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BCSJ Award Article

Synthesis of Diketones and ω-Hydroxy Ketones from Methyl Ketones and α,ω-Diols by an $[IrCl(cod)]_2/PPh_3/KOH$ System

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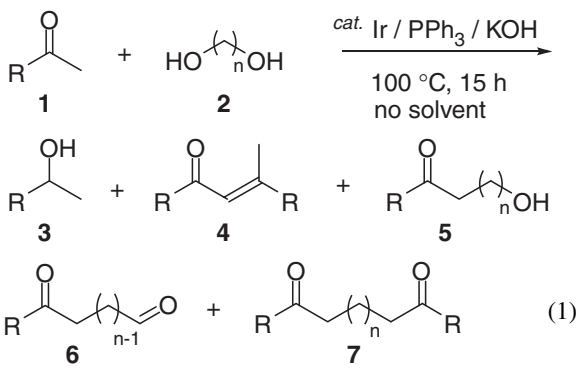
ω-Hydroxy ketones and diketones, which are important starting materials for the synthesis of cycloalkanones and heterocyclic compounds, were prepared by the one-step reaction of methyl ketones with α,ω-diols under the influence of an iridium complex and a base. The selectivity of ω-hydroxy ketones and diketones could be controlled by varying the starting ratio of methyl ketones to α,ω-diols. For example, reaction using acetophenone (5 equiv) with respect to 1,6-hexanediol (1 equiv) in the presence of $[IrCl(cod)]_2$, PPh_3, and KOH without solvent gave 1,10-diphenyl-1,10-decanedione in almost quantitative yield, while reaction using acetophenone (1 equiv) to 1,6-hexanediol (4 equiv) led to 8-hydroxy-1-phenyl-1-octanone in 92% yield. This methodology was successfully extended to the reaction of arylacetonitriles with α,ω-diols leading to diaryldinitriles.

Hydroxy ketones and diketones are a very important class of compounds which are ubiquitous in nature and represent a basic key structure in organic synthesis. Acyloin condensation[1] and aldol reaction[2] are well-known synthetic methods to obtain α-hydroxy and β-hydroxy ketones, respectively. On the other hand, a variety of synthetic methods for the preparation of diketones have been disclosed,[3] since diketones are important starting materials for the synthesis of cycloalkanones and heterocyclic compounds. To the best of our knowledge, however, there have been few methods reported so far for the preparation of hydroxy ketones and diketones via the same methodology. Therefore, it seems very attractive to explore a facile synthetic route to diketones from readily available starting materials. In the course of our study to extend iridium-catalyzed synthetic reactions,[4] we have found that α-alkylation of ketones with alcohols leading to higher alkylated ketones is efficiently promoted by iridium complexes like $[IrCl(cod)]_2$.[5] Many groups have also reported related work on iridium- or ruthenium-catalyzed α-alkylations using alcohols as alkylating agents.[6,7] If our strategy could be extended to the reaction between ketones and α,ω-diols, the reaction would provide a very convenient synthetic tool for preparing ω-hydroxy ketones and diketones. In this paper, we would like to report a novel synthetic method for preparing ω-hydroxy ketones and diketones from methyl ketones and α,ω-diols by the action of iridium complexes (eq 1).



(1)

In order to confirm optimum reaction conditions, the reaction of acetophenone (**1a**) with 1,6-hexanediol (**2a**) was chosen and examined in the presence of several Ir complexes and KOH under various reaction conditions (Table 1).

The reaction of **1a** (10.0 mmol) with **2a** (2.0 mmol) in the presence of $[IrCl(cod)]_2$ (0.1 mmol), PPh_3 (0.4 mmol), and KOH (0.4 mmol) without any solvent at 100 °C for 15 h (standard conditions) gave a homogeneous solution and was found to produce double-alkylated product, 1,10-diphenyl-1,10-decanedione (**7aa**), in almost quantitative yield (>99%) (86% isolated yield) along with a small amount of aldol condensate of **1a**, 1,3-diphenyl-2-buten-1-one (**4a**) (10%) (Entry 1). When the amount of **1a** was reduced to 2 equiv (4.0 mmol) needed for the double-alkylation with **2a**, **7aa**

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Table 1. Reaction of Acetophenone (**1a**) with 1,6-Hexanediol (**2a**) Catalyzed by Ir Complexes under Various Conditions[a)]

Entry	Ir Complex	Product/%[b)]				
		3a[c)]	**4a**[c)]	**5aa**	**6aa**	**7aa**
1	$[IrCl(cod)]_2$	0	10	0	0	>99(86)
2[d)]	$[IrCl(cod)]_2$	0	11	0	0	60
3[e)]	$[IrCl(cod)]_2$	58	14	9	2	27
4[f)]	$[IrCl(cod)]_2$	0	0	0	0	0
5	$[IrCl(coe)_2]_2$	70	8	11	2	22
6[g)]	Ir(acac)(cod)	0	29	0	0	>99
7[e),g),h)]	$IrCl(PPh_3)_3$	0	9	2	2	74
8[h)]	$[Cp^*IrCl_2]_2$	0	7	20	4	20
9[g),i)]	$IrCl_3 \cdot 3H_2O$	0	0	0	0	0

