Communication

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Multicatalytic Processes Using Diverse Transition Metals for the Synthesis of Alkenes

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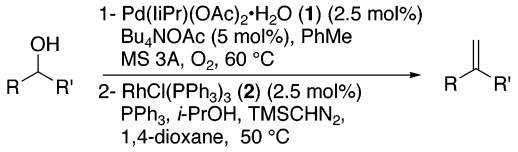
A number of useful transition metal-catalyzed processes have been developed over the years.[1] Although those denote a significant improvement by minimizing the amount of the required reagents, a traditional step-by-step approach in which each intermediate needs to be purified is generally required. The development of a multicatalytic process, which mimics the biosynthesis in living cells, would greatly enhance the efficiency of organic synthesis. Not only would such a process eliminate intermediate recovery steps, but it also would considerably decrease the amount of generated waste, a particularly important concern in industrial process chemistry.[2] Many examples of cascades using biocatalysts are described in the literature.[3] In addition, the combination of enzymes and metal catalysts has been reported to be a powerful strategy in dynamic kinetic resolution.[4] In contrast, one-pot procedures that utilize more than one metal complexes to catalyze independent reactions are scarce.[5,6] The development of this approach would greatly expand the possibilities in multicatalytic processes since the number of reported transition metal-catalyzed reactions is constantly growing.[1] In this communication, we present the first example of a cascade process that involves up to three different transition metal catalysts in the same vessel.

Our interest in de novo synthesis of alkenes prompted us to study the development of a new catalytic one-pot process for the conversion of alcohols into alkenes. The isolation and purification of the potentially unstable aldehyde intermediate is then avoided. Indeed, a number a stoichiometric one-pot oxidation−olefination procedures have been developed over the years.[7] Those procedures were typically restricted to benzylic, allylic, and primary alcohols and involved the use of an excess of the phosphorus ylide, which is usually derived from carboxymethylenephosphonium salts. We decided to focus our attention on the palladium-catalyzed aerobic oxidation of alcohols, recently reported by Sigman and co-workers,[8] in combination with the rhodium-catalyzed methylenation of carbonyl derivatives developed in our group.[9,10]

Treatment of the alcohol with 2.5 mol % palladium catalyst **1**[11] and 5 mol % tetrabutylammonium acetate under an atmosphere of oxygen led to the formation of the corresponding carbonyl derivative, either an aldehyde or a ketone. The reaction mixture was then submitted to the methylenation reaction conditions, in the presence of Wilkinson's catalyst (**2**), triphenylphosphine, 2-propanol, and trimethylsilyldiazomethane in 1,4-dioxane (Table 1). Not only was there no deleterious interaction between the two transition metal catalysts during the methylenation, but also the isolated yields for the corresponding terminal alkenes were superior to those obtained with the step-by-step procedure. This cascade process is compatible with both primary aliphatic and benzylic alcohols, which provide the corresponding terminal alkenes **4** and **6**, respectively, in good yields (entries 1 and 2).

Moreover, this one-pot procedure could be used for the synthesis of 2,2-disubstituted alkenes from secondary alcohols (entries 3−6).

Table 1. One-Pot Palladium-Catalyzed Oxidation and Rhodium-Catalyzed Methylenation Reaction



entry	substrate	olefination product	yield[a,b]
1	TBSO(CH2)4OH (**3**)	TBSO(CH2)4CH=CH2 (**4**)	78% (65%)
2	MeO-C6H4-CH2OH (**5**)	MeO-C6H4-CH=CH2 (**6**)	82% (61%)[c]
3	1,3-benzodioxole-CH(OH)CH3 (**7**)	1,3-benzodioxole-C(=CH2)CH3 (**8**)	92% (84%)
4	BnO(CH2)4CH(OH)CH3 (**9**)	BnO(CH2)4C(=CH2)CH3 (**10**)	84%
5	OBn-cyclohexyl-OH (**11**)	OBn-cyclohexyl=CH2 (**12**)	65% (50%)
6	BnO(CH2)3CH(OH)CH3 (**13**)	BnO(CH2)3C(=CH2)CH3 (**14**)	87% (62%)
7	BnO(CH2)3CH(OH)CH2OH (**15**)	BnO(CH2)3C(=CH2)CH3 (**14**)	54%

[a] Isolated yield. [b] In parantheses, literature yield[9a] for step-by-step procedure. [c] Ref 7c.

