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Acetalization of α,β-Unsaturated Carbonyl Compounds Catalyzed by Complexes of Pt(II)

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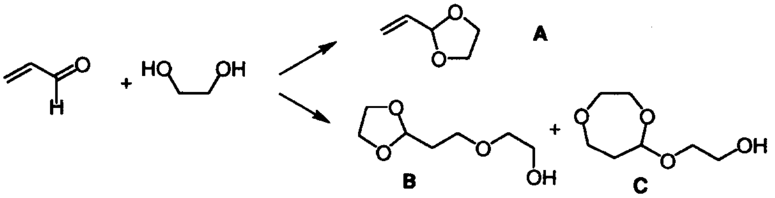
Abstract

A class of cationic diphosphine complexes of Pt(II) are sufficiently Lewis acidic to catalyze the acetalization of aldehydes and ketones. α,β-Unsaturated substrates can be easily acetalized with ethylene glycol under mild conditions in high yield and avoiding side reactions leading to formation of undesired by-products arising from the nucleophilic addition to the carbon-carbon double bond conjugated to the carbonyl group. A comparison of the behavior of a Pt complex with respect to PTSA as catalysts under identical conditions shows the superior selectivity of the former in many cases. © 1999 Published by Elsevier Science Ltd. All rights reserved.

The acetalization reaction is a process that is widely used in organic synthesis to protect the carbonyl group of aldehydes and ketones [1] and for the synthesis of enantiomerically pure compounds [2], that find practical application in the field of synthetic carbohydrate [3], steroid [4], pharmaceutical and fragrance [5], and polymer chemistry [6]. This reaction is normally acid catalyzed, although the use of transition metal complexes as Lewis acid catalysts has been occasionally reported in the literature [7]. We have recently reported [8] the first unambiguous example of the use of noble metals as possible catalysts for this reaction by testing a variety of diphosphine cationic complexes of palladium and platinum of the type [(P-P)Pt(μ-OH)]$(BF_4)_2$ (P-P = a variety of diphosphines). In this work we wish to report some unusual results observed when using these complexes as catalysts in the acetalization of α,β-unsaturated aldehydes and ketones.

Scheme 1



Acetals from the latter substrates are generally prepared by indirect methods such as transacetalization or diastereoselective cyclopropanation of cyclic ketones and have been successfully employed in the synthesis of natural products [9]. The problem complicating the reaction (Scheme 1) is the (extensive)

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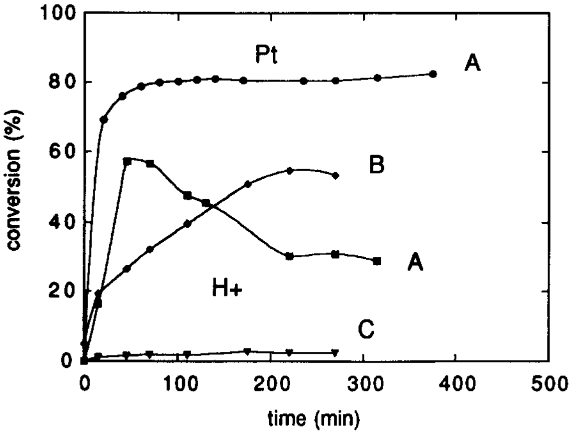


Fig. 1: Product formation vs. time in the reaction between acrolein and ethylene glycol catalyzed by either [(dppb)Pt(μ-OH)](BF$_4$)$_2$ or PTSA. Notations A, B and C refer to the products of Scheme 1. Conditions: catalyst 10 mmol, acrolein 5 mmol, ethylene glycol 5 mmol, DCE 2.5 ml, T 82°C.

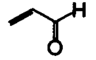
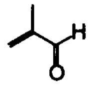
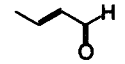
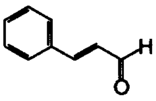
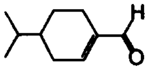
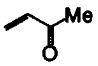
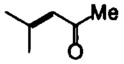
formation of undesired by-products arising from a nucleophilic addition to the carbon-carbon double bond conjugated to the carbonyl group. Partial success has been found using *p*-toluenesulfonic acid (PTSA), especially when associated with the use of drying agents to increase the yields [10], or the use of more expensive reagents such as alkoxytrimethysilanes and trimethylsilyltriflate as catalyst [11].

Initially, we have tested the complex [(dppb)Pt(μ-OH)](BF$_4$)$_2$ (dppb = 1,4-bis(diphenylphosphino)butane[2] as a catalyst in the acetalization of acrolein with ethylene glycol. As a control, the same reaction was performed using *p*-toluenesulfonic acid (PTSA) as the catalyst under the same experimental conditions.[3] As can be seen from Fig. 1, the reaction profile in the two cases is dramatically different. The Pt complex leads to clean formation of the unsaturated acetal (**A** with reference to eq. 1) as the exclusive product, whereas with PTSA products **B** and **C** also form, with **B** becoming the major product after about 40 min. Other complexes of the same type containing different diphosphines such as dppe or dppp gave very similar results.

