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Guerbet Reaction of Primary Alcohols Leading to *β*-Alkylated Dimer Alcohols Catalyzed by Iridium Complexes

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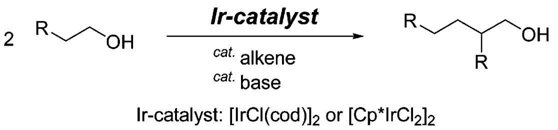
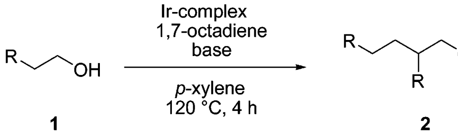


$[IrCl(cod)]_2$ and $[Cp^*IrCl_2]_2$ complexes catalyzed efficiently the Guerbet reaction of primary alcohols to *β*-alkylated dimer alcohols in good yields. For instance, the reaction of 1-butanol in the presence of $[Cp^*IrCl_2]_2$ (1 mol %), *t*-BuOK (40 mol %), and 1,7-octadiene (10 mol %) produced 2-ethyl-1-hexanol in 93% yield. Various primary alcohols undergo the Guerbet reaction under the influence of Ir complexes to give the corresponding dimer alcohols in good yields. This method provides an alternative direct route to *β*-alkylated primary alcohols which are prepared by aldol condensation of aldehydes followed by hydrogenation.

The Guerbet reaction is recognized as a useful synthetic tool to obtain *β*-alkylated dimer alcohols by the self-condensation of primary alcohols as exemplified by the conversion of 1-butanol to 2-ethyl-1-hexanol.[1] The reaction is usually carried out in the presence of alkali metal hydroxides or alkoxides and hydrogenation/dehydrogenation catalysts such as Raney Ni at higher temperature (220 °C) and pressure.[2] In 1972, the Guerbet reaction was first examined using transition-metal complexes such as Rh, Ru, Pt, and Ir which makes it possible to carry out the Guerbet reaction under much milder conditions of 110−140 °C at atmospheric pressure.[3] Among the metal complexes examined, the catalytic activity of $RhCl_3 \cdot 3H_2O/4P(C_4H_9)_3$ is shown to be very high compared with that of Ru and Ir complexes, but Pd and Au complexes are inactive because of the difficulty of the generation of stable hydride metal complexes.[3] Burk et al. reported the Rh-promoted Guerbet reaction of 1-butanol and 1-pentanol and clarified the multiple roles of Rh and alkoxide catalysts.[4,5] Carlini et al. disclosed the Guerbet reaction of 1-butanol to 2-ethyl-1-hexanol under homogeneous and heterogeneous Pd-based catalysts such as $PdCl_2(dppe)$ and Pd/C, respectively, in the presence of sodium butoxide but using a higher reaction temperature (200 °C).[6]

Previously, we reported the α-alkylation of ketones with alcohols leading to α-alkylated ketones by Ir complexes in the presence of a small amount of KOH (10 mol %) without any solvents.[7] This method provides a very convenient synthetic tool which makes it possible to introduce a carbonyl function to the desired position of ketones by reacting methyl ketones with various primary alcohols. In the course of this study, our attention has been focused on the Guerbet reaction, alkylation of primary alcohols giving *β*-alkylated higher alcohols.[8,9] In this paper, we wish to report a highly efficient Ir-catalyzed Guerbet reaction of various primary alcohols (eq 1).



(1)

1-Butanol (**1a**) was chosen as a model substrate for the Guerbet reaction and allowed to react under various iridium complexes (Table 1).

A *p*-xylene solution (0.5 mL) of $[IrCl(cod)]_2$ (1 mol %), 1,7-octadiene (10 mol %), and KOH (20 mol %) was stirred for 2 h at room temperature, and then **1a** (2 mmol) was added and reacted at 120 °C for 4 h to afford 2-ethyl-1-hexanol (**2a**) in 62% yield at 84% conversion of **1a** (entry 1). The reaction using $[Ir(OH)(cod)]_2$ under these conditions gave **2a** in a higher yield (70%) (entry 2), whereas $IrCl(PPh_3)_3$ resulted in **2a** in poor selectivity (entry 3). $IrCl_3$ did not catalyze the present reaction (entry 4). Among the iridium complexes used, $[Cp^*IrCl_2]_2$ was found to be the best catalyst and led to **2a** in 77% yield (entry 5). The use of *t*-BuOK in place of KOH as a base resulted in a slight improvement of the yield of **2a** (entry 6).