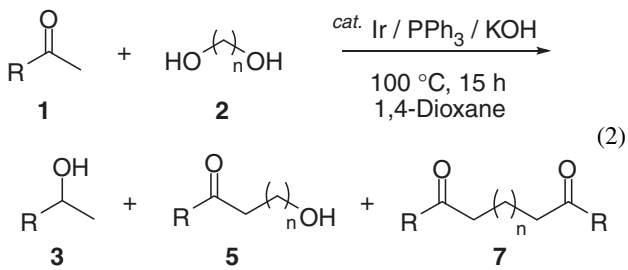
a) **1a** (10.0 mmol) was allowed to react with **2a** (2.0 mmol) in the presence of Ir complex (0.1 mmol), PPh_3 (0.4 mmol), and KOH (0.4 mmol) without solvent at 100 °C for 15 h. b) GLC yields based on **2a** unless otherwise noted. The number in parentheses shows isolated yield. c) Based on **1a** used. d) **1a** (4.0 mmol) was used. e) Reaction was performed without addition of PPh_3. f) Reaction was performed in the absence of KOH. g) Ir complex (0.2 mmol) was used. h) Reaction was performed with KOH (0.8 mmol) in 1,4-dioxane (1.0 mL). i) Reaction was performed at 120 °C.

was formed in 60% yield (Entry 2), but hydroxy ketone, 8-hydroxy-1-phenyl-1-octanone (**5aa**), which is a precursor of **7aa**, was found to be scarcely formed. This indicates that **5aa** was more reactive than diol **2a**. In a previous paper, we showed that the selectivity of the alkylation of ketones with alcohols is considerably affected by phosphine ligands.[5] In the present reaction, the $[IrCl(cod)]_2$ complex, without a phosphine ligand, catalyzed preferentially hydrogen transfer from **2a** to **1a** rather than alkylation of **1a** with **2a** to lead to 1-phenylethanol (**3a**) (58%) in preference to **5aa** (9%) and **7aa** (27%) (Entry 3). Recently, we reported that the alkylation of active methylene compounds like cyanoacetates with alcohols is promoted by $[IrCl(cod)]_2$ in the absence of any base to give α-alkylated derivatives.[8] Unfortunately, however, the present reaction was not induced at all in the absence of base (Entry 4). We next examined the catalytic performance of several iridium complexes in the double-alkylation of **1a** with α,ω-diol **2a**. $[IrCl(coe)_2]_2$ complex, which displayed high catalytic activity in the alkylation of cyanoacetates with alcohols[8] and the oxidative dimerization of primary alcohols to esters,[9] was less active than $[IrCl(cod)]_2$ to form **7aa** (22%) in low yield (Entry 5). It is difficult to explain the lower activity of the $[IrCl(coe)_2]_2$ complex compared to the $[IrCl(cod)]_2$ complex, but the $[IrCl(coe)_2]_2$ complex seems to easily liberate the weakly coordinated cyclooctene (coe) ligand from the iridium metal. On the other hand, Ir(acac)(cod) complex was very active leading to **7aa** in almost quantitative yield (Entry 6). It is interesting to note that the catalytic activity of $IrCl(PPh_3)_3$ complex was high without further addition of phosphine ligand to form **7aa** in 74% yield (Entry 7). These results indicate that Ir complexes bearing strongly coordinated ligands are appropriate for the present alkylation reaction. On the other hand, trivalent iridium complex $[Cp^*IrCl_2]_2$, which exhibited high activity for the Guerbet reaction of primary alcohols,[10] showed low catalytic activity (Entry 8). $IrCl_3 \cdot 3H_2O$ was inactive even at 120 °C (Entry 9).

On the basis of these results, several methyl ketones were reacted with α,ω-diols under the standard conditions as shown in Entry 1 in Table 1 (Table 2).

The reaction of **1a** with various α,ω-diols **2b**, **2c**, **2d**, and **2e** afforded the corresponding diketones **7ab**, **7ac**, **7ad**, and **7ae** in high yields (Entries 1–4). However, the reaction of **1a** with lower carbon-numbered α,ω-diols like 1,4-butanediol and 1,5-pentanediol did not produce diketones at all. This is believed to be due to the occurrence of homo-aldol reaction between aldehydes derived from the diols in preference to the cross-aldol reaction with **1a**. In fact, the reaction of 1,4-butanediol alone under these conditions resulted in a complex mixture of poly-aldol products. Several aliphatic methyl ketones **1b**–**1e** were allowed to react with **2a** under similar conditions to form the corresponding diketones **7ba**, **7ca**, **7da**, and **7ea** in 75–80% yields (Entries 5–8). The reaction of acetone with **2a** led to oligoketones rather than diketone as major products, since both methyl groups in acetone are capable of undergoing alkylation with **2a**.

Reaction of excess α,ω-diols with methyl ketones would be expected to provide ω-hydroxy ketones by the present method. Thus, reaction of **1** with **2** to obtain ω-hydroxy ketones was performed under several reaction conditions (eq 2) (Table 3). In the preceding reaction where methyl ketones **1** are used in excess with respect to α,ω-diols **2** (vide supra), it was possible to carry out the reaction without any solvent since viscous α,ω-diols are readily dissolved in methyl ketones existing in excess to form a clean non-viscous solution. However, reactions using excess viscous α,ω-diols to prepare ω-hydroxy ketones gave highly viscous liquids which are difficult to stir magnetically. Thus, the reaction to prepare ω-hydroxy ketones was carried out by adding a small amount of solvent like 1,4-dioxane.



