A readily prepared neutral heterobimetallic titanium(IV)–rhodium(I) catalyst for intramolecular hydroacylation†

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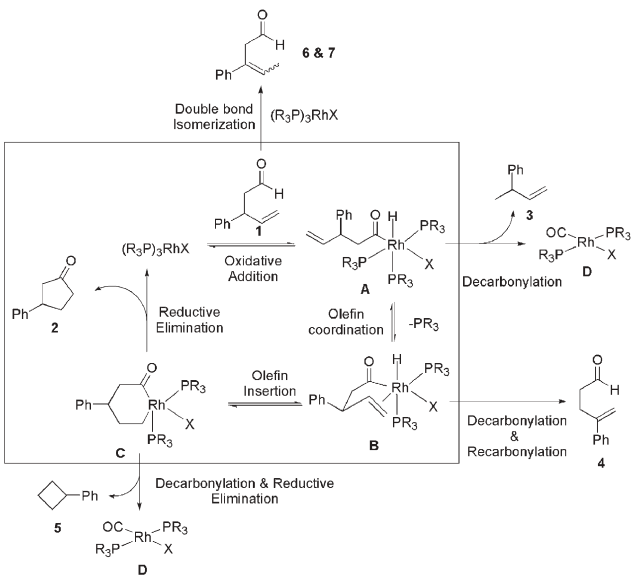
The combination of $HOCMe_2CH_2PPh_2$, $Ti(OiPr)_4$, and $[Rh(cod)Cl]_2$ (3:1:1) in either benzene or dichloromethane produces a discrete species (tentatively formulated as complex 14) that is an active catalyst for intramolecular hydroacylation reactions of 3-substituted pentenals.

Catalysts with multiple metal centers can show a breadth of reactivity that often exceeds their monometallic counterparts.[1] Each metal center may play a unique catalytic or structural role in the overall "multimetallic catalyst system." A necessary condition for the use of two (or more) metals is their compatibility, a situation that has been addressed in "early–late" bimetallic transition metal complexes.[2–4] Ultimately both the identity of the metals and their proximity to each other may lead to "synergistic" effects, in which one metal perturbs the reactivity of the other in an advantageous manner.[5] This metal–metal cooperativity has recently been suggested in hydrocarbonylation chemistry, one of our continuing interests.[6]

A specific hydrocarbonylation process (hydroacylation) was targeted for initial investigation with a proposed heterobimetallic catalyst involving rhodium(I) (Scheme 1).[7] The most active Rh(I) catalysts (developed by Bosnich and coworkers) were BINAP-derived *cationic* rhodium(I) systems which demonstrated remarkable reactivity for the cyclization of 4-substituted pentenals.[8] Recently however, Peters has shown that *zwitterionic* metal–metalloid rhodium–boronate complexes demonstrate the highest turnover frequency of all cationic rhodium systems (Fig. 1).[9] In each case the *cis* configuration of phosphines, locked by chelation, prevents significant sequestering of catalyst as the inactive form **D** (in Scheme 1).

The high activity of these boronate complexes indicates that electronic perturbation of the cationic rhodium(I) center by a proximally located charged heteroatom can dramatically increase hydroacylation reactivity. Rather than work with complexes containing a cationic rhodium atom, we chose instead to focus on *neutral* rhodium, due to its vastly improved stability relative to the cationic systems.[7f] Additionally there is significant room for improvement in neutral rhodium(I) hydroacylation catalysts; a general, highly active neutral rhodium system is currently unknown.[10] In this Communication, we report the construction and hydroacylation catalysis of a unique neutral rhodium(I) bimetallic complex.

The leading results of Wolczanski, *et al.* prompted us to focus on titanium(IV) as the second metal center in the heterobimetallic complex.[11] This previous report revealed that complex **13** (Fig. 2) could be readily synthesized from $TiCl_4$, but the product eluded full characterization due to the facile formation of aggregates. We were surprised to find that switching to $Ti(OiPr)_4$ resulted in the formation of a discrete Rh–phosphine complex without the concomitant formation of by-products. Notably, the reaction is carried out in two steps: first, $Ti(OiPr)_4$ is added to a solution of 3 eq. ligand $HOCMe_2CH_2PPh_2$ **10** (Fig. 2(a)) in dry dichloromethane.[12] Within 0.5 h the entirety of the ligand has complexed the titanium, evidenced by a small (1.5 ppm) upfield shift in the $^{31}P\{^1H\}$ NMR spectrum (Fig. 2(b)) and the formation of a persistent light yellow color. Subsequently $[RhCl(cod)]_2$ is added and the formation of a sharp doublet at 18.19 ppm occurs



Scheme 1 Mechanism for Rh(I)-catalyzed intramolecular hydroacylation using a Wilkinson's-type complex. For neutral complexes, X is typically a halide; for cationic complexes X represents an empty coordination site.

