DALTON
FULL PAPER

Evidence for the hydride mechanism in the methoxycarbonylation of ethene catalysed by palladium–triphenylphosphine complexes

Robert P. Tooze,*[a] Keith Whiston,[a] Andrew P. Malyan,[b] Michael J. Taylor[b] and Nigel W. Wilson[b]

[a] *Strategic Projects Group, Ineos Acrylics, PO Box 90, Wilton, Middlesbrough, UK TS90 8JE. E-mail: robert_tooze@ineos-a.com*
[b] *ICI Technology, PO Box 90, Wilton, Middlesbrough, UK TS90 8JE*

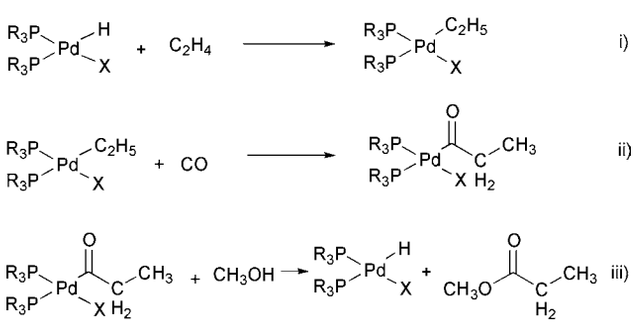
Received 29th June 2000, Accepted 11th August 2000
First published as an Advance Article on the web 18th September 2000

Analysis of the phosphorus containing by-products from the catalytic methoxycarbonylation of ethene using a palladium triphenylphosphine complex with a combination of High Performance Liquid Chromatography (HPLC) and Mass Spectrometry (MS) indicated increasing levels of phosphonium salts through the course of the reaction, major ones being methyltriphenylphosphonium, ethyltriphenylphosphonium and 3-oxopentyltriphenylphosphonium ($CH_3CH_2C(=O)CH_2CH_2PPh_3$) cations, isolated as the sulfonate salts. The latter are shown to be produced by metal mediated pathways and believed to be indicative of the operation of the hydride mechanism.

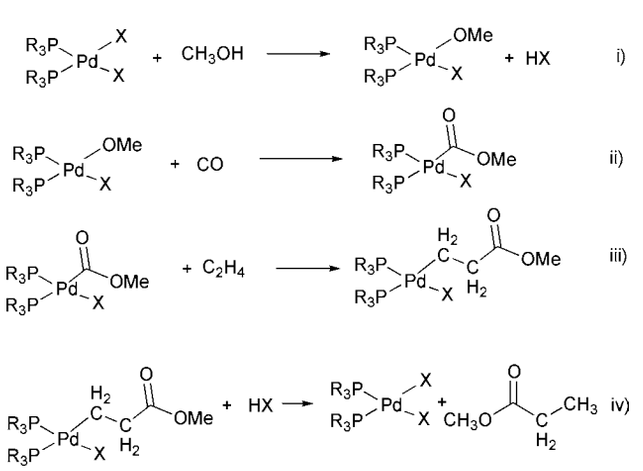
Introduction

The formation of new carbon–carbon bonds by the carbonylation of unsaturated substrates is of increasing importance. In this transformation it is broadly accepted that two distinct mechanistic pathways are possible, often acting in parallel. These are shown in Schemes 1 and 2 and are referred to as the hydride and the alkoxycarbonyl route.

Faced with the indisputable fact that true catalytic intermediates are highly reactive and therefore difficult to isolate and given the problems associated with direct "*in situ*" observation of intermediates at realistic concentrations and conditions of pressure and temperature, evidence for particular mechanistic pathways has relied on indirect methods. These have included end group analysis of polymers,[1] isotopic labelling,[2] the effect of modifying catalyst structure on product identity[3] and use of model compounds as precursors.[4] Unfortunately all such approaches have limitations for example the instability of palladium hydrides largely precludes their use as model compounds.[5] (However very recently strong evidence has been presented for the involvement of palladium hydrides in the carbonylation of styrene using a similar catalyst system[6] and some of us have reported the characterisation of all of the intermediates involved in the "hydride" cycle by NMR studies of stoichiometric reactions.[7]) Given these problems associated with individual methods a combination of techniques is probably the best approach.



