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Gold Catalysts Open a New General Chemoselective Route to Synthesize Oximes by Hydrogenation of α,*β*-Unsaturated Nitrocompounds with H_2

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Oximes are highly valuable organic molecules considering their numerous applications for polymers,[1] fungicides,[2] biochemicals,[3] fragrances,[4] or simply as latent protected forms of aldehydes and ketones. Particularly, the manufacture of cyclohexanone oxime represents a key step in the sequence of the Nylon 6 production, so that the development of easy and clean procedures for obtaining this oxime results in high interest. Traditionally, oximes are synthesized by condensation of an aldehyde or a ketone with hydroxylamine, but the use of this reagent is less desirable for large-scale processes owing to its intrinsic toxicity and unstability. Other functional group transformations, and particularly partial reduction and isomerization of the nitro groups, require harsh reaction conditions, and are characterized by poor selectivity. The hydrogenation of α,*β*-unsaturated nitrocompounds to produce oximes is not trivial (see Scheme 1) because of the presence of the easily reducible double bond, as well as the possibility of undesired secondary reactions in molecules with sensitive groups. Currently, the only possibility in achieving certain selectivity of the oxime, when reacting α,*β*-unsaturated nitrocompounds, was the use of stoichiometric amounts of organic hydrogen donors[5] (e.g., ammonium formate, decaborane, formic acid, etc). However, the use of these organic or inorganic reductants is not industrially sustainable from an environmental point of view, owing to the high *E* factor[6] value of such processes.

We have recently presented[7] that gold catalysts can selectively reduce nitro into amino groups when other easily reducible groups, such as double bond and carbonyls, are present. It would be also extremely valuable from the synthetic point of view if, using H_2 as reductant, gold could selectively hydrogenate α,*β*-unsaturated nitrocompounds into the corresponding oximes. In fact, the nitro to oxime transformation, combined with the Henry reaction, would open a powerful synthetic route for complex molecules starting from aldehydes or ketones under mild conditions. Indeed, the Henry condensation of an aldehyde or ketone with a nitroalkane, followed by dehydration of the resulting *β*-nitro alcohol, is the most versatile method for preparation of nitroalkenes, and from it a whole array of derivatives (α,*β*-unsaturated aldehydes or ketones, nitroalkanes, amines, and nitrogenated compounds, etc).[8]

In this work, we present a general chemoselective catalytic process for the transformation of α,*β*-unsaturated nitrocompounds into oximes, using H_2 as reducing agent, and gold (Au/TiO_2) as catalyst. Gold, unlike other noble metal-based catalysts, such as commercial Pd/C or Pt/C, shows a unique selectivity and quite general use for converting substituted nitro compounds into the corresponding oximes. The reaction is considerably greener than any of the known alternatives and involves an easy work up (see Supporting Information).

Table 1 shows the reaction conditions and catalytic results for the hydrogenation with H_2 of several substituted α,*β*-unsaturated nitrocompounds, using 1.5 wt % Au/TiO_2 and commercial 5 wt % Pd/C (Fluka, 75992) and 5 wt % Pt/C catalysts (Fluka, 80982). First, the selectivity toward the oxime formation in the presence of a conjugated double bond was examined by reacting the *trans*-*β*-nitrostyrene (see Table 1). While the activity of Pd, and Pt catalysts is higher than that of the Au catalyst, the yield to oxime is notably poorer with the former metals because of the occurrence of secondary reactions. Pd/C catalyst produces 28% of the corresponding saturated nitro compound, showing that simultaneous reduction of the nitro and the double bond occurs. Other secondary reactions, such as the formation of *N*,*N*-bis(2-phenylethyl)amine (19%) or the complete hydrogenation of the substrate to the saturated amine compound (5%) were also observed. Pt/C provides a slightly better selectivity to the oxime than Pd/C, although 5% of the saturated nitro compound and an important amount of *N*,*N*-bis(2-phenylethyl)amine (18%) are observed. Contrarily, the Au/TiO_2 system is very selective to the oxime, avoiding both the hydrogenation of the double bond and the formation of other products and giving selectivity above 97% to the oxime at levels of conversion close to 99%. The byproducts observed were the nitro saturated and the amino saturated compounds, always in amounts below 3%.

