ORGANIC LETTERS

2002
Vol. 4, No. 14
2361−2363

Mild and Chemoselective Synthesis of Lactones from Diols Using a Novel Metal–Ligand Bifunctional Catalyst

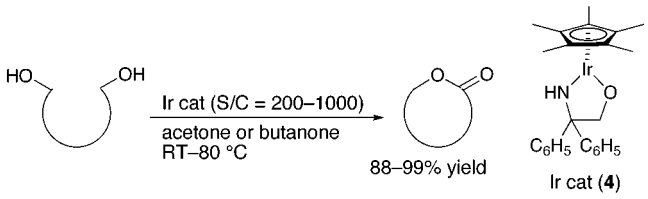
Takeyuki Suzuki, Kenji Morita, Mika Tsuchida, and Kunio Hiroi*

Department of Synthetic Organic Chemistry, Tohoku Pharmaceutical University, 4-4-1 Komatsushima, Aoba-ku, Sendai, Miyagi 981-8558, Japan

khiroi@tohoku-pharm.ac.jp

Received April 27, 2002

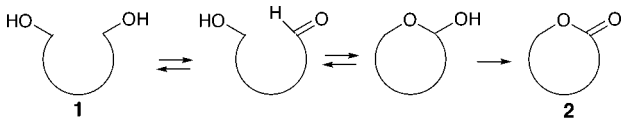
ABSTRACT



A novel amino alcohol-based Ir bifunctional complex acts as an efficient catalyst for oxidative lactonization of 1,4- or 1,5-diols with a substrate-to-catalyst molar ratio of 200–1000 in acetone or butanone. The reaction proceeds with broad functional group tolerance to give lactone in high yield at room temperature. The catalyst precursor Cp*IrCl[$OCH_2C(C_6H_5)_2NH_2$] is isolated and characterized by a single-crystal X-ray analysis.

The oxidative lactonization of diols is useful for the synthesis of a variety of natural products.[1,2] The reaction is considered to proceed via two steps: the initial chemoselective oxidation to hydroxy aldehyde, which is in equilibrium with the lactol, and then oxidation of the lactol to lactone (Scheme 1).

Scheme 1



A common approach for this reaction is to use a stoichiometric amount of silver carbonate on Celite.[1,3] This reagent, however, is not free of problems, as often a large excess (10−26 equiv) of expensive silver salts is required and the reagent is inhibited by sulfide groups.[3] To date, several catalytic reactions have been developed,[4] and the reactions required high temperatures (>180 °C)[4a,f] or co-oxidants such as tolane,[4b] PhBr,[4c] α,β-unsaturated ketone,[4d,e,j,k] allyl methyl carbonate,[4g] or *N*-methylmorpholine *N*-oxide[4h,i] to be performed under lower temperature. During the past decade, some catalytic reactions[5] using clean cooxidants such as

(1) (a) Procter, G. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming. I., Ley, S. V., Eds.; Pergamon: Oxford, 1991; Vol. 7, pp 312−318. (b) Kano, S.; Shibuya, S.; Ebata, T. *Heterocycles* **1980**, *14*, 661−711.

(2) For recent examples of the natural product synthesis, see: (a) Suzuki, T.; Ohmori, K.; Suzuki, K. *Org. Lett.* **2001**, *3*, 1741−1744. (b) Zhu, X.; Yu, B.; Hui, Y.; Higuchi, R.; Kusano, T.; Miyamoto, T. *Tetrahedron Lett.* **2000**, *41*, 717−719. (c) Amaike, M.; Mori, K. *Liebigs Ann.* **1995**, 1451−1454. (d) Ley, S. V.; Norman, J.; Pinel, C. *Tetrahedron Lett.* **1994**, *35*, 2095−2098.

(3) Fetizon, M.; Golfier, M.; Louis, J.-M. *Tetrahedron* **1975**, *31*, 171−176.

