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Synthesis of Acetals from Alkenes by One-Pot Hydroformylation-Transacetalization Reactions Catalysed by Rhodium Complexes and Pyridinium *p*-Toluenesulphonate

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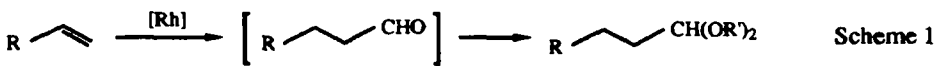
Abstract: Efficient conversion of alkenes to acetals has been achieved by consecutive hydroformylation-acetalization reactions catalyzed by rhodium complexes and pyridinium p-toluenesulphonate or by a zwitterionic rhodium catalyst.

Recently, it has been shown that Pt-Sn hydroformylation catalysts allow acetals to be obtained from alkenes in "one-pot" reactions, resulting in the direct protection of the reactive aldehyde functions from unwanted side reactions, such as elimination or racemization;[1] this latter effect, however, seems not to be general.[2] Apart from the intrinsic Lewis acidity of the transition metal complex, $SnCl_2$ has been demostrated to be a useful catalyst in acetalization[3] and acetal hydrolysis[4] and its presence as co-catalyst for the hydroformylation reaction undoubtedly has a strong influence on the efficiency of the acetalization process. Related Rh(I)-$SnCl_2$[5] complexes are known, but no catalytic activity reported.[6]

On the other hand, some rhodium complexes have been used as catalysts in acetalization and transacetalization of carbonyl compounds under mild conditions; principally acidic Rh(III), complexes such as $[RhClH_2(PPh_3)_2]$[7] or [Rh(triphos)Cl_3] derivatives,[8] were used with this purpose. Rhodium (I) complex $[Rh_2Cl_2(CO)_4]$,[9] a relatively strong Lewis acid,[10] has also been used with the same objective, although the presence of Rh(III) species during the reaction course cannot be excluded.[10,11] However, a transformation of alkenes into acetals, similar to the described for platinum catalysts, using a rhodium catalyst has not been described.

Here we report an efficient and selective "one-pot" conversion of alkenes into acetals catalyzed by rhodium complexes and PPTS through consecutive hydroformylation and acetalization reactions.



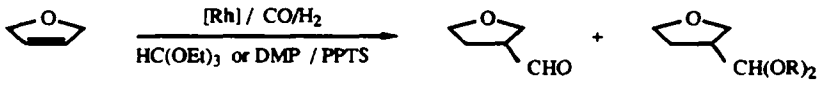
Scheme 1

Rhodium (I) catalytic systems have been very active in the hydroformylation of dihydrofurans,[12] and we chose a similar rhodium catalytic system for the hydroformylation/acetalization of 2,5-dihydrofuran, which is known to provide a single hydroformylation product,[13] to prevent the formation of mixtures.

Preliminary experiments in hydroformylation of 2,5-dihydrofuran carried out with the catalytic system $[(Rh_2(\mu\text{-}OMe)_2(cod)_2]$ (1) /10 PPh_3 and $HC(OEt)_3$ or 2,2-dimethoxypropane (DMP) as solvent at 50 bar and 60°C gave only small amounts of acetals after 48 hours of reaction, although the conversion to aldehydes was complete. In order to favour the formation of acetals $SnCl_2$[1,2,3] was added to the reaction mixture; however, this caused the conversion percentages to aldehyde felt down (Table 1, Entry 3).

On the other hand, the use of *p*-toluenesulphonic acid (PTSA) as the acetalization catalyst inhibited the hydroformylation because of the precipitation of the phosphine co-catalyst as triphenylphosphonium *p*-toluenesulphonate salt. Since the phosphine type ligands are necessary for the rhodium catalyst activity under mild conditions, the use of strong acids as acetalization catalysts is precluded. The weak acid triphenylphosphonium *p*-toluenesulphonate should be compatible with the phosphorus ligand, but unfortunately the hydroformylation rate was very low in this case and consequently the rate of acetal formation was also low.

Table 1. Consecutive Hydroformylation-Acetalization of 2,5-Dihydrofuran with the Catalytic System $[Rh_2(\mu\text{-}OMe)_2(COD)_2]$+10 PPh_3.



Entry	Solvent	Acetalization catalyst	t(h)	Conversion(%)	Products(%) THF-3-CHO	Products(%) THF-3-CH(OR)$_2$
1	$HC(OEt)_3$	-	48	100	96	4[a]
2	DMP[b]	-	48	100	100	-
3	$HC(OEt)_3$	$SnCl_2$	24	27	98	2[a]
4	DMP	PTSA[c]	48	0	-	-
5	DMP	Ph_3PH^+ PTS^-	24	94	44	56[d,e]
6	DMP	PPTS[f]	24	100	18	82[d]
7	DMP	PPTS	24	100	3	97[d,g]
8	DMP	PCS[h]	24	100	5	95[d]
9	$HC(OEt)_3$	PPTS	4	100	8	92[a]
			12	100	0	100[a]

[a] R=Et. [b] 2,2-Dimethoxypropane. [c] *p*-toluenesulphonic acid. [d] R=Me. [e] 97% of conversion to 3-CH(OR)$_2$ derivative in 48h. [f] Pyridinium *p*-toluenesulphonate. [g] 12h at 60°C and 12h at 90°C. [h] Pyridinium camphorsulphonate.

A weaker acid like pyridinium *p*-toluenesulphonate[14] has no influence on the hydroformylation rate and working in 2,2-dimethoxypropane as the solvent allowed us to obtain the dimethylacetal in 82% yield within 24h (Table1, Entry 6). Since the hydroformylation reaction is almost complete after 12h, increasing the temperature then to 90°C the acetal was quantitatively obtained in 24 hours (Table1, Entry 7). Pyridinium camphorsulphonate gave similar results.