The reaction conditions have been optimized by changing the temperature, the catalyst/acrolein/glycol ratios or using EtOH as both the reagent and the solvent of reaction. Lowering the temperature to 25°C results in a drastic decrease of the conversion (29% instead of 75% shown in Fig. 1 after 5 hr reaction time) and the latter can be increased to 57% only by using ethylene glycol as the solvent. The best catalyst/acrolein/glycol ratio in DCE as solvent and 82°C as the reaction temperature was found to be 1/500/500 and is the one used throughout this work. Finally, the use of EtOH as both the solvent and reagent results in a lowering of the yield (13%). In all cases the selectivity observed with the Pt complex as the catalyst was always > 98%.

These findings have been extended to the study of other α,β-unsaturated aldehydes and ketones and the results obtained are summarized in Table 1. As can be seen, the total conversions observed with both catalysts are very similar. In all cases tested the Pt complex displays complete selectivity towards the

Table 1: Comparison of the Reactivity of a Pt Catalyst (**2d**) and PTSA in the Acetalyzation of α,β-Unsaturated Substrates[a]

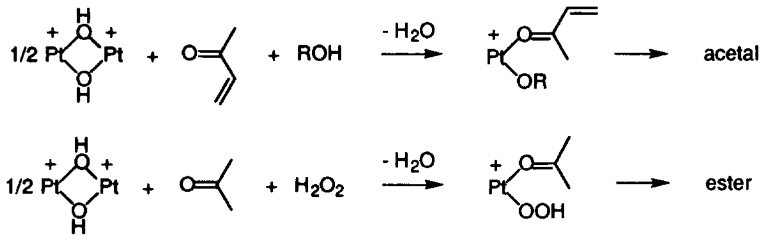
substrate	catalyst	yield[b] (5 hr)		
		A	B	C
	Pt	83	0	0
	PTSA	28	52	5
	Pt	68	0	0
	PTSA	64	0	0
	Pt	71	0	0
	PTSA	12	35	2.5
	Pt	62	0	0
	PTSA	66	0	0
	Pt	38	1.8	0
	PTSA	20	1.5	0
	Pt	10	1	0
	PTSA	10	21	34
	Pt	8	0	0
	PTSA	17	3	3

a. Reaction conditions as in footnote 4. The notation **A**, **B** and **C** refers to products of the type indicated in Scheme 1. b. based on GC analysis.

formation of the acetal, whereas the behavior of PTSA under the same conditions is irregular, sometimes the selectivity is the same as the Pt catalyst (see methacrolein, *trans*-cinnamaldehyde, or perillaldehyde albeit with a higher conversion) while in other cases the selectivity is bad with predominant formation of products of type **B**. Water formation appears to influence neither the selectivity nor the yields, at variance with what is known with PTSA as a catalyst [10]. Addition of $MgSO_4$ as a drying agent to the reaction mixture produces no effects. It has to be pointed out that the yields reported in Table 1 refer to a standard reaction time of 5 hr, however, the time necessary for the reaction to go to completion may be significantly shorter when using the Pt catalyst as shown in Fig. 1. For example, this is the case of methacrolein for which the yield indicated in Table 1 is obtained in 230 min. Alternatively, in the case of ketones, which are much less reactive as substrates, the yields can be increased by a longer reaction time (12% yield in 1700 min in the case of mesityl oxide) or by carrying out the reaction in neat ethylene glycol without solvent.

In conclusion, although the results here reported are largely preliminary, the excellent selectivity towards acetal formation observed in all α,β-unsaturated carbonyl compounds tested so far suggests the possible practical use of these Pt complexes as catalysts, at least in those cases in which other methods fail. The origin of this unusual selectivity could be related to the ability of Pt to mediate the reaction through the binding of both the alcohol and the carbonyl group (preferentially with respect to the olefin) in a way that has been already suggested by Ott *et al.* [7a] with Rh complexes (Scheme 2) and identified in the Baeyer-Villiger oxidation of ketones with hydrogen peroxide catalyzed by the same class of Pt complexes [13].

Scheme 2



Acknowledgements

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Footnotes

1. E-mail address: strukul@unive.it
2. The complex was prepared according to the method of Li and Sharp [12] by reacting (dppb)PtCl$_2$ in acetone/CH$_2$Cl$_2$ with a twofold amount of AgBF$_4$.After removing AgCl the solution is concentrated *in vacuo* and addition of excess Et$_2$O leads to precipitation of [(dppb)Pt(μ-OH)](BF$_4$)$_2$ as a white solid. The crude is redissolved in CH$_2$Cl$_2$, extracted twice with water, concentrated and precipitated with Et$_2$O.
3. In a preparative run the synthesis of 2-vinyl-1,3-dioxolane was performed using the procedure reported in footnote 4, starting from 100 mmol acrolein, 100 mmol ethylene glycol and 0.2 mmol catalyst. After the reaction was finished, DCE was carefully removed *in vacuo* and the residue was extracted twice with 20 ml portions of Et$_2$O. The Et$_2$O solution was concentrated and finally distilled *in vacuo* (130 torr) to yield 2-vinyl-1,3-dioxolane (62 mmol) [14].
4. Reactions were performed at 82°C in a round bottomed flask equipped with a reflux condenser and a side arm fitted with a silicone septum. The catalyst (10 μmol) was dissolved in DCE (2.5 ml) followed by addition of the substrate (5 mmol) and ethylene glycol (5 mmol). The mixture was heated under reflux and vigorously stirred. Periodic sampling allowed us to monitor the reaction by GC. Products were identified by comparison with authentic samples and by GC-MS analysis.