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Alkyl migration reactions—the direct observation of the preferential migration of branched over linear alkyl groups

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Abstract

Three binuclear metal alkyl complexes were synthesised, viz. $[Cp(CO)_2Fe\{CH(CH_3)CH_2CH_2\}Fe(CO)_2Cp]$ (**I**), $[CpFe(CO)_2\{CH(CH_3)CH_2CH_2CH_2\}Fe(CO)_2Cp]$ (**II**) and $[CpMo(CO)_3\{CH(CH_3)CH_2CH_2\}Mo(CO)_3Cp]$ (**III**) ($Cp = \eta^5$-cyclopentadienyl). These compounds were then reacted with PPh_3 in order to induce alkyl migration (CO insertion) reactions. The products obtained were monosubstituted phosphine acyl species. In all cases, the branched chain alkyl fragment (viz. $M–CH(CH_3)$) was observed to react preferentially over the linear fragment (viz. $M–CH_2CH_2$). These results are rationalised in terms of the relative importance of steric and electronic effects in alkyl migration reactions. © 2000 Elsevier Science S.A. All rights reserved.

Keywords: Alkyl migration; Catalysis; Selectivity; Branched; Linear

1. Introduction

A very high proportion of asymmetric catalysts that have been developed are organometallic compounds. High selectivity can be achieved by selecting the proper catalyst, substrate and reaction conditions. Many of the elementary steps of enantioselective catalytic reactions are reversible and it is the first irreversible step which involves chiral transition states that determines the nature of the products. To achieve a high degree of stereoselectivity, efforts must be focused towards a single, chirality-determining transition state.

An important application of asymmetric catalysis is the hydroformylation of prochiral olefins such as vinyl aromatics and other vinylic species, e.g. vinyl acetate, to produce aldehydes which are intermediates in the synthesis of steroids, pheromones, antibiotics and anti-inflammatories [1]. A catalytic cycle for rhodium-catalysed olefin hydroformylation is shown in Scheme 1. The initial step in the cycle is loss of a CO ligand followed by coordination of the substrate olefin to form a metal hydrido olefin complex (reaction (i)). Hydride migration onto the coordinated olefin then occurs, but this can occur via two routes, either anti-Markovnikov migration to give the linear alkyl species (reaction (ii)) or Markovnikov migration to give the branched alkyl species (reaction (vii)). It is the further reactions of this alkyl species, either linear or branched, which determines the nature of the products obtained from the reaction.

It has been shown that at higher temperatures, reaction (vii) can be reversible for branched alkyl species obtained from certain vinylic substrates [2,3]; the alkyl intermediate undergoes a facile β-hydride elimination reaction to revert back to the hydride olefin complex. This can then react again to form either the linear or branched alkyl species. In asymmetric catalysis, the branched species is the desired product as it contains the new chiral centre. The β-hydride elimination reaction is thus detrimental to the selectivity of asymmetric hydroformylation (and other) reactions and should be minimised as it constitutes a 'draining away' of the chiral alkyl intermediate. One way of overcoming this problem is to facilitate the alkyl migration reaction (reactions (iv) and (ix)) so that the branched alkyl group rapidly migrates to form the branched acyl species, for which β-hydride elimination does not occur.

Thus, there are two selectivities which need to be optimised in asymmetric catalytic reactions, viz. re-

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gioselectivity (linear versus branched) and enantioselectivity (R versus S). While there is a great deal of work being done on optimising the enantioselectivity of a reaction by, for example, the use of chiral ligands and auxiliaries [1,4], the issue of regioselectivity has received considerably less attention. The key intermediates formed during catalytic hydroformylation reactions are metal carbonyl alkyl species and the way in which they react further, especially how linear species react relative to branched species, is crucial in determining the overall selectivity of the reaction.

