Chelation Control in the Hydroformylation of Terminal Alkenes

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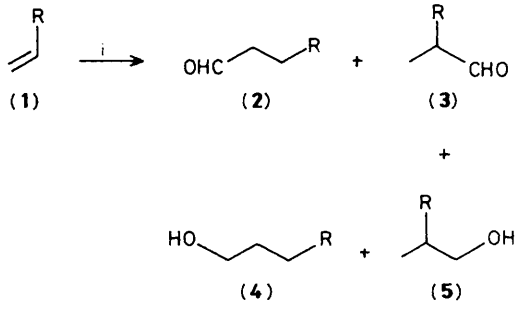
Hydroformylation of phosphine-bearing terminal alkenes can lead to a complete reversal of regioselection to that observed for simpler alkenes.

Over the last few decades the hydroformylation of alkenes (the 'oxo' reaction) has found important applications in industrial syntheses.[1,2] The emphasis in these processes has been on selective production of *linear* products (**2**) and (**4**) (Scheme 1), which has been achieved through the appropriate choice of metal and ligands.[3]



Scheme 1. i, H_2/CO,[M^0] (M = Rh, Co).

From a synthetic standpoint it is the *branched* isomers (**3**) and (**5**) which appear to be the more interesting and useful. As typical reaction conditions involve a rhodium(0) catalyst associated with a phosphine ligand, inclusion of a phosphine in the alkene framework might lead to a more selective reaction. Adjustment of the distance of the phosphine from the alkene might then provide a means for fine-tuning selectivity (Scheme 2).

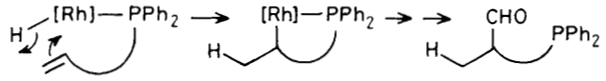
In order to test these ideas we have prepared a series of alkenylphosphines (**6**) and (**11**).† Each of these was then subjected to the same set of hydroformylation conditions {except where otherwise indicated in Table 1,

† (**6a**) and (**6b**) were prepared by reaction of the appropriate Grignard reagent with chlorodiphenylphosphine (ref. 4). (**6c**) and (**6d**) were prepared by reaction of lithium diphenylphosphine with the appropriate bromoalkene (ref. 5). (**11**), the phosphine oxide of (**6b**) was prepared by either coupling chlorodiphenylphosphine oxide with the appropriate Grignard reagent (ref. 4) or oxidation of (**6b**) (air, or H_2O_2 in acetone).

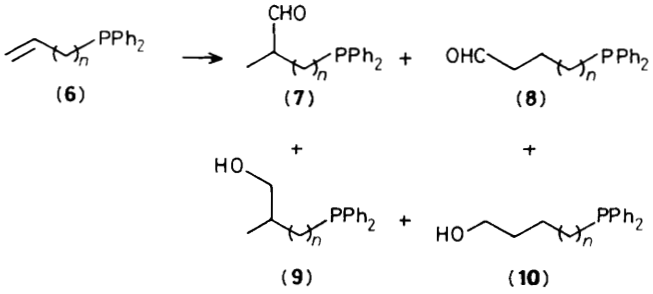
Table 1. Results of the hydroformylation of various diphenylphosphinylalk-1-enes.

		% Ratio of product[a]				
Entry	Alkene	(7)	(8)	(9)	(10)	% Yield[b]
1	(6a)[c]	—	—	30	20	68
2	(6b)	—	—	100	—	86
3	(6b)[d]	—	—	75	25	85[g]
4	(6c)[c]	21—26	2—9	27—52	—	64—95
5	(6d)[c]	60	32	—	—	96
6	(6d)[e]	50	27	13	8	54
7	(11)	36	64	—	—	55[f]
8	(1; R = Bu[n])	25(3)	75(2)	—	—	71

[a] Product ratios determined from the 300 MHz ^{1}H n.m.r. spectra of the crude product in each case, for at least two runs. [b] Yield after distillation. All crude yields were close to quantitative, however significant decomposition accompanied distillation in each case. [c] The remainder of product was the alkane. [d] 50 equiv. of PPh_3 added. [e] No PPh_3 added. [f] After recrystallisation from ethyl acetate–light petroleum; crude yield 94%. [g] Crude yield.



Scheme 2

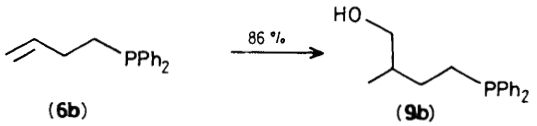


a; $n = 1$
b; $n = 2$
c; $n = 3$
d; $n = 4$

Scheme 3

alkene : PPh_3 : $[Rh(OAc)_2]_2$, (200 : 4 : 1), H_2/CO (1 : 1, 400 psi), EtOAc, 100 °C, 5 h}. Consistent with earlier studies of rhodium-catalysed hydroformylations no significant amounts of aldol by-products were formed.[6] The results, for the reactions summarised in Scheme 3, are collected in Table 1.‡

Several trends emerge from these results. First, in a number of cases, reduction of the product aldehydes (**7**) and (**8**) had occurred yielding the corresponding alcohols (**9**) and (**10**). A linear correlation was observed between the number of intervening methylenes and the oxidation state of the products. For short chains, $n = 1$ or 2, only alcohols were formed,



(**6b**) (**9b**)

Scheme 4

whereas for the longer chain, $n = 3$, a mixture was produced. The longest chain, $n = 4$, yielded only aldehydes (Table 1, entry 5).

Secondly, in all cases selection for the branched isomers was better than that for a hydrocarbon analogue, hex-1-ene (entry 8). Most notably, 4-diphenylphosphinylbut-1-ene (**6b**) yielded only *one* product (**9b**) and in high yield (86%) (Scheme 4). This represents the first example of the total reversal of regioselection in hydroformylation reactions. Although its homologue, (**6c**), produced a mixture of aldehydes and alcohols, the regioselection was again good. In this case alone, however, the yields and product distribution proved difficult to reproduce (Table 1, entry 4).

Thirdly, variation in the amount of PPh_3 present influenced the product distribution. Thus, addition of a large excess of PPh_3 led to a reduction in regioselection (*cf.* entries 2 and 3). This is to be expected if intramolecular chelation is controlling the reaction. Alternatively, the absence of PPh_3 resulted in the appearance of some alcohols in the products without significant change in the regioselection (*cf.* entries 5 and 6).

Finally, hydroformylation of (**11**), the phosphine oxide of (**6b**), was also carried out (entry 7). Only aldehydes were produced in this case and in a ratio which is only slightly different to that for hex-1-ene (entry 8).

In conclusion, we have demonstrated that terminal alkenes bearing a phosphine group undergo the hydroformylation reaction with high regioselection. This selection is the reverse to that for simple hydrocarbon alkenes. Secondly, we have shown that a simple correlation exists between the oxidation state of the products and the number of intervening methylenes in the phosphinylalkene. These observations appear to reflect the influence of a cyclic transition state, the result of *intramolecular* chelation (Scheme 2), on the nature of the products. These ideas may have potential application to more complex alkenes as well as to other reaction types.§

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‡ All new compounds gave satisfactory spectroscopic and elemental analyses.

§ While this manuscript was in preparation a report of the application of a chelation-controlled hydroformylation reaction to the preparation of (+)-phyllanthocin appeared: S. D. Burke and J. E. Cobb, *Tetrahedron Lett.*, 1986, **27**, 4237.