When the reaction was carried out in $HC(OEt)_3$ as the solvent the rate of acetalization increased, 92% of the corresponding diethylacetal being obtained in 4h (Figure 1). However, the high boiling point of this solvent makes the purification of the reaction mixture more difficult, especially when products have a low boiling point.

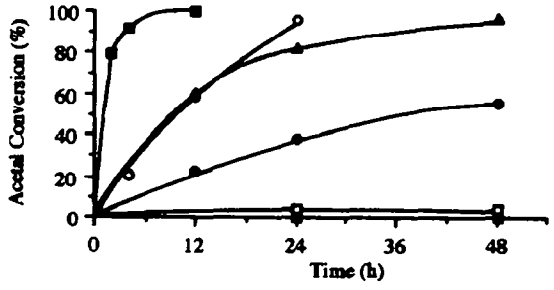
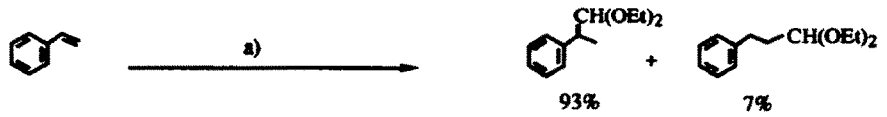


Figure 1: Evolution of the hydroformylation/acetalyzation of 2,5-dihydrofuran: (△) DMP; (▲) DMP, PPTS; (○) DMP, PPTS (12 h at 60°C and 12h at 90°C); (●) DMP, PPh_3H^+PTS; (□) $HC(OEt)_3$; (■) $HC(OEt)_3$, PPTS.

Typical procedure as follows: The substrate (5 mmol), previously stirred with alumina for 24 h, was added to a solution of the catalyst (0.05 mmol of [Rh(μ-OMe)(COD)]$_2$), the phosphorus co-catalyst (0.5 mmol of PPh_3) and 60 mg of PPTS in 15 ml of previously deoxygenated solvent ($HC(OEt)_3$ or DMP); the resulting solution was introduced into the evacuated autoclave, pressurized at 50 bar with a 1:1 mixture of CO/H_2 and heated at 60 °C. After the specified time at the indicated temperature, the autoclave was carefully depressurized and opened. The resulting solution was analyzed by gas chromatography, ^1H and ^{13}C NMR spectroscopy.

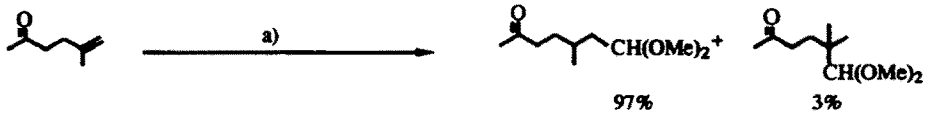
In the same way, styrene is converted into the diethyl acetals with a ratio n/iso similar to the one obtained when the hydroformylation is carried out in other more common solvents (Scheme 2).



Scheme 2

a) 1+10PPh_3/PPTS, $HC(OEt)_3$, 50 bar, 60°C, 24 h, 100%.

The different reactivity of the triethyl orthoformate and 2,2-dimethoxypropane could be successfully exploited to selectively hydroformylate the aldehyde function formed in the reaction in the presence of slightly hindered ketones ; thus, hydroformylation of 5-methyl-5-hexen-2-one gave almost exclusively the dimethylacetal of the aldehydes (Scheme 3).



Scheme 3

a) 1+10P(O-*o*-*t*-BuC_6H_4)$_3$/PPTS, DMP, 50 bar, 60°C, 24 h, 100%.

Vinyl acetate had been asymmetrically hydroformylated using (-)-DIOP as auxiliary ligand.[15] When the hydroformylation was carried out with 1+(-)-DIOP as catalytic system in DMP as the solvent the obtained ee was 25% (Scheme 4). The PPTS media and the conditions of the hydroformylation-acetalization process are compatible with the presence of sensitive substituents as the acetate group, and even result in a excellent regioselectivity in the hydroformylation of vinyl acetate (Scheme 5). On the other hand, these reaction conditions didn't significantly improve the ee in asymmetric hydroformylation reaction but it is clear they did not have a negative influence.

Scheme 4

a) 1+10(-)-DIOP, DMP, 20 bar, 70°C, 24 h, 100%.

Scheme 5

a) 1+10(-)-DIOP/PPTS, DMP, 20 bar, 70°C, 24 h, 100%.

Finally, it is noteworthy that the zwitterionic rhodium complex[$Rh_2(\mu\text{-}S(CH_2)_3NMe_2H)_2(cod)_2$] $[PF_6]_2$[16,17] is able to catalyze the hydroformylation of 2,5-dihydrofuran at a similar hydroformylation rate to the

neutral complex, although the acetalization reaction rate was slower than when PPTS was used, requiring 48 hours for the quantitative conversion to acetal when $HC(OEt)_3$ was used as the solvent.

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17. The zwitterionic complex, $[Rh_2(\mu\text{-}S(CH_2)_3NMe_2H)_2(cod)_2][PF_6]_2$, was synthetized from $[Rh_2(\mu\text{-}S(CH_2)_3NMe_2)_2(cod)_2]$[14] by adding 2 mol of HPF_6 per mol of the complex in ether solution. The zwitterionic rhodium complex precipitated and was isolated as slightly yellow needles that gave correct elemental analysis and spectroscopical data.

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