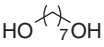
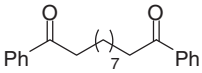
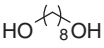
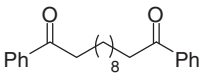
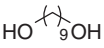
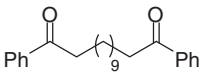
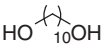
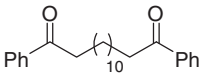
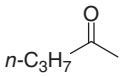
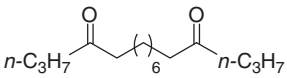
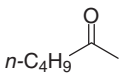
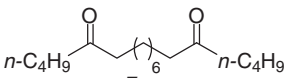
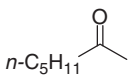
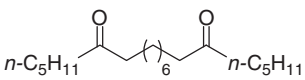
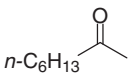
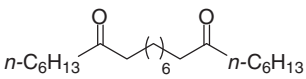
(2)

The reaction of methyl ketones **1** (2.0 mmol) with α,ω-diols **2** (8.0 mmol) was examined in 1,4-dioxane (1.0 mL) under several reaction conditions (Table 3).

By the use of 4 equiv of diol **2a** with respect to **1a** under the influence of $[IrCl(cod)]_2$, PPh_3, and KOH at 100 °C for 15 h, ω-hydroxy ketone **5aa** was obtained in 92% yield (Entry 1). In spite of the use of excess **2a** which serves as a hydrogen donor to **1a**, hydrogen-transfer from **2a** to **1a** leading to **3a** was suppressed up to 3%. The reaction of **1a** with various aliphatic α,ω-diols **2b**–**2e** produced the corresponding ω-hydroxy ketones **5ab**–**5ae** in good yields (84–91%) (Entries 2–5), while the reaction of aliphatic methyl ketones **1b**–**1e** with **2a** resulted in ω-hydroxy ketones **5ba**–**5ea** in substantial yields (ca. 70%) (Entries 6–9).

Although Grigg et al. and our group have shown the monoalkylation of arylacetonitriles with primary alcohols by an iri-

Table 2. Synthesis of Diketones **7** from Methyl Ketones **1** and α,ω-Diols **2** Catalyzed by $[IrCl(cod)]_2$[a)]

Entry	Ketone	Diol	Product	Yield/%[b)]
1	**1a**	 **2b**	 **7ab**	96 (84)
2	**1a**	 **2c**	 **7ac**	>99 (88)
3	**1a**	 **2d**	 **7ad**	>99 (91)
4	**1a**	 **2e**	 **7ae**	87 (85)
5[c)]	 **1b**	**2a**	 **7ba**	76 (69)
6[c)]	 **1c**	**2a**	 **7ca**	80 (71)
7[c)]	 **1d**	**2a**	 **7da**	75 (72)
8[c)]	 **1e**	**2a**	 **7ea**	79 (75)

a) **1** (10.0 mmol) was allowed to react with **2** (2.0 mmol) in the presence of $[IrCl(cod)]_2$ (0.1 mmol), PPh_3 (0.4 mmol), and KOH (0.4 mmol) without solvent at 100 °C for 15 h. b) GLC yields. The numbers in parentheses show isolated yields. c) KOH (0.6 mmol) and 1,7-octadiene (0.6 mmol) were used.

Table 3. Synthesis of ω-Hydroxy Ketones **5** from Methyl Ketones **1** and α,ω-Diols **2** Catalyzed by $[IrCl(cod)]_2$[a)]

Entry	Ketone	Diol	Product/%[b)]		
			3	**5**	**7**
1	**1a**	**2a**	**3a** (3)	**5aa** (92[87])	**7aa** (5)
2	**1a**	**2b**	**3a** (1)	**5ab** (84[77])	**7ab** (7)
3	**1a**	**2c**	**3a** (1)	**5ac** (87[84])	**7ac** (6)
4	**1a**	**2d**	**3a** (2)	**5ad** (89[81])	**7ad** (8)
5	**1a**	**2e**	**3a** (2)	**5ae** (91[82])	**7ae** (7)
6[c)]	**1b**	**2a**	**3b** (8)	**5ba** (69[66])	**7ba** (3)
7[c)]	**1c**	**2a**	**3c** (6)	**5ca** (70[64])	**7ca** (3)
8[c)]	**1d**	**2a**	**3d** (7)	**5da** (70[65])	**7da** (4)
9[c)]	**1e**	**2a**	**3e** (7)	**5ea** (70[67])	**7ea** (5)

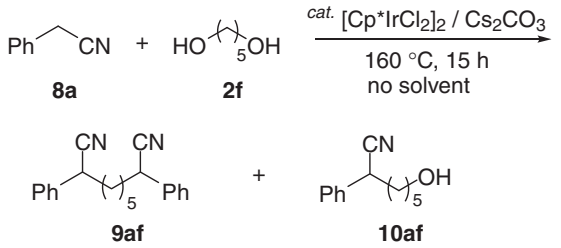
a) **1** (2.0 mmol) was allowed to react with **2** (8.0 mmol) in the presence of $[IrCl(cod)]_2$ (0.05 mmol), PPh_3 (0.2 mmol), and KOH (0.2 mmol) in 1,4-dioxane (1.0 mL) at 100 °C for 15 h. b) GLC yields based on **1** used. Numbers in brackets show isolated yields. c) KOH (0.3 mmol) and 1,7-octadiene (0.3 mmol) were used.

dium complex in the presence of a base like KOH,[11] the present methodology was successfully extended to the double-alkylation of arylacetonitriles with α,ω-diols, although the reaction must be conducted at higher temperatures.

Phenylacetonitrile (**8a**) (10.0 mmol) was allowed to react with 1,5-pentanediol (**2f**) (2.0 mmol) in the presence of an iridium complex and a base at 160 °C for 15 h to afford 2,8-diphenylnonanedinitrile (**9af**) in fair to good yield (Table 4).