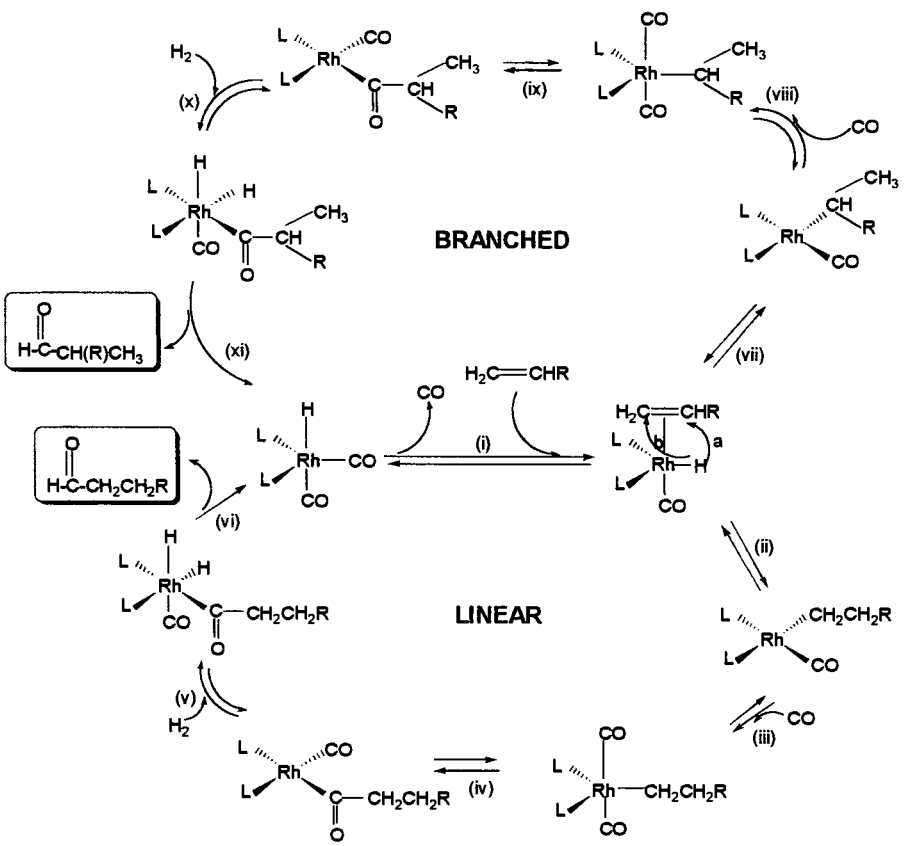
It is thus surprising that very little is known about the relative migratory aptitudes of linear versus branched alkyl groups. A few isolated studies would seem to indicate that branched alkyl groups migrate more rapidly than linear alkyl groups [5–8]; however, not all of these studies provided a complete analysis of the results. Both steric and electronic parameters should be taken into account and these can often give conflicting expectations as to the outcome of a reaction. These factors are discussed in more detail in the Section 2.

We now report our results on the synthesis and alkyl migration reactions of three binuclear complexes, viz. $[CpFe(CO)_2Fe\{CH(CH_3)CH_2CH_2\}Fe(CO)_2Cp]$ (**I**), $[Cp(CO)_2Fe\{CH(CH_3)–CH_2CH_2CH_2\}Fe(CO)_2Cp]$ (**II**) and $[Cp(CO)_3Mo\{CH(CH_3)CH_2CH_2\}Mo(CO)_3Cp]$ (**III**). These complexes all contain a bridging alkyl unit which contains both a branched alkyl moiety attached to the metal ($M–CH(CH_3)$) and a linear alkyl moiety attached to the metal ($M–CH_2CH_2$). Reactions of **I**, **II** and **III** with one equivalent of PPh_3 should result in substitution at only one end of the bridging alkyl unit, either linear or branched. The purpose of this study was to determine (a) whether reaction would occur at the linear or at the branched end and to rationalise this in terms of steric and electronic factors and (b) whether the iron complexes would react in the same way as the molybdenum complexes.

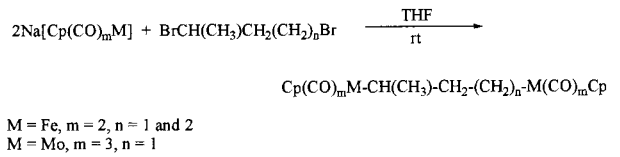
2. Results and discussion

2.1. Synthesis

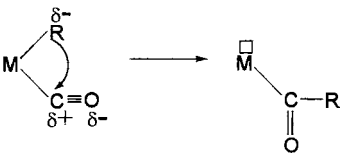
Compound **I**, $[Cp(CO)_2Fe\{CH(CH_3)CH_2CH_3\}Fe(CO)_2Cp]$, has been reported previously [9]. We have synthesised it again by an analogous route to that used before, and also the new compounds $[Cp(CO)_2Fe\{CH(CH_3)CH_2CH_2CH_2\}Fe(CO)_2Cp]$ (**II**) and $[Cp(CO)_3Mo\{CH(CH_3)CH_2CH_2\}Mo(CO)_3Cp]$ (**III**). All three compounds were synthesised by reaction of the cyclopentadienyl metal carbonyl anion with the appropriate dibromoalkane, as shown in Scheme 2. **I, II**



Scheme 1. Hydroformylation of olefins, showing both linear and branched products.