It is interesting to note that the present reaction could be carried out using KOH as a base and without continuous removal of the resulting water, in contrast to the Rh-catalyzed Guerbet reaction of **1a** and 1-pentanol (**1b**) where sodium butoxide for **1a** and sodium pentoxide for **1b** are used as bases and the resulting water is continuously removed through a column packed with 4 Å molecular sieves. Sodium alkoxides are hydrolyzed by the water generated to form NaOH, which induces the formation of carboxylate salts and esters by the Tischenko reaction and/or the Canizzaro reaction of aldehydes.[3] In the present Ir-catalyzed Guerbet reaction, however, a small amount of a hydrogen acceptor such as 1,7-octadiene was needed. The reaction without 1,7-octadiene resulted in the

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[6] Carlini, C.; Macinai, A.; Raspolli Galletti, A. M.; Sbrana, G. *J. Mol. Catal. A: Chem.* **2004**, *212*, 65.

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[8] Quite recently, *β*-alkylation of secondary alcohols with primary alcohols is reported via the in situ generation of methyl ketones. Fujita, K.; Kitatsuji, S.; Yamaguchi, T.; Hanasaka, F.; Yamaguchi, R. *Org. Lett.* **2005**, *7*, 4017.

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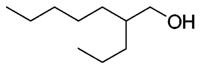
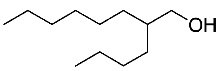
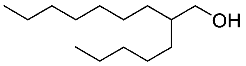
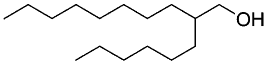
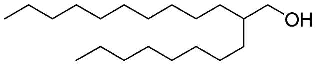
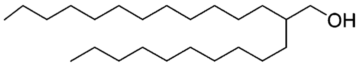
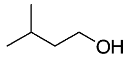
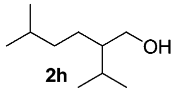
TABLE 1. Guerbet Reaction of 1a to 2a by Ir Complexes Combined with KOH under Various Conditions[a]

entry	Ir complex	conversion/%	yield/% (selectivity/%)
1	$[IrCl(cod)]_2$	84	62 (74)
2[b]	$[Ir(OH)(cod)]_2$	90	70 (78)
3	$IrCl(PPh_3)_3$	71	39 (55)
4	$IrCl_3 \cdot 3H_2O$	30	4 (13)
5	$[Cp^*IrCl_2]_2$	84	77 (92)
6[c]	$[IrCl(cod)]_2$	86	67 (78)
7[d]	$[Ir(OH)(cod)]_2$	37	23 (62)
8[b]	$[Cp^*IrCl_2]_2$	95	83 (87)
9[e]	$[Cp^*IrCl_2]_2$	94	93 (99)[f]
10[d]	$[Cp^*IrCl_2]_2$	66	49 (74)
11[g]	$[Cp^*IrCl_2]_2$	80	63 (79)
12[h]	$[Cp^*IrCl_2]_2$	89	73 (82)
13[i]	$[IrCl(cod)]_2$	71	51 (72)
14[j]	$[IrCl(cod)]_2$	91	79 (87)

[a] **1a** (2 mmol) was reacted in the presence of an Ir complex (1 mol %), 1,7-octadiene (10 mol %), and KOH (20 mol %) in *p*-xylene (0.5 mL) at 120 °C for 4 h. [b] KOH (30 mol %) was used. [c] *t*-BuOK (20 mol %) is used in place of KOH. [d] Without 1,7-octadiene. [e] *t*-BuOK (40 mol %) was used. [f] In this reaction, the isolated yield of **2a** was 70%. [g] Cyclooctene (20 mol %) was used instead of 1,7-octadiene. [h] 1-Octene (20 mol %) was used instead of 1,7-octadiene. [i] 100 °C, 20 h. [j] **1a** (2 mmol) containing about 30% of KOH was used without *p*-xylene.

TABLE 2. Guerbet Reaction of Various Alcohols Catalyzed by Ir Complexes in the Presence of a Base[a]

entry	alcohol	product	yield (%)
1	*n*-$C_5H_{11}OH$ **1b**	 **2b**	98 (71)
2	*n*-$C_6H_{13}OH$ **1c**	 **2c**	98 (77)
3[b]	**1c**	**2c**	83
4	*n*-$C_7H_{15}OH$ **1d**	 **2d**	79
5	*n*-$C_8H_{17}OH$ **1e**	 **2e**	81
6[b]	**1e**	**2e**	76
7	*n*-$C_{10}H_{21}OH$ **1f**	 **2f**	43
8	*n*-$C_{12}H_{25}OH$ **1g**	 **2g**	86
9	 **1h**	 **2h**	50

