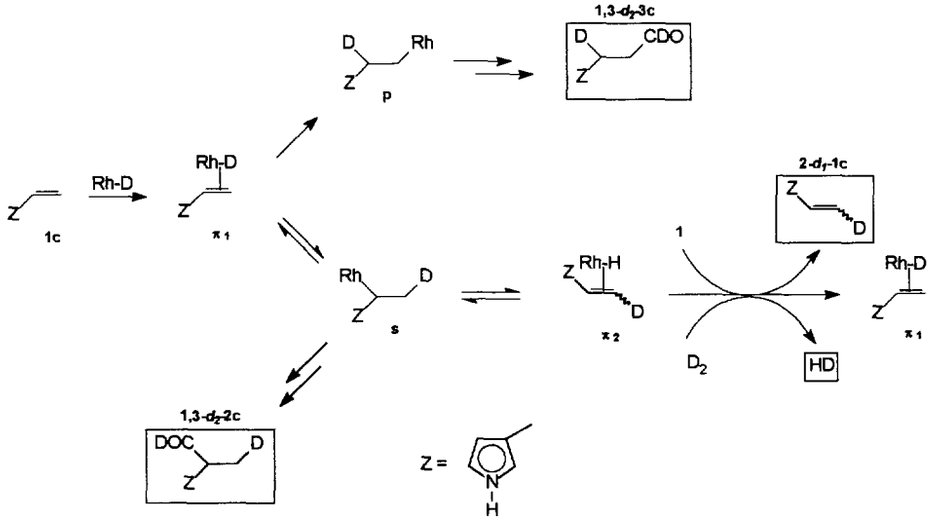
olefin in competition with an irreversible β-addition. More likely, the β-addition product is much more reactive towards acyl transfer, to give the corresponding normal aldehyde, than towards β-hydride elimination. On the contrary the branched alkyl **s** partially converts into branched aldehyde and partially regenerates the π_2 rhodium complex (Scheme 3). As a consequence the secondary alkyl partially isomerizes to the primary one, the regioisomeric ratio of the corresponding aldehydes varying in favor of the normal isomer.

In addition the presence of HD and H_2 in the residual reaction gases indicates that the rhodium hydride present in the complex π_2, formed by the β-hydride elimination from **s**, rapidly reacts with the excess of D_2 and undeuterated olefin, the prevalent species at low conversion, giving rise to free deuterated olefin and the original complex π_1 (Scheme 3). A similar fate can be hypothesized for all the branched rhodium–alkyl intermediates involved in the hydroformylation of the other vinyl substrates.

At room temperature no β-hydride elimination takes place for both **s** and **p** alkyls and hence the alkyl–rhodium intermediate formation is not reversible. Under these conditions the regioselectivity reflects the relative rates of formation of the isomeric alkyl–rhodium intermediates. As previously discussed, the presence of the polarizable pyrrole ring directly bonded to the partially negative carbon atom favors the branched isomer **s** over the linear alkyl **p** and then the branched aldehyde over the linear one (Scheme 2). This effect overcomes the structure differences between the vinylpyrroles examined (closeness of the vinyl moiety to the ring nitrogen atom, presence of the tosyl group), showing a similar value of regioselectivity in these conditions.

The increase of the linear aldehydic isomer **3**, observed at high temperatures and explained on the basis of the above considerations, is not the same for all the examined vinylpyrroles. For 1-vinylpyrrole **1a**, 2-vinylpyrrole **1b** and 3-vinylpyrrole **1c** the closer the vinyl moiety to the nitrogen atom the smaller is the entity of the above mentioned increase. This behaviour can be attributed to a $-I$ inductive electronic effect that, in addition to the presence of the polarizable aromatic ring, further stabilizes the branched alkyl–rhodium intermediate **s** also at high temperature. The same effect results evident from a direct comparison between 3-vinylpyrrole **1c** (Fig. 1) and 3-vinyl-1-tosylpyrrole **1c′** (Fig. 2); the latter substrate shows a smaller increase of the linear aldehydic isomer **3c′** due to the electronic-withdrawing effect of the tosyl group bonded to the ring nitrogen atom. By contrast in the case of 2-vinyl-1-tosylpyrrole **1b′** (Fig. 2), a greater amount of the corresponding linear aldehyde **3b′** with respect to 2-vinylpyrrole **1b** (Fig. 1) is observed at high temperatures: it can be assumed that the migratory insertion of the branched alkyl **s** on a CO group coordinated to the rhodium atom to give the acyl species, and hence the corresponding branched aldehyde, is more hindered for **1b′** than for **1b** because of steric effects due to the proximity of the tosyl group to the vinyl moiety [18].

In conclusion, the decrease of the α-regioselectivity observed for all the examined substrates can be con-



Scheme 3.

nected to a β-hydride elimination process occurring at high temperature for the branched alkyl–rhodium intermediate only: the entity of this process depends on the substrate nature and it increases with increasing temperature.

The above results constitute the first systematic study of the influence of reaction temperature on the chemo- and regioselectivity in the rhodium-catalyzed hydroformylation of vinyl heteroaromatic substrates. It is also to remark that the stability shown by the pyrrole nucleus under hydroformylation conditions also at high temperatures together with the very good reaction selectivity gives interesting perspectives in a synthetic employment of this process.

4. Experimental

Benzene was dried over molecular sieves and distilled under nitrogen. $Rh_4(CO)_{12}$ was prepared according to a well-known procedure [19]. 1-vinylpyrrole **1a** was obtained by direct *N*-vinylation of pyrrole with acetylene [20]. 2-vinylpyrrole **1b** was prepared by Wittig reaction on 2-formylpyrrole [21,22]. 2-vinyl-1-tosylpyrrole **1b′** was obtained by Wittig reaction on 2-formyl-1-tosylpyrrole, prepared by treatment of 2-formylpyrrole with *p*-toluensulfonyl chloride [23]. 3-vinylpyrrole **1c** was obtained from the corresponding 3-vinyl-1-tosylpyrrole **1c′** by treatment with NaOH in 2-propanol/water [24]. 3-vinyl-1-tosylpyrrole **1c′** was prepared through dehydration of the corresponding secondary carbinol derived from the reduction of the 3-acetyl-1-tosylpyrrole as described in literature [24].

GC analyses of the reaction mixtures were performed on a Perkin-Elmer 8500 chromatograph equipped with a 12 m × 0.22 mm bp1 capillary column, using helium as carrier gas. ^2H NMR spectra of the crude reaction mixture in benzene were recorded on a Varian VXR 300 spectrometer operating at 46 MHz for ^2H. Chemical shifts were referred to C_6D_6 as external standard.

4.1. Hydroformylation and deuterioformylation experiments: General procedure

*4.1.1. Hydroformylation and deuterioformylation of 3-vinylpyrrole (**1c**)*

A solution of 3-vinylpyrrole (**1c**) (1 g, 10.7 mmol) and $Rh_4(CO)_{12}$ (40 mg, 0.054 mmol) in benzene (5 ml) was introduced by suction into an evacuated stainless-steel autoclave. Carbon monoxide was introduced, the autoclave was then rocked and heated to the desired temperature, and hydrogen or deuterium was rapidly introduced to 120 atm total pressure. When the gas absorption reached the value corresponding to the desired conversion, the reaction vessel was rapidly cooled, the reaction mixture siphoned out and GC used to determine the isomeric composition. The degree of conversion was measured by GLC, using *o*-xylene as internal standard.

Acknowledgements

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