Scheme 2.



Scheme 3. Alkyl migration. □, vacant coordination site.

and **III** were isolated as yellow crystalline solids and were characterised by melting point, microanalysis, IR and ^{1}H-NMR. Characterisation data are reported in Tables 1 and 2.

2.2. Reaction of *I, II and III* with PPh_3

Alkyl migration onto a coordinated carbonyl ligand, or CO insertion as it is often referred to, is an intramolecular nucleophilic attack of the alkyl group on to the carbon atom of the carbonyl ligand to form a metal acyl species, as represented in Scheme 3.

Branched alkyl groups should therefore migrate faster in to the carbonyl ligand than linear alkyl groups as they will be more electron-donating and will thus experience a greater electrostatic attraction towards the δ^+ carbon atom. In addition, the resultant acyl species is electron-deficient and will be stabilised to a greater extent by branched alkyls than linear alkyls. The faster migration of more electron-donating alkyl groups has already been established [10,11].

However, on steric grounds the situation can be reversed. A branched alkyl group is bulkier than its linear analogue and might thus migrate on to the adjacent carbonyl ligand more slowly than the smaller linear group. This has also been established previously [10–13]. In addition, the product containing the bulkier branched alkyl group adjacent to the incoming nucleophile (e.g. PPh_3) will experience a greater degree of unfavourable steric interactions. There is, however, an alternative steric effect which might operate in some cases, which is that if the entering group (e.g. PPh_3) is not involved in the reaction at all, then one could argue that the bulkier (branched) alkyl should react faster since steric strain is being alleviated on going from the more hindered alkyl to the open acyl. These two oppos-

Table 1
Data for compounds **I**, **II** and **III** and products of reaction with PPh_3

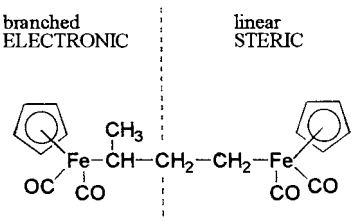
Compound No.	Yield (%)	M.P. (°C)	IR ν(CO) (cm^{-1}) [a]	Elemental analysis	
				C; Found (calc.)	H Found (calc.)
I	26	86–88	2006vs, 211vs, 1949vs	52.9 (52.7)	4.7 (4.4)
II	31	90–93	2006vs, 2001vs, 1947vs	53.5 (53.8)	4.5 (4.7)
III	18	76–80	2046m, 2019s, 1981s, 1931s	44.3 (44.0)	3.5 (3.3)
I + PPh_3	52	105–108	2005mw, 1948m, 1920mw, 1661w	64.1 (64.4)	4.3 (4.8)
II + PPh_3	63	112–116	2005mw, 1945m, 1919mw, 1657w	64.5 (64.8)	4.6 (5.0)
III + PPh_3	57	98–102	2046mw, 2020mw, 1932m, 1665w	57.1 (57.5)	4.0 (4.3)
I [b]	22	84–87	2009vs, 2003vs, 1955vs	52.4 (52.7)	4.7 (4.4)

[a] KBr discs; vs = very strong, s = strong, m = medium, w = weak.
[b] Data taken from Ref. [5].

Table 2
^{1}H-NMR data for compounds **I**, **II** and **III** [a] and products of reaction with PPh_3

Compound no.	M–C*H* or M–COC*H*	M–CH(CH_3) or M–COCH(CH_3)	M–CH_2	M–CH$_2$(CH_2)$_n$	Cp	PPh_3
I	2.2 (c, 1H)	1.05 (d, 3H, J = 7Hz)	1.35 (br, 2H)	1.56 (c, 2H)	4.73 (s, 10H)	
II	2.1 (c, 1H)	1.09 (d, 3H, J = 6Hz)	1.38 (br, 2H)	1.63 (c, 4H)	4.72 (s, 10H)	
III	2.5 (c, 1H)	1.42 (br, 3H)	1.75 (br, 2H)	2.18 (c, 2H)	5.30 (s, 10H)	
I + PPh_3	1.9 (c, 1H)	0.81 (br, 3H)	1.33 (br, 2H)	1.59 (c, 2H)	4.72 (br, 10H)	7.62 (c, 15H)
II + PPh_3	1.86 (c, 1H)	0.82 (br, 3H)	1.38 (br, 2H)	1.65 (br, 4H)	4.72 (c, 10H)	7.66 (c, 15H)
III + PPh_3	2.7 (c, 1H)	1.25 (br, 3H)	1.75 (br, 2H)	2.18 (c, 2H)	5.28 (c, 10H)	7.82 (c, 15H)
I [b]	2.48 (br, 1H)	1.36 (d, 3H, J = 6Hz)	1.63 (m, 4H)	1.63 (m, 4H)	4.70 (s, 10H)	