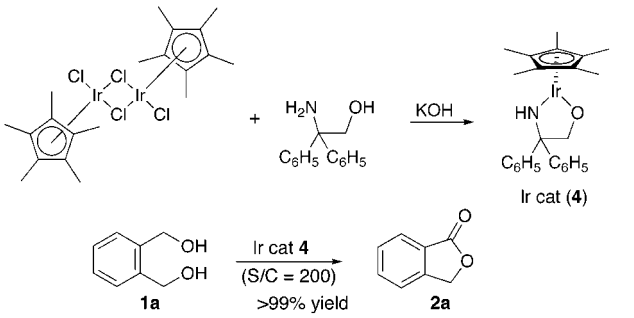
(4) (a) $2CuO{\cdot}Cr_2O_3$: Kyrides, J. P.; Zienty, F. B. *J. Am. Chem. Soc.* **1946**, *68*, 1385−1385. (b) $Ru_3(CO)_{12}$−tolane: Shvo, Y.; Blum, Y.; Reshef, D.; Menzin, M. *J. Organomet. Chem.* **1982**, *226*, C21−C25. (c) $Pd(OAc)_2$−PhBr: Tamaru, Y.; Yamada, Y.; Inoue, K.; Yamamoto, Y.; Yoshida, Z. *J. Org. Chem.* **1983**, *48*, 1286−1292. (d) $RhH(PPh_3)_4$−α,β-unsaturated ketone: Ishii, Y.; Suzuki, K.; Ikariya, T.; Saburi, M.; Yoshikawa, S. *J. Org. Chem.* **1986**, *51*, 1, 2822−2824. (e) $RuH_2(PPh_3)_4$−α,β-unsaturated ketone: Ishii, Y.; Osakada, K.; Ikariya, T.; Saburi, M.; Yoshikawa, S. *J. Org. Chem.* **1986**, *51*, 2034−2039. (f) $RuH_2(PPh_3)_4$−acetone: Murahashi, S.-I.; Naota, T.; Ito, K.; Maeda, Y.; Taki, H. *J. Org. Chem.* **1987**, *52*, 4319−4327. (g) $RuH_2(PPh_3)_4$−allyl methyl carbonate: Minami, I.; Tsuji, J. *Tetrahedron* **1987**, *43*, 3903−3915. (h) $n\text{-}Pr_4N^+RuO_4$−NMO: Block, R.; Brillet, C. *Synlett* **1991**, 829−830. (i) Ley, S. V.; Norman, J.; Griffith, W. P.; Marsden, S. P. *Synthesis* **1994**, 639−666. For enantioselective reactions: (j) Ishii, Y.; Osakada, K.; Ikariya, T.; Saburi, M.; Yoshikawa, S. *Chem. Lett.* **1982**, 1179−1182. (k) Nozaki, K.; Yoshida, M.; Takaya, H. *J. Organomet. Chem.* **1994**, *473*, 253−256.

10.1021/ol026091h CCC: $22.00 © 2002 American Chemical Society
Published on Web 06/12/2002

acetone,[5a,7b,c] hydrogen peroxide,[5b] or molecular oxygen[5c] were reported; however, there is much room for improvement of the catalytic activity and selectivity. We now disclose a new efficient method using a novel metal−ligand bifunctional catalyst[6,7] and acetone or 2-butanone as a cooxidant. This method is high-yielding, clean, operationally simple, and chemoselective. Therefore, it meets the standards for the contemporary of organic synthesis.

Treatment of a mixture of pentamethylcyclopentadienyliridium chloride dimer $[Cp^*IrCl_2]_2$[8] and 2,2-diphenylglycinol[9] in CH_2Cl_2 with aqueous KOH solution at room temperature for 30 min under argon afforded the dark red Ir catalyst in quantitative yield. Thus, when a 1 M solution of 1,2-bis(hydroxymethyl)benzene (**1a**) in dry acetone (13.6 mol equiv) containing the Ir catalyst (S/C = 200) was stirred at room temperature for 4 h, phthalide (**2a**) was obtained in quantitative yield.[10] The reaction of **1a** using reagent grade of acetone proceeds equally well, giving the lactone quantitatively (Scheme 2).