[a] Alcohol (2 mmol) was reacted under the influence of $[Cp^*IrCl_2]_2$ (1 mol %), 1,7-octadiene (10 mol %), and *t*-BuOK (40 mol %) in *p*-xylene (0.5 mL) at 120 °C for 4 h. Number in parentheses shows the isolated product. [b] The reaction was carried out using $[Ir(OH)(cod)]_2$ (1 mol %), 1,7-octadiene (10 mol %), and *t*-BuOK (20 mol %) without *p*-xylene.

decrease of both the conversion of **1a** and the selectivity of **2a** (entries 7 and 10). When the amount of KOH was increased to 30 mol %, **2a** was obtained in higher yield (83%) (entry 8). Cyclooctene and 1-octene could be used as hydrogen acceptors in place of 1,7-octadiene (entries 11 and 12). These results indicate that a hydrogen acceptor is needed to initiate smoothly the hydrogen transfer from 1-butanol **1a**. Needless to say, no reaction took place by removing KOH from the catalytic system. The reaction at 100 °C was difficult to carry out, but **2a** was obtained in 51% yield after 20 h (entry 13). When solid KOH was added to the reaction solution, we observed that KOH was gradually dissolved during the reaction. Therefore, when a **1a** solution containing about 30% of KOH was reacted under the influence of $[IrCl(cod)]_2$ (1 mol %) in the presence of 1,7-octadiene (10 mol %) without *p*-xylene, **2a** was obtained in good yield (79%) and selectivity (87%) (entry 14). This shows that the Guerbet reaction can be carried out by using a KOH solution of **1a** without any solvent.

Table 2 shows the results for the Guerbet reaction of several primary alcohols in the presence of catalytic amounts of $[Cp^*IrCl_2]_2$ or $[Ir(OH)(cod)]_2$ and *t*-BuOK.

1-Pentanol (**1b**) and 1-hexanol (**1c**) were reacted in the presence of $[Cp^*IrCl_2]_2$ and *t*-BuOK at 120 °C for 4 h to give 2-propyl-1-heptanol (**2b**) and 2-butyl-1-octanol (**2c**) in almost quantitative yields (entries 1 and 2). From higher alcohols such as 1-octanol (**1e**) and 1-decanol (**1f**), the corresponding Guerbet alcohols, 2-hexyl-1-decanol (**2e**) and 2-octyl-1-dodecanol (**2f**), were obtained, although their yields were slightly decreased compared with those of **1b** and **1c** (entries 4 and 5). The reaction of **1c** and **1e** using $[Ir(OH)(cod)]_2$ without solvent resulted in **2c** and **2e**, respectively, in slightly lower yields than those of $[Cp^*IrCl_2]_2$. Branched primary alcohols such as 3-methyl-1-butanol (**1h**) and 2-methyl-1-propanol (**1i**) were allowed to react under the same conditions. Although no Guerbet-type alcohol was obtained from **1i**, **1h** gave the corresponding Guerbet alcohol, 5-methyl-2-(1-methylethyl)-1-hexanol (**2h**), in 50% yield (entry 9). These higher alcohols find application in cosmetics as oily components with favorable solvent properties.[10]

In conclusion, we have developed an Ir-catalyzed Guerbet reaction of primary alcohols to dimer alcohols in high yields under mild conditions. This method provides an alternative route to β-alkylated higher alcohols which are used as plasticizer materials and detergent alcohols.

Experimental Section

General Procedures. All starting materials were commercially available and used without any purification. GLC analysis was performed with a flame ionization detector using a 0.2 mm × 25 m capillary column (OV-1). ^1H and ^{13}C NMR were measured at 270 and 67.5 MHz, respectively, in $CDCl_3$ with Me_4Si as the internal standard.

A typical reaction procedure is as follows: To a *p*-xylene (0.5 mL) solution of $[Cp^*IrCl_2]_2$ (0.02 mmol), 1,7-octadiene (0.2 mmol), and *t*-BuOK (0.8 mmol) was added alcohol (2 mmol) under Ar. The reaction mixture was stirred at 120 °C for 4 h. The product was isolated by column chromatography (230−400 mesh silica gel, *n*-hexane/ethyl acetate = 10−5:1). The conversions and yields of products were estimated from the peak areas based on the internal

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standard technique using GC. The products **2b**[11] and **2d**[12] were reported previously. **2a**, **2c**, and **2e**−**h** were commercially available.

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra for compounds **2b**−**h**. This material is available free of charge via the Internet at http://pubs.acs.org.

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