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Catalytic nucleophilic activation of acetonitrile via a cooperative catalysis of cationic Ru complex, DBU, and $NaPF_6$

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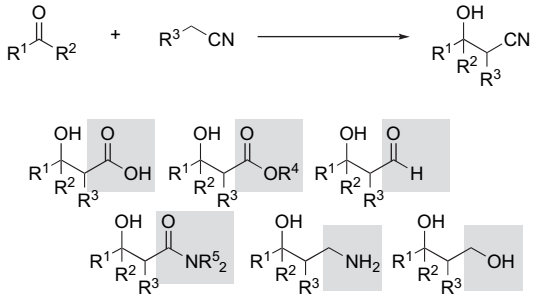
Dedicated to Professor Hisashi Yamamoto for his outstanding contribution to Lewis acid chemistry

Abstract—The development of an efficient catalytic system for the direct addition of acetonitrile under mild amine basic conditions is described. A cooperative catalysis of CpRu complex, DBU, and $NaPF_6$ enables chemoselective and catalytic generation of nucleophiles from barely acidic acetonitrile, which is integrated into the addition to aldehydes, imines, and activated ketones. Mechanistic investigations revealed that the three catalyst components work together to achieve high catalytic efficiency.

1. Introduction

Coupling of carbon nucleophiles and carbonyl compounds is a fundamental tool for the construction of carbon–carbon bonds in organic synthesis. Conventionally, preactivated carbon nucleophiles, such as metalated enolates or silicon-based nucleophiles, are widely utilized with concomitant formation of undesired waste.[1] Catalytic generation of carbon nucleophiles through proton transfer and subsequent integration into a carbon–carbon bond formation is now increasingly recognized as a more advantageous strategy because it provides a nearly ideal atom-economical process[2] with minimal waste generation. Over the last decade, there have been considerable advances in this area, making the use of pronucleophiles like ketones, aldehydes,[1b,3] and ester equivalents[4] fairly feasible. Alkylnitriles constitute a unique class of carbon pronucleophiles that are frequently utilized in various scenes of organic synthesis.[5] From the synthetic point of view, alkylnitriles are stable, easy to handle, and in the same oxidation state as carboxylic acid, which enables facile transformation into a range of functionalities (Scheme 1). The potential functional group interconversion of nitriles makes the alkylnitrile nucleophile a versatile synthon with wide functional potency. There have been few attempts to catalytically generate nucleophiles from alkylnitrile, however, likely because of its poor acidity (pK_a 31.3 in DMSO, 28.9 in H_2O)[6] except for much more acidic α-arylnitriles (pK_a ~21.9 in DMSO) or β-cyanocarbonyls (pK_a ~13 in DMSO).[7] Chemoselective deprotonation of much less acidic alkylnitrile over carbonyl compounds (pK_a ~15.7–16.9 in H_2O)[8] was indispensable to the direct catalytic addition of alkylnitrile to carbonyl compounds (Scheme 2, eq. 1). This type of reaction faces the dilemma of taking strong base or substrate generality; strong base causes undesirable reactions, whereas weak base fails deprotonation. Recent progress in this regard has been made by using strongly basic catalysts such as proazaphosphatrane[9] (pK_a of its conjugate acid ~34) or metal alkoxide[10] at the expense of substrate compatibility. A milder alternative remains to be developed. We hypothesized that catalytic chemoselective deprotonation of alkylnitrile could be realized by focusing on the soft Lewis basic nature of the nitrile functionality (Scheme 2). Upon exposure to a soft Lewis acid, alkylnitrile would predominantly coordinate over a carbonyl electrophile, which usually shows hard Lewis basicity ([A]). The acidity of a coordinated nitrile would then be sufficiently enhanced to be deprotonated by the amine base, which would leave the



Scheme 1. Coupling of alkylnitrile nucleophiles and carbonyl electrophiles, and further elaboration of nitrile functionality into a range of functional groups.