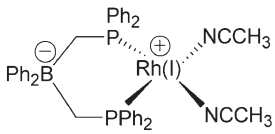


Fig. 1 Rhodium(I) catalyst with a proximally located charged heteroatom shows enhanced reactivity.[9]

† Electronic supplementary information (ESI) available: experimental procedures and catalyst characterization. See http://www.rsc.org/suppdata/cc/b5/b504195c/

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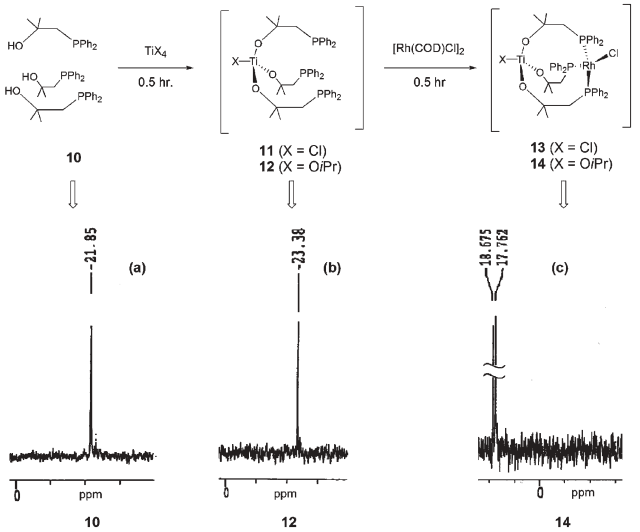
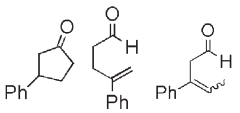


Fig. 2 *In situ* preparation of (iPrO)Ti(μ:η^1,η^1-$OCMe_2CH_2PPh_2)_3$RhCl (**14**) with associated ^{31}P spectra. Complete spectra are supplied in Supporting Information.

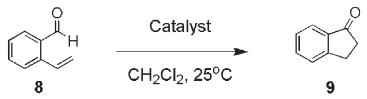
over 0.5 h (J_{RhP} = 147 Hz, Fig. 2(c)). The resulting complex, tentatively formulated as (*i*PrO)Ti(μ:η^1,η^1-$OCMe_2CH_2PPh_2)_3$RhCl, **14**, decomposes to an oily solid under vacuum,[13] but it is stable in solution for over 36 hours. Catalyst synthesis (and the hydroacylation reactions) can be readily carried out on the benchtop in dry glassware under a nitrogen atmosphere; a glovebox is not required. Several attempts to crystallize the complex were unsuccessful.

Complex **14** can perform the clean intramolecular hydroacylation ring-closure reaction of 3-phenyl-4-pentenal **1** and styrene 2-carboxaldehyde **8** (Table 1 and Scheme 2). In particular, compound **1** can lead to 6 different possible products (**2–7** in Scheme 1) and three have been observed using cationic catalysts.[14] When compound **14** is utilized, however, the cyclopentanone is the only observable product – no rearrangement or alkene migration

Table 1 Hydroacylation of 3-substituted pentenal **1** at room temperature[a]

			Product (% yield)		
					
Substrate	Catalyst	Time	**2**	**4**	**6 & 7**
	[Rh(*S*-BINAP)]$^{+b}$	45 min	51	42	7
	[Rh(*S*,*S*-chiraphos)]$^{+b}$	45 min	21	79	0
	14[c]	8 h	98	0	0
1					

[a] See Supporting Information for full experimental details. All reactions were performed in CD_2Cl_2 at room temperature. Yields using catalyst **14** were measured by NMR integration or gas chromatography. [b] Reference 14. Catalyst loading is 1 mol%. [c] Catalyst loading is 10 mol%, prepared *in situ*.



[Rh(*S*-dppe)]$^+$ (2 mol%)	2.5 hr, **29% yield (+ 64% polymeric side product)**
14 (10 mol% *in situ*)	11 hr, **40% yield (+ 0% polymeric side product)**

Scheme 2 Hydroacylation of styrene 2-carboxaldehyde (**8**).[8]

occurs. Similarly compound **8** is known to produce significant amounts of polymeric side product when exposed to cationic rhodium catalysts (Scheme 2).[8] With **14**, the desired hydroacylation product is cleanly produced and no polymer side products are formed.

Importantly, none of the catalyst components ($[RhCl(cod)]_2$, $Ti(OiPr)_4$, or ligand) can individually (or in pairwise combination) catalyze the hydroacylation of **1**, suggesting that the active species is indeed a unique three-component complex. Compound **12** (*i.e.* without Rh) is ineffective at hydroacylation, as is the combination of $[RhCl(cod)]_2$ + $Ti(OiPr)_4$ (without added ligand). Most significantly, the mixture of $[RhCl(cod)]_2$ and 3 equivalents of ligand **10** (*i.e.* without Ti) does not produce a viable catalyst. A "carbon analogue" of the catalyst, (triphos)RhCl (triphos = *tris*-(*tris*-(diphenylphosphinomethyl)ethane), in which the titanium center is substituted by a quaternary carbon atom, also does not catalyze the hydroacylation of **1** either at room temperature or at 45 °C.[15] These control experiments indicate that the Ti(IV) center must not only organize the ligands but must also play a unique role in catalysis.