In contrast to the reaction of methyl ketones with α,ω-diols where $[Cp^*IrCl_2]_2$ was a poor catalyst, this complex was found to be the best among the catalysts examined. For instance, the reaction of **8a** with **2a** in the presence of $[Cp^*IrCl_2]_2$ under these conditions produced **9af** in 93% yield (Entry 2), but $[IrCl(cod)]_2$ afforded only 41% yield of **9af** in addition to 7-hydroxy-2-phenylheptanenitrile (**10af**) (10%) (Entry 1). Another feature of this reaction is that the double-alkylation of **8a** with **2f** proceeded smoothly without any phosphine ligand. In addition, the reaction was promoted by the addition of Cs_2CO_3 rather than KOH (Entries 2 and 4), but no reaction was induced in the absence of a base

Table 4. Reaction of Phenylacetonitrile (**8a**) with 1,5-Pentanediol (**2f**) Catalyzed by Ir Complexes[a)]



Entry	Ir Complex	Yield/%[b)]	
		9af	**10af**
1	$[IrCl(cod)]_2$	41	10
2	$[Cp^*IrCl_2]_2$	93(89)	0
3[c)]	$[Cp^*IrCl_2]_2$	19	27
4[d)]	$[Cp^*IrCl_2]_2$	79	0
5[e)]	$[Cp^*IrCl_2]_2$	0	0
6[f)]	$[Cp^*IrCl_2]_2$	62	26
7[g)]	$[Cp^*IrCl_2]_2$	49	43
8[h)]	$[Cp^*IrCl_2]_2$	10	45
9	$[IrCl(coe)_2]_2$	68	0
10[i)]	$IrCl_3 \cdot 3H_2O$	52	13

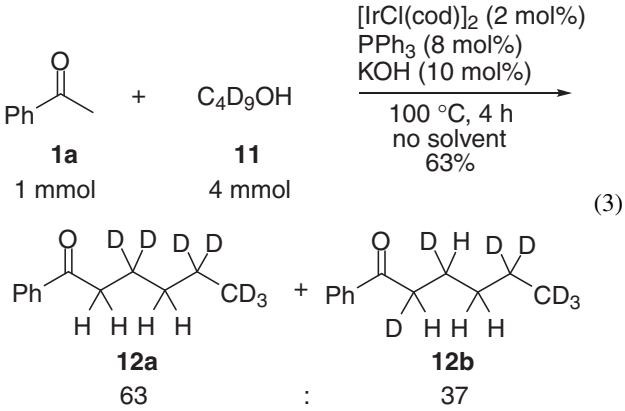
a) **8a** (10.0 mmol) was allowed to react with **2f** (2.0 mmol) in the presence of Ir complex (0.05 mmol) and Cs_2CO_3 (0.4 mmol) without solvent at 160 °C for 15 h. b) GLC yields based on **2f** used. The number in parentheses shows isolated yield. c) Reaction was performed in the presence of PPh_3 (0.2 mmol). d) KOH (0.4 mmol) was used as a base. e) Reaction was carried in the absence of base. f) Reaction was carried out at 140 °C. g) Reaction was carried out at 120 °C. h) Reaction was carried out at 100 °C. i) $IrCl_3 \cdot 3H_2O$ (0.1 mmol) was used.

(Entry 5). The reaction between methyl ketones and diols occurred at relatively lower temperature (100 °C), but the reaction of nitrile **8a** with **2f** at 100–140 °C resulted in **9af** in unsatisfactory yields (Entries 6–8). Other selected iridium catalysts such as $[IrCl(coe)_2]_2$ and $IrCl_3 \cdot 3H_2O$, which were poor for the reaction with methyl ketones, showed moderate catalytic activities (Entries 9 and 10).

Under the same reaction conditions as Entry 1 in Table 4, α,ω-diols **2a**, **2b**, **2g**, and **2h** were reacted with various arylacetonitriles **8a**–**8d** affording the corresponding diaryldinitriles **9** in moderate to good yields (Table 5).

Arylacetonitriles bearing electron-donating substituents were found to be more reactive than those bearing electron-withdrawing ones (Entries 5–7). To our surprise, the reaction of phenylacetonitrile **8a** with lower carbon-numbered 1,3-, 1,4-, and 1,5-diols, **2f**–**2h**, was promoted by $[Cp^*IrCl_2]_2$ to give the corresponding dinitriles, **9af**, **9ag**, and **9ah**, respectively, because the reaction of methyl ketones with **2f** and **2h** was not promoted at all (Table 4, Entry 2 and Table 5, Entries 1 and 2).

In order to obtain information on the reaction pathway of the present reaction, the alkylation of **1a** with butanol-d_9 (1-C_4D_9OH) (**11**) was examined as a model reaction under the conditions shown in eq 3.



(3)

^{1}H NMR spectrum showed that a 63:37 mixture of 1-phenyl-1-hexanone-d_7, **12a** and **12b**, including rearranged deuterium and hydrogen atoms is formed. The formation of **12a** and **12b** is rationally explained by considering the following reaction pathway through the generation of iridium dihydride as a key species (Scheme 1).