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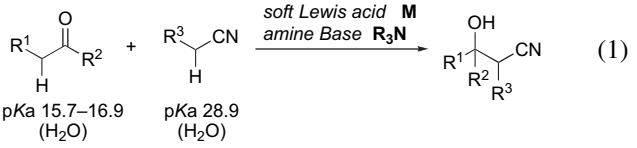
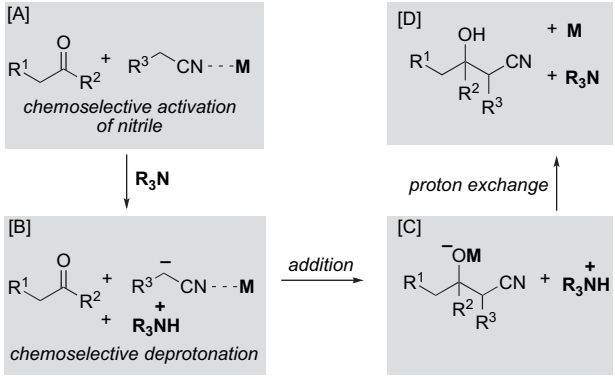




Scheme 2. Proposed catalytic cycle for the direct catalytic addition of alkylnitrile promoted by a soft Lewis acid–amine base combination.

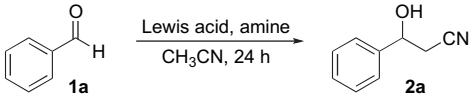
carbonyl electrophiles untouched ([B]). The addition of the thus generated α-cyano carbanion ([C]) and the following proton exchange give rise to β-hydroxynitrile and regeneration of the amine and Lewis acid catalyst ([D]).

On the basis of the scheme illustrated above, we developed a direct addition reaction of acetonitrile under amine basic conditions.[11] Herein, we report the full details of our approach toward catalytic nucleophilic activation of acetonitrile through cooperative catalysis of a cationic CpRu complex, DBU, and $NaPF_6$. Chemoselective coordination of acetonitrile to the CpRu complex renders chemoselective deprotonation of acetonitrile by DBU, with the more acidic carbonyl electrophile remaining intact, allowing for the addition of acetonitrile to carbonyl electrophiles. The basicity of the reaction media is sufficiently mild, thereby readily enolizable α,α-nonsubstituted aldehydes can be utilized as electrophiles.[11b] This chemistry was then elaborated by developing a solid phase protocol and addition to ketones. After our report,[11] Ozerov and Fan disclosed the catalytic addition of acetonitrile with a similar approach using a combination of Ni–PNP pincer ligand complex and DBU.[12]

2. Results and discussion

We set out our study with attempts to identify a suitable soft Lewis acid to activate the nitrile chemoselectively in the presence of carbonyl compounds. Although electrophilic activation of the nitrile with a soft Lewis acid is well established,[13] nucleophilic activation of a nitrile is relatively unexplored.[14] In the reaction of benzaldehyde (**1a**) and acetonitrile, various metal salts were evaluated using 2 equiv of DBU as a base (Table 1). Among the Lewis acids examined, the use of 50 mol % of cationic Cu, Pd, Ag, and Ru salts gave rise to the formation of the desired product **2a** at room temperature, whereas the reaction did not proceed catalytically in Lewis acids (entries 2–5). Ag(I) salts seemed to be reduced to Ag(0) during the reaction, suggesting that basic reaction media in the presence of aldehyde were not compatible with Ag(I) catalysis. $CpRu(CH_3CN)_3PF_6$ (**3a**)[15] gave **2a** in 23% yield and no catalytic turnover was observed. A monophosphine Ru complex, $CpRu(PPh_3)(CH_3CN)_2PF_6$ (**3b**), promoted the reaction in a catalytic manner based on the Lewis acid, possibly due to the increased stability of the Ru complex (entry 6). Less electron-rich phosphines like $P(C_6F_5)_3$ or P(2-furyl)$_3$ were expected to provide a more electrophilic Ru center with sufficient stability, but the reaction was completely prevented.[16] Less basic amines like Et_3N, Hünig's base, and pyridine were ineffective in this reaction (entries 7–9). Apparently, the deprotonation event posed the greatest barrier in this reaction, which could be overcome by raising the reaction temperature and the dielectric constant of the reaction media. The reaction at 50 °C in a CH_3CN/HMPA mixed solvent system with MS 4 Å enabled us to reduce the loading of **3b** to 10 mol % to afford **2a** in 84% yield (entry 11). Reducing the amount of DBU to 5 mol %,

Table 1. Direct addition of acetonitrile to benzaldehyde (**1a**) with soft Lewis acid and amine base combination