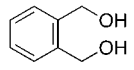
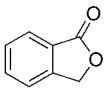
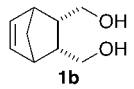
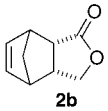
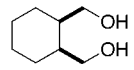
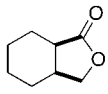
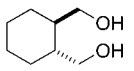
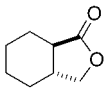
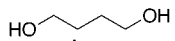
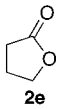
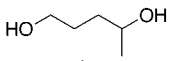
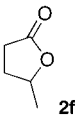
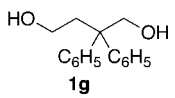
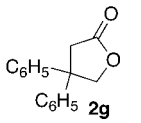
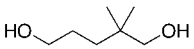
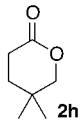
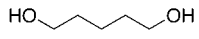
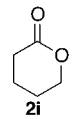
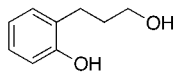
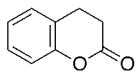
Scheme 2



A variety of 1,4- or 1,5-diols can be transformed to the corresponding lactones in high yield (Table 1). The reactions of **1b**−**d** gave corresponding lactones without epimerization. In the case of unsymmetrical diol **1g** and **1h**, the less hindered hydroxyl groups were oxidized selectively to give **2g** and **2h**. The reaction of 1,4-pentanediol (**1f**) gave γ-valerolactone (**2f**) in 88% yield. 2-(3-Hydroxypropyl)phenol (**1j**) also afforded **2j** in 95% yield.

Since transfer hydrogenation of ketones is reversible, a substrate concentration as low as 0.1 M is required for obtaining high yield in the transfer hydrogenation of acetophenone in 2-propanol (2-propanol/ketone substrate =

Table 1. Oxidative Lactonization of Diols Catalyzed by an Ir Catalyst **4**[a]

entry	diol	time, h	product	% yield[b]
1	 **1a**	4	 **2a**	>99
2	 **1b**	48	 **2b**	97
3	 **1c**	36	 **2c**	97
4	 **1d**	36	 **2d**	98
5	 **1e**	20	 **2e**	96
6[c]		48		89
7[d]	 **1f**	36	 **2f**	88
8[e]	 **1g**	20	 **2g**	98 (β,β:α,α = >99:1)[f]
9	 **1h**	26	 **2h**	>99 (γ,γ:α,α = 93:7)[f]
10	 **1i**	24	 **2i**	95
11[d]	 **1j**	5	 **2j**	95

[a] Unless otherwise stated, the reaction was carried out at room temperature using a 1.0 M solution of diol (1.0 mmol) in acetone. Diol/Ir = 200:1. [b] Isolated yield. [c] Reaction using 50 g of **1e** in 140 mL of 2-butanone (4.0 M) under reflux with S/C = 1000. [d] Reaction using a 2.0 M acetone solution. [e] The reaction was carried out using a 0.25 M solution of **1g** in CH_3CN containing 4 molar equiv of acetone. [f] Determined by ^1H NMR.

(5) (a) Metal polyhydrides−acetone: Lin, Y.; Zhu, X.; Zhou, Y. *J. Organomet. Chem.* **1992**, *429*, 269−274. (b) Heteropolyacid−H_2O_2: Ishii, Y.; Yoshida, T.; Yamawaki, K.; Ogawa, M. *J. Org. Chem.* **1988**, *53*, 5549−5552. (c) $Pd(OAc)_2$−O_2: Nishimura, T.; Onoue, T.; Ohe, K.; Uemura, S. *J. Org. Chem.* **1999**, *64*, 6750−6755.