Scheme 1 Idealised hydride mechanism for the alkoxycarbonylation of alkenes.



Scheme 2 Idealised alkoxycarbonyl mechanism for the alkoxycarbonylation of alkenes.

In general the side reactions of phosphine ligands with reactants, products or intermediates is regarded as a nuisance in homogeneous catalysis and efforts have been made to reduce such reactions by ligand modification.[8] Their use as a mechanistic probe has largely been neglected.[9] We report here some results in this area suggesting that for specific reactions this could be added to the above list of techniques.

We are interested in routes to methyl propanoate (MeP) as an intermediate to methyl methacrylate (MMA) *via* the methoxycarbonylation of ethene.[10] It has been shown by others that complexes derived from palladium acetate, triphenylphosphine (TPP) and a sulfonic acid make suitable catalysts for this transformation[11] (albeit with a much lower activity than systems recently reported by some of us using a bidentate phosphine ligand[12]). In order to maintain the activity triphenylphosphine must be fed continuously. We report here the use of a combination of High Performance Liquid Chromatography (HPLC) and Mass Spectrometry (MS) to follow these side reactions.

Results and discussion

Catalyst optimisation

The work reported in this paper arose as part of a systematic study of catalysts based on palladium acetate, triphenylphosphine and sulfonic acid. Two separate statistically designed tests were carried out on the catalyst system. The first was a two level

DOI: 10.1039/b005232i

Table 1 Variables and levels employed in screening experiments

Variable	Low level	High level	Midpoint	Units
CO Pressure	10	30	25	Barg[a]
Temperature	85	115	98	°C
C_2H_4 Pressure	10	30	20	Barg[a]
H_2 Pressure	0	5	2.5	Barg[a]
Palladium concentration	0.4	1	0.7	mmol l^{-1}
Anion concentration	10	25	17.5	mmol l^{-1}
PPh_3 concentration	10	25	17.5	mmol l^{-1}
	Type I	Type 2		
Solvent	Methanol	34% MeOH in methyl propanoate	N.A.	v/v
Anion type	*p*-Toluenesulfonic acid	Methanesulfonic acid	N.A.	

[a] Barg stands for Bar gauge, the pressure registered on monitoring equipment, which takes the initial (i.e. atmospheric) pressure to be zero.

Table 2 Basis of designed experiments

Run	Reaction temperature	CO Pressure	C_2H_4 Pressure	H_2 Pressure	Solvent type	Anion type	Anion level	Palladium concentration	Ligand level
1	High	High	High	Low	Type 2	Type 2	Low	High	Low
2	Low	Low	Low	Low	Type 1	Type 1	Low	Low	Low
3	Low	High	High	High	Type 1	Type 2	High	Low	High
4	High	Low	High	Low	Type 1	Type 1	High	High	High
5	Low	Low	Low	High	Type 2	Type 2	Low	High	High
6	High	High	Low	High	Type 2	Type 1	High	Low	Low
7	High	Low	Low	Low	Type 2	Type 2	High	Low	High
8	Low	Low	High	High	Type 2	Type 1	High	High	Low
9	High	High	Low	High	Type 1	Type 1	Low	High	High
10	High	Low	High	High	Type 1	Type 2	Low	Low	Low
11	Low	High	Low	Low	Type 1	Type 2	High	High	Low
12	Low	High	High	Low	Type 2	Type 1	Low	Low	High
13	High	Low	Low	High	Type 1	Type 2	High	High	Low
14	Low	High	Low	Low	Type 2	Type 1	High	High	High
15	High	Low	High	High	Type 2	Type 1	Low	Low	High
16	Low	Low	High	Low	Type 2	Type 2	High	Low	Low
17	Low	High	High	High	Type 1	Type 1	Low	High	Low
18	High	High	Low	Low	Type 1	Type 2	Low	Low	High
19	Low	High	Low	High	Type 2	Type 2	Low	Low	Low
20	Low	Low	High	Low	Type 1	Type 2	Low	High	High
21	High	High	High	Low	Type 1	Type 1	High	Low	Low
22	High	High	High	High	Type 2	Type 2	High	High	High
23	Low	Low	Low	High	Type 1	Type 1	High	Low	High
24	High	Low	Low	Low	Type 2	Type 1	Low	High	Low