This is the first example of a successful one-pot process that involves ketone intermediates. A four-reaction sequence was also achieved with diol **15**, which was converted to the corresponding diene **14** with 54% yield, indicating that each individual step afforded more than 80% yield (entry 7).

Metathesis reactions of terminal alkenes have been established as a powerful synthetic method to produce stereodefined substituted alkenes.[12] The development of a cascade process in which a carbonyl derivative is converted to a diene, which then undergoes a metathesis reaction, will further improve the efficiency of this method.[13] The mildness of our rhodium-catalyzed methylenation of carbonyl derivatives prompted us to study a one-pot methylenation−methasis procedure to produce functionalized alkenes. A number of issues needed to be addressed, in particular the compatibility of both catalysts, and the compatibility of the

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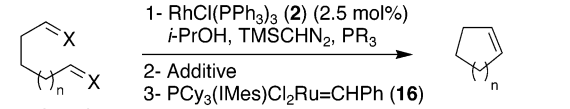
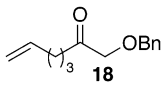
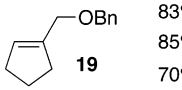
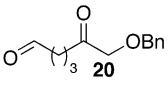
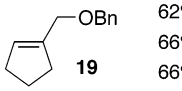
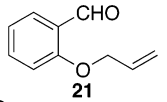
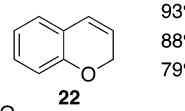
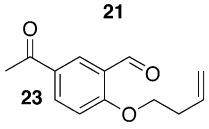
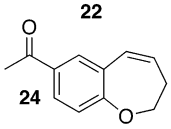
Table 2. One-Pot Methylenation−Ring Closing Metathesis Reaction

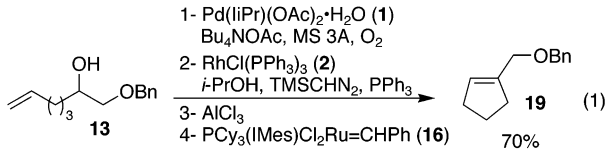


entry	substrate	conditions[a]	RCM product	yield[b]
1		A		83%
2		B		85%
3		C		70%
4		A		62%
5		B		66%
6		C		66%
7		A		93%
8		B		88%
9		Lit[c]		79%[c]
10		A		79%
11		B		80%
12		Lit[d]		74%[d]

[a] Conditions A: PPh_3; additive = $AlCl_3$. B: DPPBE (**17**); additive = oxone. C: Step-by-step approach. [b]Isolated yield. [c]Ref 17. [d]Ref 18.

ruthenium metathesis catalyst and the phosphine residues. After optimization (see Supporting Information for details), we devised two sets of reaction conditions that allowed the conversion of carbonyl compounds into cyclic alkenes (Table 2). To avoid the inhibition of the metathesis reaction by phosphine residues,[14] either oxone (an oxidant) or aluminum trichloride (a Lewis acid) was used as an additive with, respectively, DPPBE[15] or triphenylphosphine. Here again, no deleterious interaction between both catalysts was observed during the metathesis reaction when we used the second-generation ruthenium metathesis complex.[16] In the case of a monomethylenation reaction of either a ketone or aldehyde, followed by the metathesis reaction, higher yields were observed for the one-pot procedure, compared to the step-by-step approach (entries 1 and 2 vs 3; 7 and 8 vs 9; 10 and 11 vs 12). When a double-methylenation reaction was carried out, followed by the ring-closing metathesis reaction, similar yields were observed for the one-pot cascade vs the stepwise procedure (entries 4−6). Those one-pot reaction conditions are compatible with the formation of five-, six-,[17] and seven-membered[18] cyclic alkenes.

We then combined the two one-pot procedures to devise a three-reaction cascade that requires three different catalysts. The alcohol **13** was submitted to the palladium-catalyzed oxidation reaction conditions, followed by the rhodium-catalyzed methylenation and the ruthenium-catalyzed ring-closing metathesis reaction to provide the cyclic alkene **19** with 70% yield, which indicated roughly 90% yield for each individual steps (eq 1). It is remarkable that at the end of the reaction, three different transition metal catalysts were in the reaction mixture and did not interfere with the metathesis reaction.



In conclusion, we have devised a series of one-pot procedures that combined various transition metal catalysts to achieve a highly efficient synthesis of alkenes from alcohols.

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Supporting Information Available: Characterization data for new compounds and experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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