(6) For asymmetric transfer hydrogenation using a metal−ligand bifunctional catalyst, see: RuCl(Tsdpen)(μ^6-arene): (a) Hashiguchi, S.; Fujii, A.; Takehara, J.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 7562−7563. (b) Takehara, J.; Hashiguchi, S.; Fujii, A.; Inoue, S.; Ikariya, T.; Noyori, R. *Chem. Commun.* **1996**, 233−234. (c) Fujii, A.; Hashiguchi, S.; Uematsu, N.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1996**, *118*, 2521−2522. (d) Uematsu, N.; Fujii, A.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1996**, *118*, 4916−4917. (e) Haack, K.-J.; Hashiguchi, S.; Fujii, A.; Ikariya, T.; Noyori, R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 285−288. (f) Hashiguchi, S.; Fujii, A.; Haack, K.-J.; Matsumura, K.; Ikariya, T.; Noyori, R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 288−290. (g) Matsumura, K.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 8738−8739. (h) Noyori, R.; Hashiguchi, S. *Acc. Chem. Res.* **1997**, *30*, 97−102. (i) Yamada, I.; Noyori, R. *Org. Lett.* **2000**, *2*, 3425−3427. (j) Yamakawa, M.; Yamada, I.; Noyori, R. *Angew. Chem., Int. Ed. Engl.* **2001**, *40*, 2818−2821. (k) Noyori, R.; Yamakawa, M.; Hashiguchi, S. *J. Org. Chem.* **2001**, *66*, 7931−7944. Cp*MCl(Tsdiamine) (M = Rh, Ir): (l) Mashima, K.; Abe, T.; Tani, K. *Chem. Lett.* **1998**, 1199−1200. (m) Mashima, K.; Abe, T.; Tani, K. *Chem. Lett.* **1998**, 1201−1202. (n) Murata, K.; Ikariya, T.; Noyori, R. *J. Org. Chem.* **1999**, *64*, 2186−2187. (o) Mao, J.; Baker, D. C. *Org. Lett.* **1999**, *1*, 841−843.

136:1).[6a] On the other hand, the reaction using a 0.27 M solution of **1a** in toluene proceeds quantitatively in the presence of a slight excess of acetone and the Ir catalyst **4** (acetone/diol substrate/**4** = 2.5:1:0.005), while 2 molar equiv of oxidant is required by the stoichiometry for the oxidative lactonization of diols. Therefore, a 50 g scale reaction can be performed easily with high concentration with S/C = 1000 to give **2e** in 89% yield after distillation (Table 1, entry 6).

To test the tolerance of functional groups, **1a** was oxidized in acetone containing an equimolar amount of coordinative compound. The reaction proceeded without problems in >92% yield in the presence of 1-tetradecene, methyl decanoate, di-*n*-hexyl ether, benzyl cyanide, thioanisole, or *N*-methylpyrrolidinone. Moreover the acid-sensitive additive such as styrene oxide or the trimethylsilyl ether of 4-bromobenzyl alcohol also remains intact during the reaction. However, the addition of pyrrolidinone or 1-dodecyne completely retarded the reaction.

Having succeeded in catalytic lactonization, we then turned our attention to the elucidation of the catalyst structure. A catalyst precursor Ir(III) complex **3** that was prepared from a 1:2 mixture of $[Cp^*IrCl_2]_2$ and 2,2-diphenylglycinol in CH_2Cl_2 with triethyamine was isolated as a yellow crystal after recrystallization from chloroform. The single-crystal X-ray analysis illustrated in Figure 1 indicates that the 18 electron Ir(III) complex has a distorted octahedral coordination environment with Cp*, amino, alkoxide, and chloro ligands. Noteworthy is the very short Cl···HN distance of 2.71 Å, which is ascribed from intramolecular hydrogen bonding. Although this preformed mononuclear Ir complex **3** does not possess catalytic activities by itself, treating the complex **3** with aqueous KOH in CH_2Cl_2 gave the active catalyst **4**, which catalyzed the lactonization of **1a** in acetone to give **2a** quantitatively at room temperature for 4 h.