In Table 2, the catalytic turnover of the bimetallic system is compared to other monometallic *neutral* Rh(I) systems formed *in situ*. For **14**, the TOF is an order of magnitude larger than other monometallic species. Although the exact reason for this higher activity remains unclear, it is feasible that the coordination of the aldehyde to the Lewis acidic titanium center (of one catalyst complex) may activate the aldehydic C–H bond for Rh insertion (by a second catalyst complex). This activation may then lead to a faster rate of catalysis by shifting the insertion equilibrium toward the hydrido-acyl-Rh(III) species **A** (Scheme 1). However, addition of $Ti(OiPr)_4$ to the reaction between $RhCl(PPh_3)_3$ and **1** did not change reaction rate or yield, indicating that this Lewis acid-catalyzed pathway should not be relevant.

An alternative explanation is "bimetallic cooperativity," in which the cationic Ti center directly activates the Rh center by charge-charge repulsion (Scheme 3). As the Rh center becomes more electron deficient (Rh(III)), reductive elimination to Rh(I) (and therefore catalytic turnover) should be favored. Computational analysis of the complex suggests that the Rh and Ti centers lie too far apart for direct orbital overlap (greater than 3.1 Å),[16] consistent with this cooperativity model as a through-space charge–charge effect. Also proximity of the dissociated phosphine may play an important role in the reductive elimination step.

In conclusion, the 1:1:3 Rh:Ti:ligand complex **14** is an easily constructed neutral Rh(I) catalyst which exhibits hydroacylation reactivity. The catalyst components are readily available and the catalyst preparation can be easily monitored by ^{31}P NMR. The titanium center is uniquely important to the overall catalytic

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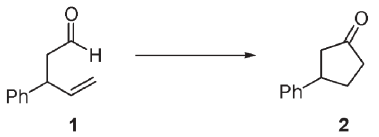
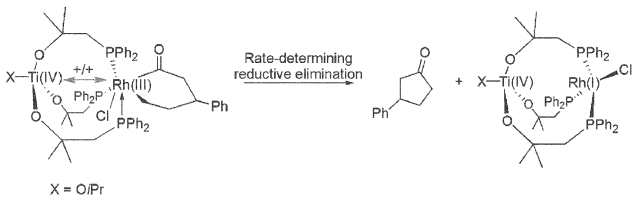
Table 2 Turnover frequencies for the intramolecular hydroacylation of **1** using various neutral hydroacylation catalysts prepared *in situ*[a]



1 **2**

Catalyst	Solvent	Time to completion	TOF (h^{-1})
(*i*PrO)Ti(μ:η^1,η^1-$OCMe_2CH_2PPh_2$)$_3$RhCl, **14**	C_6D_6	8 h	1.2
$RhCl(PPh_3)_3$	C_6D_6	Slow (23% in 16 h)	0.14
$[Rh(cod)Cl]_2$ + *R*-(+)-BINAP	C_6D_6	Slow	—
$[Rh(cod)Cl]_2$ + *R*-(+)-BINAP	CD_2Cl_2	72 h	0.14
$[Rh(cod)Cl]_2$ + *S,S*-(+)-DIOP	CD_2Cl_2	>72 h	<0.12
$[Rh(cod)Cl]_2$ + *R,R*-(+)-BDPP	CD_2Cl_2	80 h	0.13

[a] Conditions: $[Rh(cod)Cl]_2$ (3 μmol), ligand (3.5 μmol) in solvent (1 mL) at room temperature.[7f] Catalyst loading is 10 mol% for all cases. BINAP = 2,2′-*bis*(diphenylphosphino)-1,1′-binaphthyl; DIOP = (4*S*,5*S*)-*O*-isopropylidene-2,3-dihydroxy-1,4-*bis*(diphenylphosphino)butane; BDPP = (2*R*,4*R*)-2,4-*bis*(diphenylphosphino)pentane; Triphos = *tris*(diphenylphosphinomethyl)ethane.



Scheme 3 Acceleration of rate-limiting reductive elimination step by charge-charge repulsion and proximity of coordinating phosphine.

turnover of this bimetallic system. The ready ability to change both ligands and metals in the catalyst synthesis can rapidly provide a variety of structurally complex and catalytically active early-late transition metal complexes of interest.

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12 Variation of ligand stoichiometry indicates that 3:1:1 ligand:Rh:Ti is optimal: lower amounts of added ligand (2 eq.) lead to the formation of multiple metal species (detected by $^{31}P\{^1H\}$ NMR), while higher stoichiometry (4.5 eq.) leads to rapid precipitation of catalytically inactive, Rh-containing solids.

13 When the oily solid is redissolved in CD_2Cl_2, the doublet at 18.19 ppm in the $^{31}P\{^1H\}$ NMR spectrum is replaced by a singlet at 30.72 ppm (Supporting Information). The resulting yellowish solution does not show hydroacylation reactivity with **1**.

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