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Lewis Acid-Assisted Dirhodium(II) Catalyzed Ketone Hydroacylation

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Lewis Acid-Assisted Dirhodium(II) Catalyzed Ketone Hydroacylation

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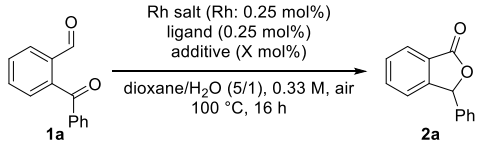
The combination of a Rh(II) salt and a Lewis acid, $Sc(OTf)_3$, as a highly active and robust cooperative catalyst system for ketone hydroacylation was developed. The catalyst system showed high turnover numbers (up to ca. 400) even under air, whereas the corresponding $Rh(I)/Sc(OTf)_3$ system did not work well. Application of the Rh(II)/Sc system was also extended to hydroacylation of olefins and an enantioselective reaction.

Lewis acids are an important class of catalysts that can coordinate to Lewis basic functionality such as carbonyl and imine groups to activate electrophiles. They can catalyze many fundamental reactions, such as aldol reactions, Mannich reactions, Michael additions, and Diels–Alder reactions.[1] Compared with single Lewis acid catalyst systems, the use of a combination of Lewis acid and another catalyst such as a transition-metal catalyst[2] or organocatalyst[3] as a cooperative catalyst can be a more powerful tool to develop new reactions and/or to enhance catalytic turnover. Our group also recently found a synergistic effect between metal nanoparticle catalysts and Lewis acid catalysts for hydrogen autotransfer processes[4] and asymmetric 1,4-addition reactions.[5]

Hydroacylation, which involves aldehyde C–H bond activation and subsequent insertion into a multiple bond, is an atom economical and attractive transformation to produce carbonyl compounds. Since the first report of intramolecular hydroacylation by Sakai and co-workers in 1972,[6] significant progress in this field has been achieved to extend applicable substrates.[7] In particular, intramolecular ketone hydroacylation of 2-formylarylketones is an effective synthetic method to access phthalide derivatives that are frequently found in natural products exhibiting biological activities and that can act as versatile building blocks in organic synthesis.[8] In 2009, Dong and co-workers developed chiral Rh(I) complex catalyzed asymmetric ketone hydroacylation that can produce a broad range of chiral phthalides with excellent enantioselectivity.[9] However, their systems required a relatively high loading of an expensive Rh catalyst (5–10 mol%) and a relatively long reaction time and thus more active catalyst systems are desired. Herein, we report a novel cooperative catalyst system consisting of Rh and a Lewis acid as a highly active catalyst system for intramolecular hydroacylation reactions.

At the outset, ketone hydroacylation was examined in the reaction with 2-benzoylbenzaldehyde (**2a**) by using a very small amount (0.25 mol%) of a Rh catalyst and a diphosphine ligand (Table 1). We hypothesized that use of a Lewis acid that can coordinate to a substrate may accelerate the reaction. It was initially discovered that, in addition to a Rh(II) catalyst, the use of water-compatible Lewis acid, $Sc(OTf)_3$, as a co-catalyst dramatically accelerated the reaction to give the corresponding lactone **2a** in excellent yield (entry 1), although the reaction barely proceeded in the absence of $Sc(OTf)_3$ (entry 2). The reaction could work even in the presence of water under air, demonstrating robustness of this catalyst system. A Rh(I) catalyst, which is a conventional catalyst for ketone hydroacylation,[9] did not work for this reaction under the same conditions, and the starting material was fully recovered (entry 3) Even a cationic Rh(I) complex prepared from Rh chloride salt and AgOTf in situ, which was the one of the most reactive complex for this reaction,[9] did not afford any products under our conditions (entry 4). For the Rh(I) catalyst system, a high catalyst loading of $Sc(OTf)_3$ was required to give the product (entry 5). No catalytic activity of $Sc(OTf)_3$ itself was confirmed (entry 6). It is noted that the combination of Rh(II) and $Sc(OTf)_3$ is essential to achieve a high catalyst turnover number.