The oxidative addition of C_4D_9O–H to an Ir complex is followed by β-hydride elimination to give butanal-d_8 and LnIrHD. Under the present strongly basic conditions, the deuterium atoms at the α-position of butanal-d_8 may undergo rapid H–D exchange with C_4D_9O–H, which exists in excess in the reaction system, through enolate formation to give eventually butanal-d_6. Aldol condensation with **1a** would produce 1-phenyl-2-hexen-1-one-d_6 (**13**) followed by hydrogenation by LnIrHD to lead to **12a** and **12b**. The deuterium exchange at the α-position of the resulting **12b** with formed water and/or butanol seems to contribute to the preferential formation of **12a** rather than **12b**.

Although a detailed reaction mechanism of the double alkylation is not confirmed at this stage, the reaction of methyl ketones **1** with α,ω-diols **2** is thought to proceed in a similar way to the iridium-catalyzed α-alkylation of **1** using butanol-d_9 shown above (Scheme 2). First, the iridium catalyst serves as hydrogen acceptor from **2** giving mono-aldehyde **A** and an iridium dihydride species. Then, the formed **A** reacts with **1** via base-catalyzed aldol condensation giving α,β-unsaturated ω-hydroxy ketone **B** and water. Subsequently, **B** was hydrogenated with the iridium dihydride species to give the saturated ω-hydroxy ketone **5**. When the reaction was performed with excess **1**, the resulting **5** reacted further with **1** in a similar way through the formation of **C** and **D** to give diketones **7**.

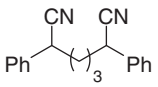
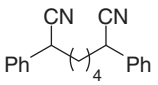
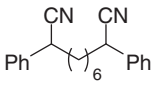
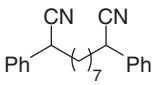
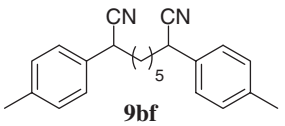
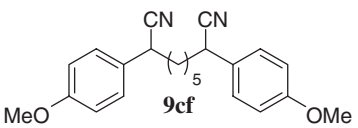
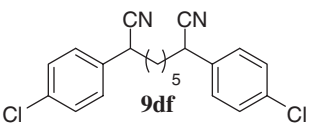
Conclusion

In conclusion, we have developed an iridium-catalyzed reaction of methyl ketones with α,ω-diols which provides a useful approach to diketones and ω-hydroxy ketones. This reaction was extended to the reaction of arylacetonitriles with α,ω-diols to afford diaryldinitriles in good yields.

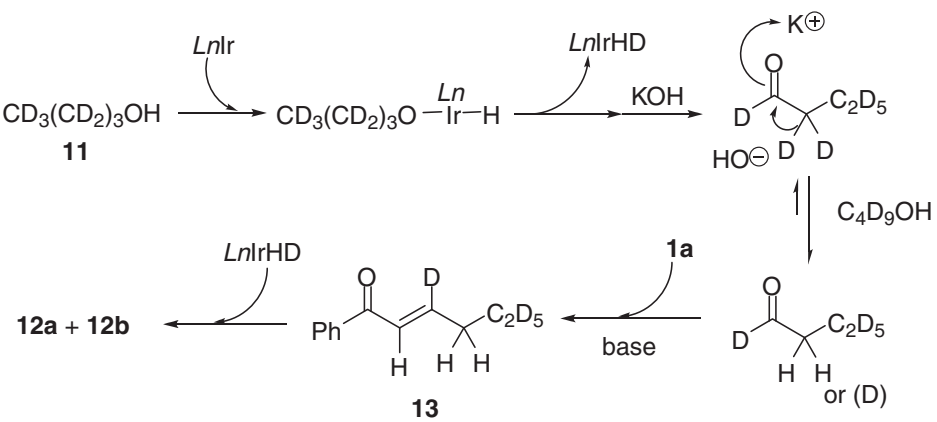
Experimental

All starting materials were commercially available and used without any purification. GLC analysis was performed with a flame ionization detector using a 0.22 mm × 25 m capillary column (BP-5). ^{1}H and ^{13}C NMR were measured in $CDCl_3$ with

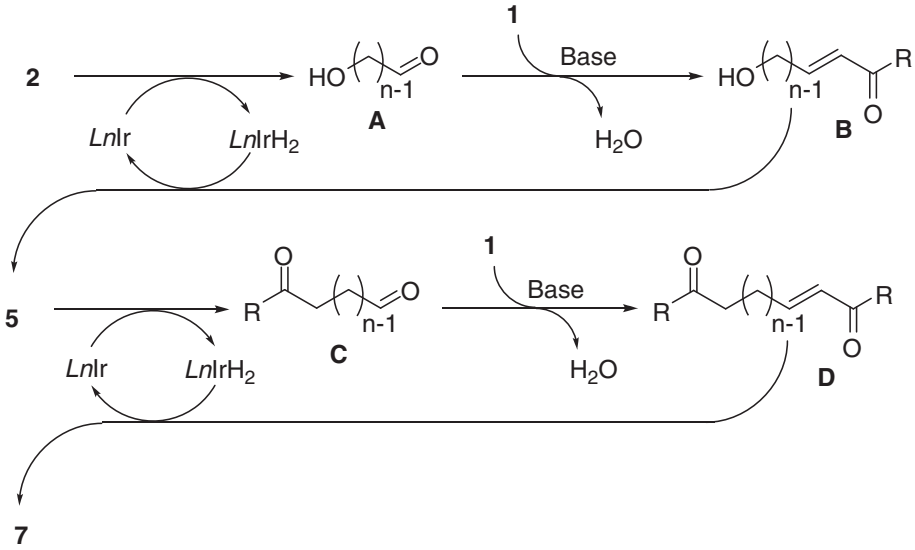
Table 5. Synthesis of Diaryldinitriles from Arylacetonitriles and α,ω-Diols Catalyzed by $[Cp^*IrCl_2]_2$[a)]