[a] In $CDCl_3$, relative to TMS (δ = 0.00 ppm), s = singlet, d = doublet, br = broad, c = complex, m = multiplet
[b] Data taken from Ref. [5].



Scheme 4. Linear versus branched reactivity.

ing steric effects have been discussed in depth by Cotton and Markwell [13], who introduce the concept of a 'steric window' within which reactivity is enhanced. The more typical effect, however, is the first, viz. that bulkier alkyl groups undergo migratory insertion more slowly than do smaller groups; studies reported by ourselves and other groups have shown this to be the case [10–13].

When comparing linear and branched alkyl groups and their expected migratory aptitudes, there are thus two opposing effects to consider, viz. on electronic grounds, branched alkyl groups should migrate faster, whereas on steric grounds, the linear alkyl groups should migrate faster. We thus synthesised compounds **I**, **II** and **III** as they contain both linear and branched alkyl moieties. Reaction of these complexes with only one equivalent of nucleophile should thus result in reaction at only one end of the molecule. If reaction occurs at the linear end of the molecule (M–CH_2CH_2), this then indicates that steric factors dominate over electronic factors, whereas if reaction occurs at the branched end of the molecule (M–$CH(CH_3)$), this would indicate that electronic factors dominate. This is represented in Scheme 4. These experiments thus represent a direct comparison between migratory insertion reactions of linear and branched alkyl groups. In addition, these complexes approximate actual catalytic intermediates more closely than do separate studies on linear and branched alkyl species. A catalytic reaction, at any given time, will contain a mixture of both linear and branched alkyl species and it is the relative rates of the two different species, which will determine the regioselectivity of reaction. Thus, performing a competition experiment, as we have done, is a more accurate comparison to in situ catalytic processes than performing two separate studies.

Compounds **I**, **II** and **III** were reacted with one equivalent of PPh_3, as represented in Scheme 5, in order to determine which end of the molecule (linear or branched) would react preferentially. All reactions were performed in hexane at 45°C.

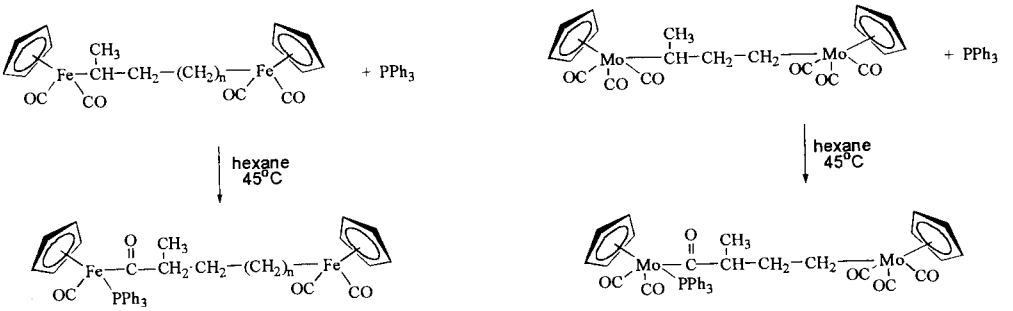
The products of the reaction were the phosphine-substituted acyl complexes where reaction had occurred at the branched end of the molecule. The reactions were monitored by FTIR and the reaction products characterised by FTIR, ^{1}H-NMR and elemental analysis, as reported in Tables 1 and 2. ^{1}H-NMR was used to identify which end of the complex had reacted. In all cases, the signals for M–C*H* and M–CH(CH_3) had shifted position, whereas the signal for M–CH_2 remained unchanged.

^{1}H-NMR spectra were also run of the crude reaction mixture prior to recrystallisation of the PPh_3-substituted products in order to ascertain that we were not selectively recrystallising only one product. In all cases, the NMR spectra of the crude mixtures showed that only one product had formed.