Table 1. Optimization of reaction conditions of ketone hydroacylation



Entry	Rh salt	Ligand	Additive (mol%)	Yield (%)[a]
1	$Rh_2(OAc)_4$	dppp	$Sc(OTf)_3$ (1)	>95
2	$Rh_2(OAc)_4$	dppp	-	4
3	$[Rh(C_2H_4)_2Cl]_2$	dppp	$Sc(OTf)_3$ (1)	0
4	$[Rh(C_2H_4)_2Cl]_2$	dppp	Ag(OTf) (0.25)	0
5	$[Rh(C_2H_4)_2Cl]_2$	dppp	$Sc(OTf)_3$ (10)	89
6	–	dppp	$Sc(OTf)_3$ (10)	0
7	$Rh_2(OAc)_4$	dppp	$Yb(OTf)_3$ (1)	>95
8	$Rh_2(OAc)_4$	dppp	Ag(OTf) (1)	26
9	$Rh_2(OAc)_4$	dppp	HOTf (1)	>95
10	$Rh_2(OAc)_4$	dppe	1	71
11	$Rh_2(OAc)_4$	dppb	1	32
12	$Rh_2(OAc)_4$	dppf	1	3

[a] Determined by ^{1}H NMR analysis.

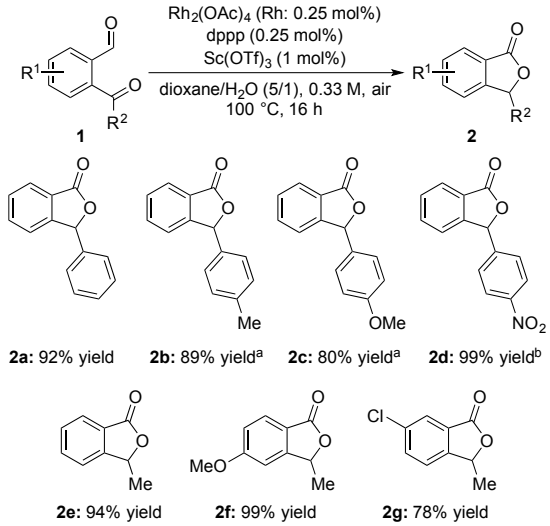
Other types of acid additives were also tested. Similar with $Sc(OTf)_3$, another water-compatible Lewis acid, $Yb(OTf)_3$ could efficiently promote the reaction (entry 7) while AgOTf gave low yield (entry 8) indicating that these additives might not be a just triflate anion supplier. Surprisingly, it was found that strong Brønsted acid additive, HOTf, could accelerate the reaction well too (entry 9). To clarify whether a Lewis acid-assisted pathway really exists or not, the initial reaction rate was compared. Indeed, $Sc(OTf)_3$ showed the faster reaction rate than that in the case of HOTf[10] and judging from relatively large pK_h (K_h = hydrolysis constant) value of Sc^{3+},[11] we concluded that the Lewis acid-

assisted pathway was dominant and more effective than Brønsted acid-assisted pathway.[12] The effect of diphosphine ligand structures was then briefly surveyed (entries 10–12) and the results showed that 1,3-bis(diphenylphosphino)propane (dppp) is the best choice. In the case of 1,4-bis(diphenylphosphino)butane (dppb) and 1,1′-bis(diphenylphosphino)ferrocene (dppf), a relatively large amount of benzophenone side product (18% and 67%, respectively) was observed, which may form through decarbonylation. In contrast, 1,2-bis(diphenylphosphino)ethane (dppe) and dppp showed good selectivity with respect to the production of **2a**.

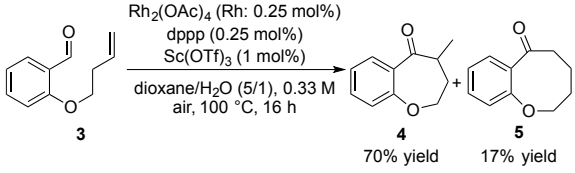
Substrate scope was surveyed under the optimized conditions (Table 2). Substrates with electron-donating groups substituted on the benzoyl part showed less reactivity than **1a**, and a slight increase in the catalyst loading (Rh and ligand) afforded the desired product in high yields (**2b** and **2c**). The presence of a nitro group on the benzoyl part further decreased the reactivity and a higher catalyst loading was required to achieve a full conversion. In this case, the product **2d** was obtained in almost quantitative yield. The co-catalyst system was also applicable for the reaction with 2-acetylbenzaldehyde to afford the product **2e** in excellent yield. Substitution on the benzene ring of 2-acetylbenzaldehyde was examined, and substrates bearing either a methoxy or chloro group were smoothly converted into the desired product **2f** or **2g** in high yield.

