

Iridium-Catalyzed Oppenauer Oxidations of Primary Alcohols Using Acetone or 2-Butanone as Oxidant

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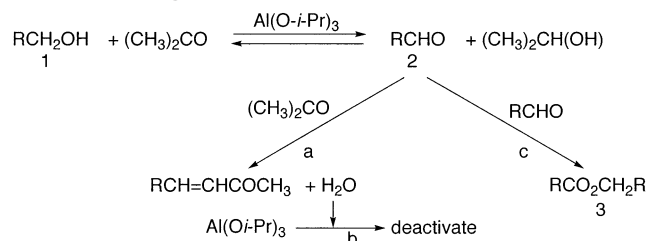
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Abstract: The first Oppenauer oxidation of primary alcohols with acetone or 2-butanone by an amino alcohol-based Ir bifunctional catalyst was accomplished. The reaction proceeds with 1 mol % catalyst in acetone or 2-butanone at 30–80 °C to give the corresponding aldehydes in 33–96% yield.

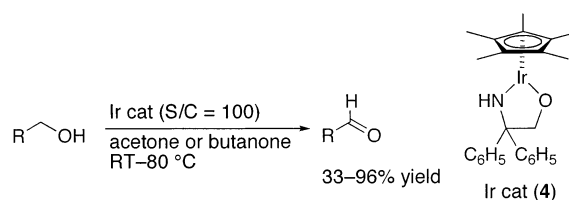
In 1937 Oppenauer reported that the oxidation of steroids bearing secondary alcohol functions proceeded using acetone as an oxidant in the presence of an Al(O-*t*-Bu)₃ catalyst.¹ The main advantage of this reaction lies in the high selectivity of various functional groups, and the method is often used to prepare ketones. However, the oxidation of primary alcohols does not occur easily for the following reasons (see Scheme 1): (a) the product aldehyde **2** reacts with acetone to give an aldol condensation product, (b) water formed by the aldol condensation deactivates the moisture-sensitive aluminum alkoxide catalyst, and (c) the product aldehyde **2** may cause a Tishchenko reaction to give dimeric esters **3**.²

To date, many attempts for improvements of the Oppenauer oxidation of primary alcohols using other hydrogen acceptors³ and metal catalyst⁴ systems have been reported, but there has been no report of oxidizing a primary alcohol to form an aldehyde using inexpensive acetone or 2-butanone as the oxidant. We have recently developed an efficient oxidative lactonization of diols using a novel Ir–ligand bifunctional catalyst, **4**.⁵ Due to the neutral character of the catalyst, we hypothesized that this catalyst system would be effective for the oxidation of primary alcohols without the accompanying

SCHEME 1. Oppenauer Oxidation of Primary Alcohol Using Acetone and Side Reactions



aldol reaction. On the basis of the present results, we report herein the first Oppenauer oxidation of primary alcohols to aldehydes using inexpensive acetone or 2-butanone as an oxidant (eq 1).



When a 0.1 M solution of 4-methoxybenzyl alcohol (**1b**) in acetone-containing Ir complex **4** (acetone:**1b**:**4** = 13600:100:1) was stirred under Ar at 30 °C for 16 h, we found that *p*-anisaldehyde (**2b**) was obtained in 78% yield without aldol condensation (Table 1, entry 1). The yield was improved by raising the temperature (entry 2), and the best result was obtained by heating the solution in butanone at 80 °C (entry 3). To obtain the aldehyde in high yield, the reaction should be performed with a substrate concentration as low as 0.08 M. The high-dilution condition has the following two merits: (1) because the reaction is reversible, use of the excess oxidant makes the equilibrium shift toward the product side and (2) the formation of dimeric ester **3**, which is a major side product in the reaction of **1f**, is suppressed under the low-concentration condition (entries 6–8).⁶

Having succeeded in optimizing the reaction condition, we examined the scope and limitations of the reaction with substrates. As shown in Table 2, the oxidation of the benzyl alcohol with an electron-donating substituent gave the desired aldehyde in high yield (entries 1–3). Moreover, the oxidation of the substrate **1d** with a substituent such as the sulfide, which is easy to oxidize, proceeded with no problems (entry 4). The oxidation of the allyl alcohol **1g** afforded the corresponding aldehyde in good yield. However, the oxidation of the saturated aliphatic alcohol gave octanal in low yield due to the lower redox potential of butanone (entry 8).⁷

(6) Although a detailed mechanism has not yet been determined, it seems possible that the dimeric ester **3** was formed via the corresponding hemiacetal intermediate. The reaction of bromobenzaldehyde (**2f**) in the presence of the Ir catalyst **4** (**2f**:**4** = 100:1 mole ratio) gave a trace amount of **3f** under reflux for 16 h, indicating that the contribution of the mechanism via the acylhydridometal complex is negligible. For the mechanism via the acylhydridometal complex, see: Horino, H.; Ito, T.; Yamamoto, A. *Chem. Lett.* **1978**, 17–20.