Plackett–Burman[13] test designed to screen the effect of nine process parameters on the catalyst performance criteria of activity, lifetime and selectivity. Plackett–Burman tests are designed to screen large numbers of variables for their effect on a response in the minimum number of tests. The nine experimental parameters selected were reaction temperature, ethene pressure, carbon monoxide pressure, hydrogen pressure, palladium concentration, phosphine concentration, acid concentration and type and solvent composition. The details of the high and low levels for the parameters and the design are collected in Tables 1 and 2. Analysis of the results was carried out using the analysis of variance technique (ANOVA).[14] The second trial was an optimisation exercise which looked in more detail at the effects of temperature and the initial concentrations of triphenylphosphine and sulfonic acid. Analysis here provided a descriptive mathematical model of catalyst performance (*e.g.* activity) in the form of an additive polynomial function of the variables used in the design. This is not a factorial kinetic model but rather a method of calculating what level of reaction rate can be obtained with a selected catalyst formulation. The results can be displayed as a response surface holding one of the variables constant as shown in Fig. 1.

This analysis required that samples were taken at regular intervals from catalytic runs and cooled rapidly to quench the reaction prior to analysis by gas chromatography (GC) of the organic products. This also showed the presence of a much less

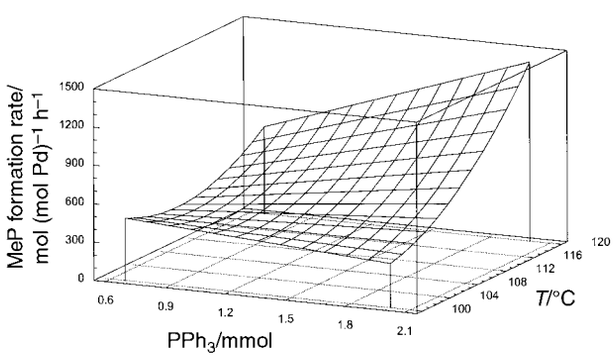


Fig. 1 Methyl propanoate formation rate as a function of temperature and triphenylphosphine concentration at constant concentration of *p*-toluenesulfonic acid (0.67 mmol).

volatile species, initially this was believed to be a higher oligomer of general formula $H[CH_2CH_2C(=O)]_nOCH_3$; however further analysis of these samples using liquid chromatography (LC) showed the presence of a number of products. Their structure was then ascertained using coupled LC-MS and Tandem Mass spectrometry (see Experimental section). In addition to TPP and its oxide $Ph_3P=O$, the most significant products were the methyl-, ethyl- and in particular the 3-oxopentyl-triphenylphosphonium cations, CH_3PPh_3 **1**, $C_2H_5PPh_3$ **2**, and C_2H_5-

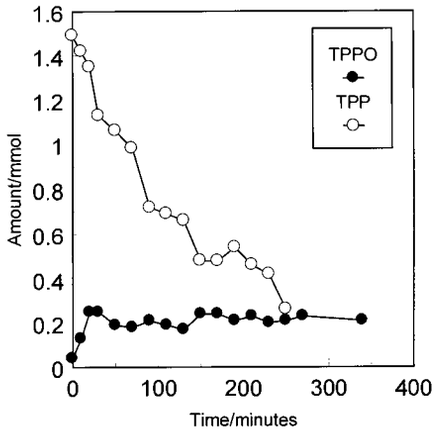


Fig. 2 Amount of individual phosphorus containing species as a function of reaction time at 100 °C, (TPPO = triphenylphosphine oxide).