Hydroacylation of an olefin[13] was also demonstrated by using the Rh(II)/Sc system (Scheme 1). The desired seven-membered ring product **4** was obtained in good yield under the optimized conditions, whereas the eight-membered ring **5** formed as a side product.

Table 2. Substrate scope

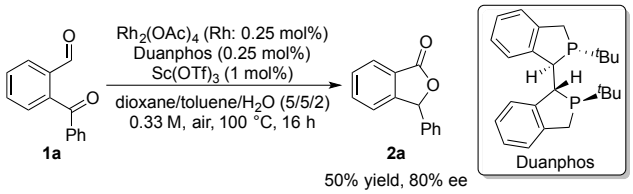


Isolated yields are shown. [a] $Rh_2(OAc)_4$ (Rh: 0.5 mol%) and dppp (0.5 mol%) were used. [b] $Rh_2(OAc)_4$ (Rh: 1.0 mol%) and dppp (1.0 mol%) were used.

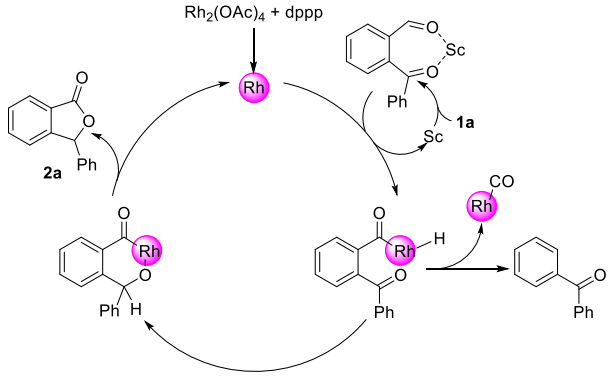


Scheme 1. Hydroacylation of olefin

Finally, we examined an enantioselective version of the reaction using a chiral diphosphine ligand. The combination of a Rh(II) salt and Duanphos, which was the best chiral ligand for the reported Rh(I) catalyzed asymmetric ketone hydroacylation,[9] could induce enantioselectivity; further solvent screening established conditions under which product **2a** was formed with good enantioselectivity (Scheme 2).[11] Interestingly, no product was generated with a Rh(I) salt and Duanphos under the conditions, even in the presence of $Sc(OTf)_3$ (10 mol%).[11] This result suggests that Rh(II)/Sc is a much more robust and highly active co-catalyst system than the conventional chiral Rh(I) complex.



Scheme 2. Asymmetric ketone hydroacylation



Scheme 3. Plausible reaction mechanism

Although there are several possible mechanisms for the formation of the lactone from 2-formylarylketones,[14] such as a Tishchenko-type pathway,[14c] we assumed that it was more likely that the reaction proceeded through i) C–H oxidation of an aldehyde by Rh, ii) Rh–H insertion to the carbonyl group, and iii) reductive elimination (Scheme 3),[15] based on the observation of the formation of a decarbonylated side product, the induction of enantioselectivity by a chiral phosphine ligand, and the finding that no catalytic activity was achieved by using the Lewis acid catalyst alone. The Lewis acid co-catalyst might coordinate to an aldehyde and/or a ketone group to facilitate the oxidative addition step and/or the Rh–H insertion step, respectively. The true role of $Sc(OTf)_3$ is unclear at present, but the latter function might be less likely because no significant change of enantioselectivity was observed by changing $Sc(OTf)_3$ to either other metal triflates or a chiral $Sc(OTf)_3$ complex.[10] A catalytically active Rh species might form after coordination of a phosphine ligand to the axial position of a Rh(II) dimer complex.[16] Several possible active species can be considered, for example, the axially ligated Rh(II) dimer itself[17] and a Rh(I) acetate complex formed in situ from disproportionation of the Rh(II) dimer.[18] To elucidate the latter possibility, a control study using $[Rh(C_2H_4)_2Cl]_2$ and Ag(OAc) to generate Rh(I) acetate

species by anion exchange was conducted in the presence of Duanphos and $Sc(OTf)_3$.[10] However, no reaction occurred, which indicates that an active Rh species in our Rh(II)/Sc system may not be a simple monomeric Rh(I) species.[19]

In conclusion, a new cooperative catalyst system consisting of a Rh(II) salt and a Lewis acid for ketone hydroacylation was developed, and high turnover number (up to ca. 400) compared with that of reported reactions was achieved. The corresponding Rh(I)/$Sc(OTf)_3$ system did not work well under such low catalyst loading and thus the use of a Rh(II) salt was essential. The Rh(II)/Sc system was also applicable for hydroacylation of olefins, and an enantioselective reaction was possible. The origin of the high activity of the Rh(II) catalyst and the role of $Sc(OTf)_3$ are under investigation in our laboratory.