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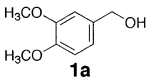
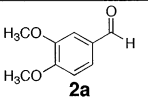
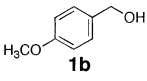
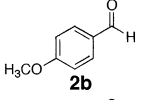
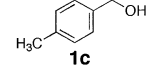
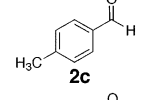
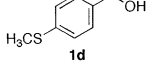
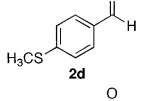
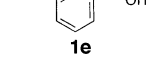
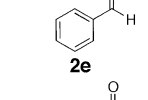
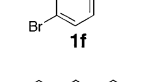
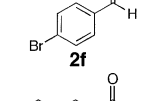
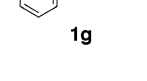
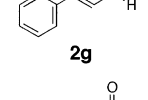
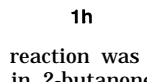
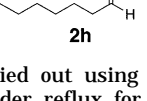
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TABLE 1. Optimization of Catalytic Oxidation of Benzyl Alcohols Using Ir Complex 4^a

entry	alcohol	oxidant	concn, ^b M (ratio) ^c	temp, °C	time, h	convn, ^d %	yield of 2 , ^d %	yield of 3 , ^d %
1	1b	acetone	0.10 (136)	30	16	78	78	0
2	1b	acetone	0.10 (136)	60	36	89	89	0
3	1b	2-butanone	0.08 (136)	80	16	94	94	0
4	1b	2-butanone	1.0 (10.3)	80	16	71	70	1
5	1b	2-butanone	3.0 (3.4)	80	16	53	47	6
6	1f	2-butanone	0.08 (136)	80	16	41	40	1
7	1f	2-butanone	1.0 (10.3)	80	16	40	10	30
8	1f	2-butanone	3.0 (3.4)	80	16	55	2	53

^a The reaction was carried out using a 0.08–3.0 M solution of benzyl alcohols in acetone or 2-butanone. Ir complex **4**/alcohol **1** = 1/100. ^b Concentration of alcohol. ^c Oxidant/alcohol ratio. ^d Determined by ¹H NMR.

TABLE 2. Oxidation of Primary Alcohols Using 2-Butanone Catalyzed by Iridium Complex 4^a

entry	alcohol	product	% yield ^b	SM recover ^b
1			96	4
2			91	7
3			92 ^c	8 ^c
4			81	19
5			71 ^c	29 ^c
6			40	59
7			72	26
8			33 ^c	64 ^c

^a The reaction was carried out using a 0.08 M solution of alcohols in 2-butanone under reflux for 16–18 h. Ir catalyst **4**/alcohol **1** = 1/100. ^b Isolated yield. ^c Determined by GC.

In summary we have developed a method by which the Oppenauer oxidation of primary alcohols to form the corresponding aldehydes can be carried out using inexpensive acetone or 2-butanone as an oxidant. This method can be used with lower catalyst loading in comparison with the known Oppenauer oxidation of

primary alcohols.⁴ The simple workup procedure does not require the decomposition step of excess oxidant; as such, after the reaction ends, filtration by short SiO₂ column chromatography and subsequent concentration give the crude product. Because this method is also environmentally benign,⁸ it might be useful for contemporary organic synthesis.

Experimental Section

General Procedure for Alcohol Oxidation. A mixture of Ir complex **4**⁵ (2.7 mg, 0.005 mmol) and alcohol (1.0 mmol) in 2-butanone (12 mL) was refluxed for 16–18 h. After the resulting solution was cooled, the mixture was passed through a short silica gel column (1.5 g, ethyl acetate) to remove the catalyst. The yields for the products **2c**, **2e**, and **2h** were determined by gas chromatography using authentic samples and appropriate correction factors. The products **2a**, **2b**, **2d**, **2f**, and **2g** were purified by silica gel column chromatography and identified by comparing their ¹H and ¹³C NMR spectra with those of authentic samples.

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Supporting Information Available: Characterization data for the products and ¹H and ¹³C NMR spectra of the products **2a**, **2b**, **2d**, **2f**, and **2g**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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