Entry	Ar⌒CN	Diol	Product	Yield/%[b)]
1[c)]	Ar = Ph **8a**	HO⌒3⌒OH **2g**	 **9ag**	56 (48)
2	**8a**	HO⌒4⌒OH **2h**	 **9ah**	94 (84)
3[d)]	**8a**	HO⌒6⌒OH **2a**	 **9aa**	79 (70)
4[d)]	**8a**	HO⌒7⌒OH **2b**	 **9ab**	80 (67)
5[e)]	Ar = p-MeC_6H_4 **8b**	HO⌒5⌒OH **2f**	 **9bf**	94 (85)
6[e)]	Ar = p-$MeOC_6H_4$ **8c**	HO⌒5⌒OH **2f**	 **9cf**	99 (89)
7[e)]	Ar = p-ClC_6H_4 **8d**	HO⌒5⌒OH **2f**	 **9df**	84 (80)

a) **8** (10.0 mmol) was allowed to react with **2** (2.0 mmol) in the presence of $[Cp^*IrCl_2]_2$ (0.05 mmol) and $CsCO_3$ (0.4 mmol) at 160 °C for 15 h without solvent. b) GLC yields based on **2** used. The numbers in parentheses show isolated yield. c) At 140 °C. d) Cs_2CO_3 (0.6 mmol) was used. e) **8** (4.0 mmol), Cs_2CO_3 (0.8 mmol), and mesitylene (1.0 mL) were used.



Scheme 1. A possible reaction pathway for the alkylation of **1a** with butanol-d_9 (**11**).



Scheme 2. A possible reaction path for the formation of **5** and **7**.

Me_4Si as an internal standard. The products were characterized by ^{1}H NMR, ^{13}C NMR, and GC-MS. The yields of products were estimated from peak areas based on an internal standard using GLC.

Compounds **5aa**,[12] **5ac**,[13] **5ae**,[14] **5ea**,[15] **6aa**,[16] **7aa**,[17] **7ab**,[18] **7ac**,[19] **7ad**,[20] **7ae**,[21] **7ba**,[22] **7ca**,[23] **7da**,[24] **7ea**,[25] **9aa**,[26] and **9ag**[27] were reported previously.

A Typical Reaction Procedure for the Formation of Diketone (7aa) by the Reaction of 1a and 2a is as Follows (Table 1, Entry 1). To a mixture of $[IrCl(cod)]_2$ (67 mg, 0.1 mmol), PPh_3 (105 mg, 0.4 mmol), and KOH (22 mg, 0.4 mmol) was added **1a** (1.20 g, 10.0 mmol) and **2a** (236 mg, 2.0 mmol) under Ar. The reaction mixture was stirred at 100 °C for 15 h. The conversions and yields of products were estimated from peak areas based on an internal standard using GC and the product **7aa** was obtained in quantitative yield along with the formation of **4a** (10%). The product **7aa** was isolated by column chromatography (230–400 mesh silica gel, Hexane/ethyl acetate = 10/1) in 86% yield (555 mg).

A Typical Reaction Procedure for the Formation of ω-Hydroxy Ketone (5aa) by the Reaction of 1a and 2a is as Follows (Table 3, Entry 1). To a mixture of $[IrCl(cod)]_2$ (34 mg, 0.05 mmol), PPh_3 (53 mg, 0.2 mmol), KOH (11 mg, 0.2 mmol) in 1,4-dioxane (1.0 mL) was added **1a** (240 mg, 2.0 mmol) and **2a** (0.95 g, 8.0 mmol) under Ar. The reaction mixture was stirred at 100 °C for 15 h. The conversions and yields of products were estimated from peak areas based on an internal standard using GC and the product **5aa** was obtained in 92% yield along with the formation of **3a** (3%) and **7aa** (5%). The product **5aa** was isolated by column chromatography (230–400 mesh silica gel, Hexane/ethyl acetate = 4/1) in 87% yield (380 mg).

A Typical Reaction Procedure for the Formation of Diaryldinitrile (9af) by the Reaction of 2f and 8a is as Follows (Table 4, Entry 2). To a mixture of $[Cp^*IrCl_2]_2$ (40 mg, 0.05 mmol) and Cs_2CO_3 (130 mg, 0.40 mmol) was added **2f** (208 mg, 2.0 mmol) and **8a** (1.17 g, 10.0 mmol) under Ar. The reaction mixture was stirred at 160 °C for 15 h. The conversions and yields of products were estimated from peak areas based on an internal standard using GC and the product **9af** was obtained in 93% yield. The product **9af** was isolated by column chromatography (230–400 mesh silica gel, Hexane/ethyl acetate = 10/1) in 89% yield (539 mg).

Reaction of 1a with 11 (eq 3). To a mixture of $[IrCl(cod)]_2$ (13 mg, 0.02 mmol), PPh_3 (21 mg, 0.08 mmol), and KOH (6 mg, 0.1 mmol) was added **1a** (120 mg, 1.0 mmol) and **11** (332 mg, 4.0 mmol) under Ar. The reaction mixture was stirred at 100 °C for 4 h. A 63:37 mixture of 1-phenyl-1-hexanone-d_7 **12a** and **12b** was isolated by column chromatography (230–400 mesh silica gel, Hexane/ethyl acetate = 10/1) in 63% yield (116 mg).