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References and Notes

1 a) H. Yamamoto, *Lewis Acids in Organic Synthesis*, Wiley-VCH, Weinheim, **2000**. b) R. H. Qiu, Y. Chen, S. F. Yin, X. H. Xu, C. T. Au, *RSC Adv.* **2012**, *2*, 10774. c) A. Corma, H. Garcia, *Chem. Rev.* **2003**, *103*, 4307. d) S. Kobayashi, K. Manabe, *Acc. Chem. Res.* **2002**, *35*, 209.

2 a) S. M. Inamdar, V. S. Shinde, N. T. Patil, *Org. Biomol. Chem.* **2015**, *13*, 8116. b) Y. Nakao, *Bull. Chem. Soc. Jpn.* **2012**, *85*, 731. c) A. E. Allen, D. W. C. MacMillan, *Chem. Sci.* **2012**, *3*, 633. d) C. Y. Wang, Z. F. Xi, *Chem. Soc. Rev.* **2007**, *36*, 1395.

3 A. Gualandi, L. Mengozzi, C. M. Wilson, P. G. Cozzi, *Chem. Asian J.* **2014**, *9*, 984.

4 G. C. Y. Choo, H. Miyamura, S. Kobayashi, *Chem. Sci.* **2015**, *6*, 1719.

5 T. Yasukawa, Y. Saito, H. Miyamura, S. Kobayashi, *Angew. Chem., Int. Ed.* **2016**, *55*, 8058.

6 K. Sakai, J. Ide, O. Oda, N. Nakamura, *Tetrahedron Lett.* **1972**, *13*, 1287.

7 a) L. Yang, H. M. Huang, *Chem. Rev.* **2015**, *115*, 3468. b) M. C. Willis, *Chem. Rev.* **2010**, *110*, 725. c) M. A. Garralda, *Dalton Trans.* **2009**, 3635.

8 R. Karmakar, P. Pahari, D. Mal, *Chem. Rev.* **2014**, *114*, 6213.

9 D. H. T. Phan, B. Kim, V. M. Dong, *J. Am. Chem. Soc.* **2009**, *131*, 15608.

10 See the Supporting Information for details.

11 S. Kobayashi, S. Nagayama, T. Busujima, *J. Am. Chem. Soc.* **1998**, *120*, 8287.

12 We also compared those two systems in the reaction using chiral ligand and more clear reactivity difference was observed. See the Supporting Information for details.

13 M. M. Coulter, P. K. Dornan, V. M. Dong, *J. Am. Chem. Soc.* **2009**, *131*, 6932.

14 a) D. C. Gerbino, D. Augner, N. Slavov, H.-G. Schmalz, *Org. Lett.* **2012**, *14*, 2338. b) S. Omura, T. Fukuyama, Y. Murakami, H. Okamoto, I. Ryu, *Chem. Commun.* **2009**, 6741. c) S. Tsunetake, N. Tetsuo, O. Makoto, *Chem. Lett.* **2006**, *35*, 824. d) A. Chan, K. A. Scheidt, *J. Am. Chem. Soc.* **2006**, *128*, 4558.

15 Z. Shen, P. K. Dornan, H. A. Khan, T. K. Woo, V. M. Dong, *J. Am. Chem. Soc.* **2009**, *131*, 1077.

16 S. Shinoda, T. Kojima, Y. Saito, *J. Mol. Catal.* **1983**, *18*, 99.

17 a) A. F. Trindade, V. André, M. T. Duarte, L. F. Veiros, P. M. P. Gois, C. A. M. Afonso, *Tetrahedron* **2010**, *66*, 8494. b) A. F. Trindade, P. M. P. Gois, L. F. Veiros, V. André, M. T. Duarte, C. A. M. Afonso, S. Caddick, F. G. N. Cloke, *J. Org. Chem.* **2008**, *73*, 4076.

18 J. P. Collman, R. Boulatov, *J. Am. Chem. Soc.* **2000**, *122*, 11812.

19 Preliminary ^{31}P NMR analysis of the mixture of $Rh_2(OAc)_4$ and dppp failed to identify the structure of active species because of very low concentration of active species. Probably, there were several kinds of Rh-P species and intensity of each species was too low to detect. See the Supporting Information for details.