

Homogeneous Catalytic Hydroformylation of Vinylarenes: A Selective Rhodium Diphosphine Catalyst System for Higher Branched/Linear Product Ratios

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A rhodium diphosphine catalyst containing electron-withdrawing substituents on the ligand is highly regioselective in the hydroformylation of vinylarenes giving high branched/linear product ratios.

The homogeneous catalytic hydroformylation of aryl vinyl compounds is potentially a very useful reaction for the preparation of fine chemicals and pharmaceuticals. Recently there has been substantial interest in the use of hydroformylation¹ (or hydrocarboxylation²) technology for the production of 2-arylpropionic acids which constitute an important class of anti-inflammatory drugs. The most notable amongst these include the studies of the preparation of the popular anti-inflammatory drugs naproxen and ibuprofen. In a recent study Stille *et al.* discovered that very high optical yields could be achieved in the homogeneous catalytic hydroformylation of styrene and other similar compounds by using a platinum catalyst containing a BPPM chiral bidentate diphosphine ligand.¹ {BPPM = (2*S*,4*S*)-*N*-(*tert*-butoxycarbonyl)-4-(diphosphino)-2-[(diphenylphosphino)methyl]pyrrolidine}. Unfortunately the regioselectivity of the reported catalyst system was not high enough. Studies of these reactions with rhodium *cis*-diphosphine catalysts also frequently gave high percentages of the undesired linear products.³ On the other hand, the studies with simple rhodium complexes without phosphine ligands,^{4,5} rhodium diphosphites,⁶ and rhodium phosphine complexes capable of forming *trans*-diphosphine configuration^{7,8} gave high regioselectivity. More recently Sakai *et al.* found that binaphthyl phosphinephosphite–rhodium complexes were highly enantioselective in the hydroformylation of vinylarenes with moderate to good regioselectivity.⁹ Unfortunately the simple rhodium complexes without phosphine ligands are rather difficult to be designed as chiral catalysts and the phosphite and phosphinite complexes are less stable under hydrolytic conditions. From a practical standpoint, it is of substantial interest to develop transition metal *cis*-diphosphine catalysts with high selectivity for the branched products in the hydroformylation of vinylarenes. It is also desirable to understand the underlying principles which govern the higher branched/linear product ratios in this reaction so that rational design of new, more effective chiral catalysts can be achieved.

Two important factors often govern the activity and selectivity of transition metal phosphine catalysts: steric and electronic effects. Since sterically hindered phosphines are expected to favour linear products, we believe that an investigation of the electronic effect of the catalysts should be meaningful. Recently, RajanBabu and Ayers studied the electronic effect of rhodium diphosphinites on the enantioselectivity of the hydroformylation of vinylarenes and found that substitution of electron-withdrawing aryl groups on the phosphorus increased enantioselectivity for the rhodium catalyst.¹⁰ Here we report a highly regioselective system based on the use of a rhodium *cis*-diphosphine catalyst with electron-withdrawing substituents on the ligand.

The first reaction we studied was the catalytic hydroformylation of styrene. A 'reference' reaction was carried out by using [Rh(NBD)(dppe)]BF₄ **1** [NBD = norbornadiene; dppe = 1,2-bis(diphenylphosphino)ethane] as a standard catalyst precursor. In benzene solvent at 55 °C and under 200 psig of a 1 : 1 mixture of CO and H₂, the hydroformylation products showed a branched/linear ratio of only 3.5. When a perfluoro analogue of dppe was used, *i.e.* 1,2-bis[bis(pentafluorophenyl)phosphino]ethane, as the phosphine ligand for the catalyst

precursor, the branched/linear ratio of the hydroformylation products was found to increase to 13.3 under otherwise identical reaction conditions.

This result was extremely interesting and encouraging. To test the generality of this effect, the hydroformylation of a variety of substituted styrenes was also studied. The substrates used included *p*-methylstyrene, methoxystyrene, chlorostyrene, and nitrostyrene. The results gave the same conclusion: catalyst

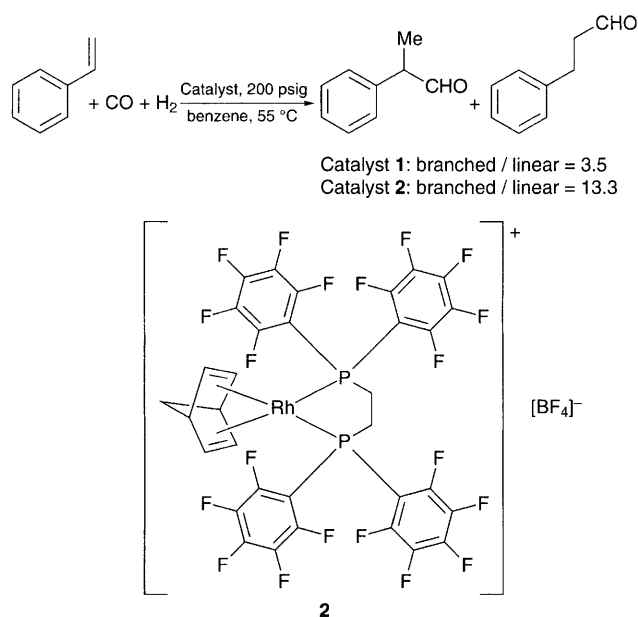


Table 1 The branched/linear product ratios in the homogeneous catalytic hydroformylation of vinyl arenes

Entry ^a	Substrate	Catalyst	Branched/linear ratio ^b
1	styrene	1	3.5
2	styrene	2	13.3
3	<i>p</i> -methylstyrene	1	3.2
4	<i>p</i> -methylstyrene	2	19
5	<i>p</i> -methoxystyrene	1	4
6	<i>p</i> -methoxystyrene	2	16
7	<i>p</i> -chlorostyrene	1	3.2
8	<i>p</i> -chlorostyrene	2	10
9	<i>p</i> -nitrostyrene	1	24
10	<i>p</i> -nitrostyrene	2	100% branched

^a Reaction conditions: benzene; 5 mol% catalyst; 200 psig 1 : 1 CO : H₂; 55 °C; 24 h. ^b 100% conversion was observed in all experiments. The branched/linear product ratios were determined by ¹H NMR.

2 gave much higher branched/linear product ratios from the hydroformylation than catalyst **1**. In the hydroformylation of *p*-nitrostyrene with catalyst **2**, essentially 100% of branched product was obtained. Since these substrates covered a wide range of electronic properties, it is obvious that the effect of the electron-deficient phosphine ligand is broad. The detailed experimental results are summarised in Table. 1.

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