5ab: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.34–1.74 (m, 13H), 2.96 (t, J = 7.4 Hz, 2H), 3.64 (t, J = 6.3 Hz, 2H), 7.43–7.98 (m, 5H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 24.3 (CH_2), 25.6 (CH_2), 29.20 (CH_2), 29.24 (CH_2), 29.4 (CH_2), 32.7 (CH_2), 38.6 (CH_2), 63.0 (CH_2), 128.0 (C), 128.5 (C), 132.9 (C), 137.1 (C), 200.6 (C); IR (neat, cm^{-1}) 689, 744, 1072, 1448, 1470, 1683, 2852, 2920, 3242; GC-MS (EI), m/z (relative intensity) 234 (3) $[M]^+$, 133 (13), 120 (100), 105 (90), 77 (42); HRMS (EI) m/z calcd for $C_{15}H_{22}O_2$ $[M]^+$ 234.1621, found 234.1618; Anal. Found: C, 76.97; H, 9.64%. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46%.

5ad: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.30–1.78 (m, 17H), 2.96 (t, J = 7.3 Hz, 2H), 3.63 (t, J = 6.4 Hz, 2H), 7.43–7.97 (m, 5H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 24.3 (CH_2), 25.7 (CH_2), 29.29 (CH_2), 29.34 (CH_2), 29.4 (CH_2), 29.5 (CH_2), 32.7 (CH_2), 38.6 (CH_2), 63.0 (CH_2), 128.0 (C), 128.5 (C), 132.8 (C), 137.0 (C), 200.6 (C); IR (neat, cm^{-1}) 688, 734, 1072, 1447, 1471, 1684, 2850, 2919, 3244; GC-MS (EI), m/z (relative intensity) 262 (5) $[M]^+$, 133 (15), 120 (100), 105 (80), 77 (34); HRMS (EI) m/z calcd for $C_{17}H_{26}O_2$ $[M]^+$ 262.1934, found 262.1925.

5ba: ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.87–1.63 (m, 16H), 2.35–2.42 (m, 4H), 3.61 (t, J = 6.6 Hz, 2H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 13.6 (CH_3), 17.1 (CH_2), 23.6 (CH_2), 25.4 (CH_2), 29.0 (CH_2), 32.5 (CH_2), 42.6 (CH_2), 44.5 (CH_2), 62.6 (CH_2), 211.6 (C); IR (neat, cm^{-1}) 724, 1068, 1383, 1414, 1465, 1697, 2852, 2931, 3221; GC-MS (EI), m/z (relative intensity) 186 (0.6) $[M]^+$, 143 (10), 125 (20), 99 (16), 86 (75), 71 (100), 58 (75), 43 (95); HRMS (EI, 70 eV) m/z calcd for $C_{11}H_{22}O_2$ $[M]^+$ 186.1621, found 186.1624.

5ca: ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.88–1.62 (m, 18H), 2.39 (t, J = 7.4 Hz, 4H), 3.62 (t, J = 6.2 Hz, 2H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 13.8 (CH_3), 22.3 (CH_2), 23.7 (CH_2), 25.5 (CH_2), 25.9 (CH_2), 29.1 (CH_2), 32.6 (CH_2), 42.5 (CH_2), 42.7 (CH_2), 62.9 (CH_2), 211.7 (C); IR (neat, cm^{-1}) 724, 1067, 1384,

1418, 1466, 1698, 2852, 2930, 3227; GC-MS (EI), m/z (relative intensity) 200 (0.3) $[M]^+$, 158 (8), 143 (9), 125 (19), 100 (25), 85 (82), 71 (30), 58 (100), 43 (28); HRMS (EI, 70 eV) m/z calcd for $C_{12}H_{24}O_2$ $[M]^+$ 200.1777, found 200.1773.

5da: ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.86–1.62 (m, 20H), 2.38 (t, $J = 7.4$ Hz, 4H), 3.63 (t, $J = 6.3$ Hz, 2H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 13.9 (CH_3), 22.4 (CH_2), 23.5 (CH_2), 23.7 (CH_2), 25.5 (CH_2), 29.1 (CH_2), 31.3 (CH_2), 32.6 (CH_2), 42.7 (CH_2), 42.8 (CH_2), 62.9 (CH_2), 211.7 (C); IR (neat, cm^{-1}) 721, 1071, 1419, 1472, 1705, 2851, 2931, 3220; GC-MS (EI), m/z (relative intensity) 214 (0.3) $[M]^+$, 158 (8), 143 (10), 125 (21), 114 (25), 99 (49), 85 (22), 71 (100), 58 (68), 43 (96); HRMS (EI, 70 eV) m/z calcd for $C_{13}H_{26}O_2$ $[M]^+$ 214.1934, found 214.1927.

9ab: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29–1.59 (m, 10H), 1.79–1.95 (m, 4H), 3.76 (t, $J = 7.3$ Hz, 2H), 7.29–7.39 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.9 (CH_2), 28.7 (CH_2), 28.9 (CH_2), 35.8 (CH_2), 37.3 (CH_2), 120.8 (C), 127.2 (C), 128.0 (C), 129.0 (C), 135.9 (C); IR (neat, cm^{-1}) 700, 757, 1455, 1495, 2240, 2859, 2930; GC-MS (EI), m/z (relative intensity) 330 (70) $[M]^+$, 214 (17), 173 (29), 131 (63), 117 (100), 91 (75); HRMS (EI, 70 eV) m/z calcd for $C_{23}H_{26}N_2$ $[M]^+$ 330.2097, found 330.2090.