3. Conclusions

The alkyl migration reaction occurred, in every case, at the branched end of the molecule. This is indicative of electronic factors being of greater significance than steric factors for the migration of an alkyl group on to a coordinated carbonyl ligand. This has implications in, for example, asymmetric hydroformylation reactions. If the rate of the overall process is increased, this may result in a greater amount of branched (chiral) product being formed. The branched alkyl intermediate should react faster than the linear intermediate, and will thus drive the catalytic cycle towards forming more branched product.

However, it should be noted (as was pointed out by a referee) that the steric demands of the two metal centres chosen in this study are not very high. The steric demand in typical hydroformylation catalysts is



Scheme 5. Reaction of **I**, **II** and **III** with PPh_3.

usually higher, so steric effects may become more important.

4. Experimental

All reactions were carried out under an atmosphere of high purity nitrogen using standard Schlenk tube techniques. Tetrahydrofuran (THF) was dried by distilling over sodium/benzophenone and hexane was dried by distilling over sodium wire under nitrogen. $[CpFe(CO)_2]_2$ and $[CpMo(CO)_3]_2$ were obtained from Strem Chemicals Inc. and the compounds $BrCH(CH_3)CH_2CH_2Br$ and $BrCH(CH_3)CH_2CH_2CH_2Br$ were obtained from Aldrich and were used without further purification. Alumina (BDH, active neutral, Brockman grade I) was deactivated before use.

Melting points were recorded on a Kofler hot-stage microscope (Reichert–Thermovar) and are uncorrected. Infrared spectra were recorded on an Atavar 360 FTIR Spectrometer as either as KBr discs or as Nujol mulls with NaCl windows.

^{1}H-NMR spectra were recorded on a Bruker AC-300 300MHz Spectrometer. The chemical shifts are relative to TMS (0 ppm).

4.1. Synthesis of $[Cp(CO)_2Fe\{CH(CH_3)CH_2CH_2\}Fe(CO)_2Cp]$ (I) and $[Cp(CO)_2Fe\{CH(CH_3)–CH_2CH_2CH_2\}Fe(CO)_2Cp]$ (III)

Compound **I** has previously been reported by Cooke et al. [9]. The same general procedure was adopted by us in this study. A solution of $Na\{CpFe(CO)_2]$ (5.65 mmol), prepared by reductive cleavage of $[CpFe(CO)_2]_2$ over Na–Hg in THF (20 ml), was added dropwise over ca. 10 min to the dibromoalkane (5.65 mmol) at 0°C with stirring. The yellow–brown solution was then stirred for 3 h at room temperature (r.t.). The solvent was removed under reduced pressure, leaving an orange–brown oily residue. This was dissolved in a minimum of hexane, transferred to a deactivated alumina chromatography column (2 cm × 10 cm) and eluted with hexane. A yellow band containing the product was eluted first, from which the solvent was removed under reduced pressure to yield a yellow oily solid. This was recrystallised from hexane at −15°C to give a yellow–orange solid in 26% yield (**I**) or 31% yield (**III**). A second, red band containing the $[CpFe(CO)_2]_2$ dimer remained on the column.

4.2. Synthesis of $[Cp(CO)_3Mo\{CH(CH_3)CH_2CH_2\}Mo(CO)_3Cp]$ (II)

A solution of $Na[CpMo(CO)_3]$ (6.12 mmol), prepared by reductive cleavage of $[CpMo(CO)_3]_2$ over Na–Hg in THF (20 ml), was added dropwise over ca. 10 min to 1,3-dibromobutane (6.12 mmol) at 0°C with stirring. The yellow–brown solution was then stirred for 4 h at r.t. The solvent was removed under reduced pressure, leaving an orange–red oily residue. This was dissolved in a minimum of hexane, transferred to a deactivated alumina chromatography column (2 cm × 10 cm) and eluted with hexane. A pale yellow band containing the product was eluted first, from which the solvent was removed under reduced pressure to yield a yellow oily solid. This was recrystallised from hexane at −15°C to give a yellow solid in 18% yield. A second, orange–red band containing the $[CpMo(CO)_3]_2$ dimer remained on the column.

4.3. Reactions of Compounds I, II and III with PPh_3

Compound **I**, **II** or **III** (0.20 mmol) was dissolved in hexane (10 ml) at 45°C. One equivalent of PPh_3 (0.20 mmol) was added to the solution. The solution was then left to stir overnight at 45°C. After this time, the Schlenk tube containing the reaction mixture was cooled down to r.t. When cool, approximately one half of the solvent was removed under reduced pressure, and the product left to crystallise at −15°C. The products were obtained as yellow crystalline solids in ca. 60% yield.

Acknowledgements

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