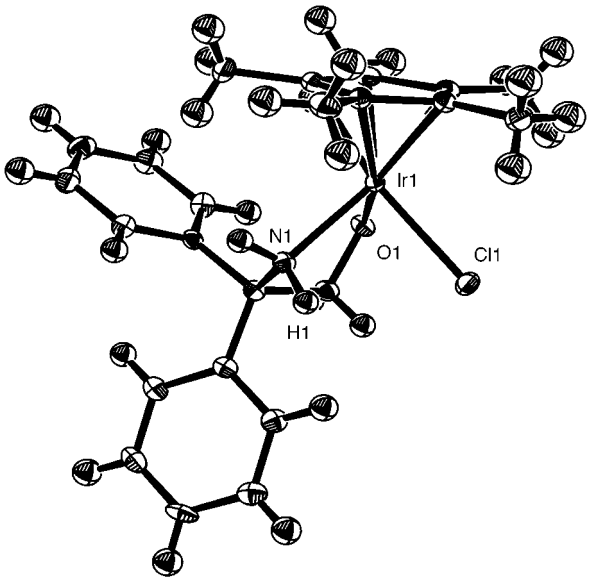


Figure 1. ORTEP plot (50% probability ellipsoids) of the molecular structure of $Cp^*IrCl[OCH_2C(C_6H_5)_2NH_2]$ (**3**).

In summary, we have accomplished the practical synthesis of lactones from diols catalyzed by a novel Ir catalyst. Further investigation for enantioselective reaction is ongoing.[11]

Acknowledgment. This work was financially supported by the Uehara Memorial Foundation. We thank Professor Ryoji Noyori of Nagoya University and Professor Takao Ikariya of Tokyo Institute of Technology for helpful discussions and Dr. Motoo Shiro of Rigaku Cooperation for the single-crystal X-ray analysis of **3**.

Supporting Information Available: The experimental procedure for the oxidative lactonization and the single-crystal X-ray information for **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL026091H

(7) Kinetic resolution of secondary alcohols using a metal−ligand bifunctional catalyst: (a) Hashiguchi, S.; Fujii, A.; Haack, K.-J.; Ikariya, T.; Matsumura, K.; Noyori, R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 288−290. Lactonization using Cp*Ru complex: (b) Ito, M.; Osaku, A.; Ikariya, T. Abstracts of Papers. *79th National Meeting of the Chemical Society of Japan*, Kobe, Mar 28−31, 2001; Chemical Society of Japan: Tokyo, 2001; Abstract 1H326. (c) Ito, M.; Osaku, A.; Ikariya, T. Abstracts of Papers. *48th Symposium on Organometallic Chemistry*, Yokohama, Sep 18−19, 2001; Kinki Chemical Society: Osaka, 2001; Abstract PB142.

(8) Kang, J. W.; Moseley, K.; Maitlis, P. M. *J. Am. Chem. Soc.* **1969**, *91*, 1, 5970−5977.

(9) Newman, M. S.; Edwards, W. M. *J. Am. Chem. Soc.* **1954**, *76*, 1840−1845.

(10) The use of other ligands such as 2-aminoethanol and *N*-tosylethylendiamine instead of 2,2-diphenylglycinol showed lower reactivity.

(11) For recent examples of oxidative desymmetrization, see: (a) Jensen, D. R.; Pugsley, J. S.; Sigman, M. S. *J. Am. Chem. Soc.* **2001**, *123*, 7475−7476. (b) Ferreira E. M.; Stoltz B. M. *J. Am. Chem. Soc.* **2001**, *123*, 7725−7726.