9af: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.33–1.48 (m, 6H), 1.79–1.90 (m, 4H), 3.74 (t, $J = 7.3$ Hz, 2H), 7.26–7.39 (m, 10H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 26.57 (CH_2), 26.59 (CH_2), 28.22 (CH_2), 28.24 (CH_2), 35.5 (CH_2), 37.2 (CH_2), 120.8 (C), 127.2 (C), 128.0 (C), 129.1 (C), 135.8 (C); IR (neat, cm^{-1}) 697, 757, 1455, 1493, 2240, 2861, 2949; GC-MS (EI), m/z (relative intensity) 302 (75) $[M]^+$, 275 (15), 156 (36), 117 (100), 91 (55); HRMS (EI) m/z calcd for $C_{21}H_{22}N_2$ $[M]^+$ 302.1784, found 302.1792.

9ah: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44–1.56 (m, 4H), 1.86–1.93 (m, 4H), 3.76 (t, $J = 7.2$ Hz, 2H), 7.29–7.39 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.3 (CH_2), 35.4 (CH_2), 37.2 (CH_2), 120.6 (C), 127.2 (C), 128.1 (C), 129.1 (C), 135.5 (C); IR (neat, cm^{-1}) 700, 759, 1455, 1491, 2240, 2861, 2926; GC-MS (EI), m/z (relative intensity) 288 (70) $[M]^+$, 260 (24), 145 (77), 117 (100), 91 (40); HRMS (EI) m/z calcd for $C_{20}H_{20}N_2$ $[M]^+$ 288.1627, found 288.1631. Anal. Found: C, 83.16; H, 6.94; N, 9.67%. Calcd for $C_{20}H_{20}N_2$: C, 83.30; H, 6.99; N, 9.71%.

9bf: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.33–1.47 (m, 6H), 1.78–1.89 (m, 4H), 2.33 (s, 6H), 3.70 (t, $J = 7.3$ Hz, 2H), 7.13 (s, 8H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 21.0 (CH_3), 26.57 (CH_2), 26.59 (CH_2), 28.3 (CH_2), 35.6 (CH_2), 36.8 (CH_2), 120.9 (C), 127.1 (C), 129.7 (C), 132.8 (C), 137.8 (C); IR (neat, cm^{-1}) 815, 1457, 1514, 2239, 2861, 2931; GC-MS (EI), m/z (relative intensity) 330 (86) $[M]^+$, 303 (38), 260 (14), 170 (44), 131 (100), 105 (81); HRMS (EI, 70 eV) m/z calcd for $C_{23}H_{26}N_2$ $[M]^+$ 330.2097, found 330.2090.

9cf: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.34–1.47 (m, 6H), 1.77–1.88 (m, 4H), 3.70 (t, $J = 7.3$ Hz, 2H), 3.78 (s, 6H), 6.87–7.22 (m, 8H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 26.6 (CH_2), 28.3 (CH_2), 35.6 (CH_2), 36.4 (CH_2), 55.3 (CH_3), 114.3 (C), 114.4 (C), 114.8 (C), 121.1 (C), 127.8 (C), 128.3 (C), 128.5 (C), 159.3 (C); IR (neat, cm^{-1}) 832, 1033, 1252, 1304, 1464, 1514, 2239, 2861, 2937; GC-MS (EI), m/z (relative intensity) 362 (38) $[M]^+$, 335 (46), 146 (100), 121 (37); HRMS (EI) m/z calcd for $C_{23}H_{26}N_2O_2$ $[M]^+$ 362.1995, found 362.1995.

9df: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.35–1.46 (m, 6H), 1.79–1.89 (m, 4H), 3.75 (t, $J = 7.3$ Hz, 2H), 7.22–7.35 (m, 8H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 26.50 (CH_2), 26.52 (CH_2), 28.16 (CH_2), 28.20 (CH_2), 35.40 (CH_2), 35.42 (CH_2), 36.65 (CH_2), 36.67 (CH_2), 120.3 (C), 128.6 (C), 129.3 (C), 134.0 (C), 134.3 (C); IR (neat, cm^{-1}) 827, 1094, 1465, 1493, 2241, 2862, 2933; GC-MS (EI), m/z (relative intensity) 370 (67) $[M]^+$, 343 (27), 207 (19), 190 (60), 151 (100), 125 (88); HRMS (EI) m/z calcd for $C_{21}H_{20}N_2Cl_2$ $[M]^+$ 370.1004, found 370.1005.

10af: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.35–2.03 (m, 9H), 3.59 (t, $J = 6.3$ Hz, 1H), 3.78 (t, $J = 7.4$ Hz, 2H), 7.27–7.40 (m, 5H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 25.1 (CH_2), 26.8 (CH_2), 32.3 (CH_2), 35.8 (CH_2), 37.3 (CH_2), 62.4 (CH_2), 120.9 (C), 127.2 (C), 128.0 (C), 129.1 (C), 135.9 (C); IR (neat, cm^{-1}) 700, 756, 1054, 1456, 1496, 2241, 2862, 2936, 3367; GC-MS (EI), m/z (relative intensity) 203 (3) $[M]^+$, 185 (32), 129 (100), 117 (60); HRMS (EI, 70 eV) m/z calcd for $C_{13}H_{17}NO$ $[M]^+$ 203.1311, found 203.1310.

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Supporting Information

^{1}H and ^{13}C NMR spectra of compounds **5**, **6**, **7**, and **9**. This material is available free of charge on the web at http://www.csj.jp/journals/bcsj/.

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