$C(=O)C_2H_4PPh_3$ **3**, isolated as the sulfonate salts. Analytically pure compounds were synthesized of the simplest materials (**1**, **2**) by the reaction of TPP with the corresponding ester of methanesulfonic acid in methanol and standard solutions of known concentration were then prepared. Development of a specific analytical method enabled good chromatographic separation to be obtained of the reaction mixtures using HPLC (see Experimental section). Combination of identification by MS and quantification by HPLC techniques thus allowed quantitative, time resolved analysis of the phosphorus containing by-products, the only assumption being that the calibration curve obtained for **1** and **2** could also be applied to **3**. Care was also taken to exclude air; earlier less rigorous attempts led to the formation of phosphine oxide as the dominant product.

Samples taken from all of the aforementioned statistically designed experiments were analysed using this combination of techniques. The most significant findings are as follows. (i) The most abundant phosphonium cation at the end of the reaction is **3**. The amount formed correlates with the ethene pressure used, the reaction temperature and the initial concentration of acid, but not with the initial phosphine concentration. (ii) The amount of compound **1** formed correlates with the initial concentration of phosphine and acid and is higher in reactions conducted in pure methanol. (iii) The levels of **2** observed did not correlate significantly with any of the experimental variables selected. (iv) The levels of **1** were higher when *p*-toluenesulfonic acid was used compared to those when methanesulfonic acid was used.

Time resolved experiments

On the basis of this work a catalyst formulation was selected to give optimum stability, this comprised palladium acetate, triphenylphosphine and *p*-toluenesulfonic acid in the molar ratio 1 : 20 : 20. This catalyst was then studied in a further series of experiments, conducted at three different temperatures whereby samples were withdrawn throughout the course of the reaction. The results of the study are shown in Figs. 2 and 3. These show the total amount of each phosphorus containing species in the autoclave as a function of time, calculated from the sample volume withdrawn and the concentration in this sample. Inspection of these shows that the formation of triphenylphosphine oxide occurs very early on and then reaches a plateau; similar behaviour is exhibited for **1** and to an extent **2**. The formation of **3** continues through the course of the reaction and dominates in the later stages.

With regards to the formation of triphenylphosphine oxide it is felt significant that the level observed approximates in molar terms to the amount of palladium acetate added to the reaction. The stoichiometric reduction of palladium acetate with the concomitant oxidation of triphenylphosphine has been

Table 3 Arrhenius data for phosphonium cation formation

Phosphonium cation	Rate/10^{-3} mmol min^{-1}			E_a/kJ mol^{-1}
	100 °C	110 °C	120 °C	
1	25.5	64.7	177.2	118.1
2	6.0	20.4	79.4	157.5
3	13.9	28.6	41.8	67.4

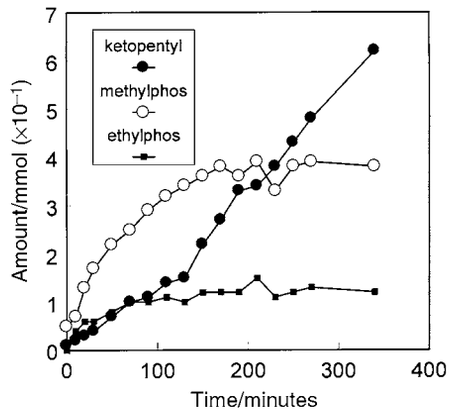


Fig. 3 Amount of individual phosphorus containing species as a function of reaction time at 100 °C. (ketopentyl = 3-oxopentyltriphenylphosphonium cation, $[C_2H_5C(=O)C_2H_4PPh_3]^+$; methyl = methyltriphenylphosphonium cation, $[CH_3PPh_3]^+$; ethyl = ethyltriphenylphosphonium cation, $[C_2H_5PPh_3]^+$.