Table 1. Catalytic Results of the Hydrogenation of Several α,*β*-Unsaturated Nitrocompounds

substrate	catalysts	% metal (mol)	*T* (°C)	*P* (bar)	time (h)	conversion (%)	selectivity[a] (%)
trans-*β*-nitrostyrene	Au/TiO_2	0.64	90	10	2.00	98.8	97.1
	Pd/C	0.32	90	10	0.03	99.2	38.1
	Pt/C	0.34	90	10	0.03	99.0	66.3
trans-4-methoxy-*β*−nitrostyrene	Au/TiO_2	0.78	90	15	3.00	99.1	91.1
	Pd/C	0.24	90	15	1.75	73.4	42.5
	Pt/C	0.30	90	15	0.25	81.9	85.3
trans-4-bromo-*β*−nitrostyrene	Au/TiO_2	0.78	100	15	3.00	94.5	91.5
	Pd/C	0.81	100	15	0.50	98.7	85.7
	Pt/C	0.44	100	15	0.25	99.1	88.6
β,2-dinitrostyrene	Au/TiO_2	0.93	110	15	3.0	95.4	95.7
	Pd/C	0.67	110	15	0.25	98.5	0.0
	Pt/C	0.52	110	15	0.25	97.9	0.5
1-Nitro-1-Cyclohexene	Au/TiO_2	0.27	110	15	0.5	99.6	90.9
	Pd/C	0.42	110	15	0.03	69.8	70.6
	Pt/C	0.23	110	15	0.03	67.1	52.6

[a] Cis/trans mixture of products, excepts for 1-nitro-1-cyclohexene.

When electron donating or withdrawing groups are present in the aromatic ring of nitrostyrene, the chemoselectivity of gold catalyst is still high. For instance (see Table 1), reaction with substituted methoxy- and bromo-*β*-nitrostyrenes also gives higher selectivity with the gold catalyst. We have not observed any secondary reaction affecting the methoxy or the halogen group (dehalogenation), under the selected reaction conditions, but the presence of methoxy and Br groups obviously influences the rate and selectivity for the production of the oxime on the different metal catalysts. Thus, while the presence of a methoxy group improves the selectivity with Pt/C, it is not still a sufficiently strong electron donor to completely suppress the double bond hydrogenation by

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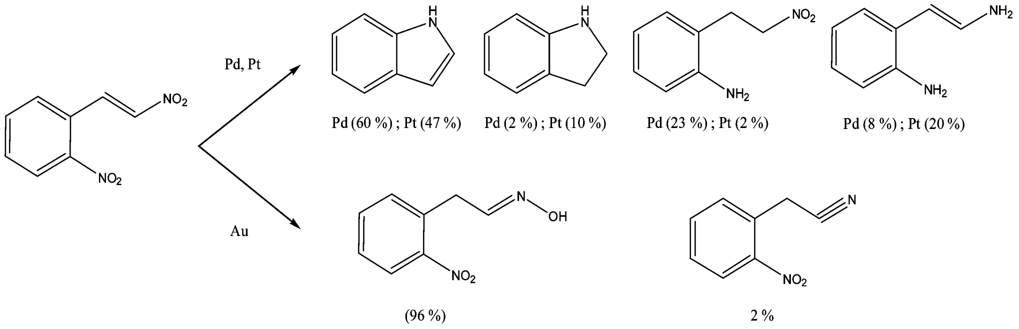
Scheme 1. Distribution of Products for the Hydrogenation of β,2-Dinitrostyrene on Pd/C, Pt/C, and Au/TiO$_2$ Catalysts



the Pd/C catalyst (48% of saturated nitrocompound is still obtained with this catalyst). The presence of a bromo group improves the selectivity with Pt and Pd, but with none of them was it possible to achieve the high selectivity observed with gold on TiO$_2$.

When a second nitro group is present in the reactant molecule (β,2-dinitrostyrene), results in Table 1 show large differences between the catalytic behavior of Pd and Pt with respect to Au/TiO$_2$. Neither the Pd nor the Pt catalysts are able to produce the aromatic oxime owing to the occurrence of other competing reactions such as hydrogenation of the double bond, reduction of one or both nitro groups to anilines, and reductive cyclizations. Indole has been found as the main byproduct (60% and 47% with Pd and Pt, respectively). On the contrary, the Au/TiO$_2$ catalyst is remarkably selective toward the oxime formation, and the reduction of the aromatic nitro group to the corresponding aniline is totally avoided (Scheme 1).

Finally, the procedure is shown to be applicable also to nonaromatic unsaturated nitro compounds, such as 1-nitro-1-cyclohexene. The reaction with the Au/TiO$_2$ catalyst allows one to obtain the industrially relevant cyclohexanone oxime in excellent yields.

In conclusion, the use of gold on TiO$_2$ as catalyst has allowed the establishment of a general and green catalytic method for obtaining oximes from α,β-unsaturated nitrocompounds with H$_2$. This opens new avenues when coupling the Henry reaction between nitroalkanes and carbonyls with the catalytic reaction described here.

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Note Added after ASAP Publication: In the version published on the Internet April 12, 2007, there were errors in the TOC graphic and in the text. The version published April 26, 2007, and the print version are correct.

Supporting Information Available: Experimental section on the synthesis of the catalyst and details on the catalytic test procedure. This material is available free of charge via the Internet at http://pubs.acs.org.

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