reported.[15] It appears that most of the added phosphine is converted into the phosphonium cations **1**,**2** and **3** rather than to oxidation products. It is believed that **1** is derived from the reaction of TPP with methyl *p*-toluenesulfonate (known to be present in solution); this reaction is not metal mediated. This differentiates it from the other cations **2** and **3**; for example, ethene, *p*-toluenesulfonic acid and TPP in methanol under reaction conditions fail to produce any **2**. It is felt that the most likely route for the production of **3** is *via* the interruption of the palladium catalysed chain growth of polyketone (arising from a further insertion of ethene into the palladium acyl, Pd–$C(=O)C_2H_5$ in Scheme 1) by interaction with TPP. This attack by phosphine can either occur in an inter- or intra-molecular fashion; more data are required unequivocally to establish this point. In the case of **3** the apparent independence of the rate of formation of **3** on free phosphine concentration seems to mitigate against the former. The level of TPP does not fall to zero but rather to a level equal to about three times the amount of palladium added on a molar basis; at this level catalyst stability is poor, visible degradation occurs and reaction ceases.

These time resolved variable temperature experiments also allowed an estimation of the activation energies of the degradation processes operating, by calculating the rate of phosphonium salt formation at each temperature. This could be used to give an activation energy for compounds **1**, **2** and **3** of 118, 157.5 and 67 kJ mol^{-1} respectively (Table 3). An overall value for phosphonium cation production was calculated to be 117 kJ mol^{-1}. The value for MeP production for this system is 64 kJ mol^{-1}. This is consistent with the observation that the catalyst system is less productive at higher temperatures due to increasing instability.

Both the ethyl and oxopentyl palladium complexes are products of the hydride catalytic cycle (Scheme 1) providing strong evidence of the operation of this pathway. The absence of any phosphonium cations derived from organometallic fragments associated with the methoxycarbonyl cycle is surprising but does not rule out the operation of this pathway. It could be for example that the phosphonium cation forming reaction

may be slower than "productive" termination reactions of these species, *e.g*. the formation of product *via* protonolysis of the palladium–carbon bond (final step, Scheme 2).

Conclusion

Statistically designed experiments have been used to optimise the catalytic methoxycarbonylation of ethene. This ensured the results and subsequent analysis were obtained from the most relevant operating conditions. The side reactions leading to phosphine consumption are normally considered undesirable but given scant attention. However by careful analysis of the phosphorus containing by-products insight has been gained not only into the degradation pathway of these catalysts but also the desired product forming cycles. Evidence for the operation of the hydride pathway has been found.

Experimental

Palladium acetate was supplied by the Aldrich Chemical Company and recrystallised from toluene prior to use; triphenylphosphine from the same supplier was recrystallised from ethanol. Methanesulfonic acid and *p*-toluenesulfonic acid were used as received, also from Aldrich. Ethene, hydrogen and carbon monoxide were high purity grade supplied by BOC.

Catalysis

Reactions were carried out in 300 cm^3 stainless steel autoclaves agitated by means of air driven Magnadrive stirrers. The desired reaction temperature was achieved by electrically heated jackets with set point control *via* an immersed coil fed by a Churchill oil-circulating bath. Gas components were always fed in the order carbon monoxide, ethene and then hydrogen to the desired pressure and the autoclave sealed. As required the unit was topped up with a 1:1 mixture of ethene and carbon monoxide (reflecting the expected reaction stoichiometry); no hydrogen was added to the reactor after the initial charge. Pressure and temperature data were acquired using a Rustrak Ranger datalogger at 30 second intervals throughout the runs. The initial reaction rate was calculated by least squares regression analysis of the recorded gas absorption data. The catalyst components, palladium acetate, triphenylphosphine and *p*-toluenesulfonic acid in a molar ratio of 1:20:20, were stirred in methanol under an inert atmosphere prior to charging to the autoclave; the amount of palladium acetate used in these experiments was 0.2 mmol. For the time resolved experiments samples were removed from the autoclave every ten minutes for the first hour and every twenty minutes thereafter. These were cooled to −78 °C and stored under an inert atmosphere prior to analysis.

Analysis

HPLC-MS experiments were performed using a ZAB2SE mass spectrometer (Micromass UK) fitted with a Continuous-Flow Liquid Secondary Ion Mass Spectrometry interface. HPLC column eluent was split using a pneumatically controlled gas-flow needle valve to achieve a post-column flow-rate of *ca*. 5–10 $cm^3\ min^{-1}$. Tandem mass spectrometry experiments on selected ions were performed on the ZABT tandem mass spectrometer (Micromass UK) which was operated at a collision-cell voltage of +4 kV and with argon as collision gas. Glycerol was used as sample matrix. HPLC was carried out using a Zorbax SB-CN column operating under ion-suppression/ion-pair reversed phase (100 mM aqueous methanesulfonic acid at a pH of 1.8 to methanol gradient) conditions. The conditions of pH and ionic strength were found necessary to get good peak shape and stable chromatography. Analysis was *via* on line UV spectral analysis. GC-MS was performed under the following standard chromatography conditions (unless stated): 25 metre CPSil 19 capillary column, 1.2 mm film thickness, helium carrier gas 5 psi, injector temperature 250 °C, oven program 50 °C for 4 minutes rising to 200 °C at 20 °C min^{-1} and holding at 200 °C.

References

1 E. Drent and P. H. Budzelaar, *Chem. Rev.*, 1996, **96**, 663.
2 A. Scrivanti, V. Beghetti, E. Campagna, M. Zanatto and U. Matteoli, *Organometallics*, 1998, **17**, 630; M. A. Zuideveld, P. C. J. Kamer, P. W. N. M. van Leeuwen, P. A. A. Klusener, H. A. Stil and C. F. Roobeek, *J. Am. Chem. Soc.*, 1998, **120**, 7977.
3 E. Drent, P. Arnoldy and P. H. Budzelaar, *J. Organomet. Chem.*, 1994, **475**, 57.
4 D. Milstein, *Acc. Chem. Res.*, 1998, **21**, 428; G. Cavinato and L. Toniolo, *J. Organomet. Chem.*, 1990, **398**, 187.
5 V. V. Grushin, *Chem. Rev.*, 1996, **96**, 2011.
6 A. Seayad, S. Jayasree, K. Damodoran, L. Toniolo and R. V. Chaudhari, *J. Organomet. Chem.*, 2000, **601**, 100.
7 G. R. Eastham, B. T. Heaton, J. A. Iggo, R. P. Tooze, R. Whyman and S. Zacchini, *Chem. Commun.*, 2000, 609.
8 C. B. Ziegler and R. F. Heck, *J. Org. Chem.*, 1978, **43**, 2941.
9 J. A. Kampmeier, S. H. Harris and R. M. Rodehorst, *J. Am. Chem. Soc.*, 1981, **103**, 1478; F. E. Goodson, T. I. Wallow and B. M. Novak, *J. Am. Chem. Soc.*, 1997, **119**, 12441.
10 *Kirk-Othmer Encyclopedia of Chemical Technology*, John Wiley & Sons, New York, 4th edn., 1995, vol. 16, p. 487.
11 W. G. Reman, G. B. J. De Boer, S. A. J. Van Langen and A. Nahuijsen (Shell), *Eur. Pat.*, EP 411 721 A3, Priority date 1st August 1989.
12 W. Clegg, M. R. Elsegood, G. R. Eastham, R. P. Tooze, X. L. Wang and K. Whiston, *Chem Commun.*, 1999, 1877.
13 R. L. Plackett and J. P. Burman, *Biometrika*, 1946, **33**, 305.
14 C. Chatfield, *Statistics for Technology*, Chapman and Hall, London, 1979.
15 C. Amatore, A. Jutand and M. M'Barki, *Organometallics*, 1992, **11**, 3009.