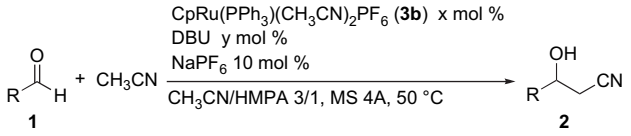
Entry	Lewis acid (mol %)	Amine (mol %)	$NaPF_6$ (mol %)	Temp (°C)	Yield (%)
1	None (—)	DBU (200)	0	rt	0
2	$Pd(CH_3CN)_4(BF_4)_2$ (50)	DBU (200)	0	rt	11
3	$Cu(CH_3CN)_4PF_6$ (50)	DBU (200)	0	rt	0
4[a]	$Ag(CH_3CN)_4BF_4$ (50)	DBU (200)	0	rt	14
5	$CpRu(CH_3CN)_3PF_6$ **3a** (50)	DBU (200)	0	rt	23
6	$CpRu(PPh_3)(CH_3CN)_2PF_6$ **3b** (50)	DBU (200)	0	rt	63
7	$CpRu(PPh_3)(CH_3CN)_2PF_6$ **3b** (50)	Et_3N (200)	0	rt	0
8	$CpRu(PPh_3)(CH_3CN)_2PF_6$ **3b** (50)	$^iPr_2NEt$ (200)	0	rt	0
9	$CpRu(PPh_3)(CH_3CN)_2PF_6$ **3b** (50)	Pyridine (200)	0	rt	0
10	$CpRu(PPh_3)(CH_3CN)_2PF_6$ **3b** (10)	DBU (200)	0	rt	40
11[b]	$CpRu(PPh_3)(CH_3CN)_2PF_6$ **3b** (10)	DBU (200)	0	50	84
12[b]	$CpRu(PPh_3)(CH_3CN)_2PF_6$ **3b** (5)	DBU (5)	0	50	46
13[b]	$CpRu(PPh_3)(CH_3CN)_2PF_6$ **3b** (5)	DBU (5)	10	50	93
14[b]	$CpRu(PPh_3)(CH_3CN)_2PF_6$ **3b** (5)	—	10	50	0
15[b]	None (—)	DBU 5	10	50	0

[a] Reaction was performed in the dark.
[b] Reaction was conducted in CH_3CN/HMPA (3:1) with MS 4 Å.

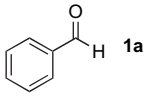
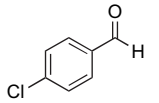
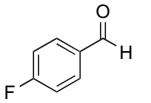
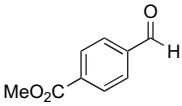
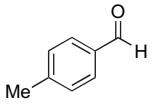
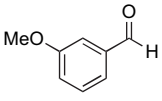
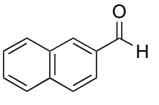
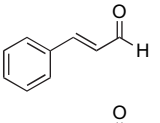
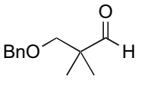
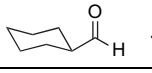
however, caused a significant decrease in the yield of **2a**, thus the reaction was virtually not catalytic in DBU (entry 12). The addition of 10 mol % of $NaPF_6$ significantly enhanced the catalytic turnover of DBU, allowing the reaction to reach completion with 5 mol % each of **3b** and DBU (entry 13). No reaction proceeded without **3b** or DBU (entries 1, 14, and 15), indicating that all three components, **3b**, DBU, and $NaPF_6$, were crucial to the present catalytic system. The conditions are supposed to be as mild as Masamune–Roush conditions for Horner–Wadsworth–Emmons reaction, in which LiCl and DBU are employed.[17]

Having identified a suitable catalytic system for the direct addition of acetonitrile under mild amine basic conditions, the substrate scope was examined with various aldehydes (Table 2). With 2.5–5 mol % of Ru complex **3b** and DBU, aromatic aldehydes bearing either electron-withdrawing or -donating substituents were smoothly converted to the desired product in high yield (entries 1–8). Ester functionality on the aromatic ring remained intact owing to the mild basicity of the reaction conditions (entry 5). The reaction proceeded in a 1,2-fashion exclusively with α,β-unsaturated aldehyde (entry 9). Sterically congested α,α-disubstituted aldehyde **1i** afforded the product in good yield, although a longer reaction time was necessary (entry 10). Cyclohexanecarboxaldehyde (**1j**), which was susceptible to self-aldol reactions under strongly basic conditions, was successfully transformed into the desired product in good yield.

Table 2. Direct addition of acetonitrile to aldehydes catalyzed by $CpRu(PPh_3)(CH_3CN)_2PF_6$ (**3b**), DBU, and $NaPF_6$

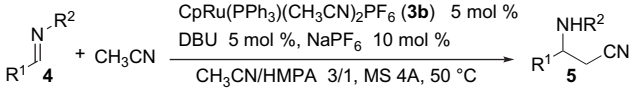


1 2

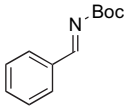
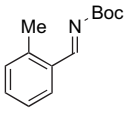
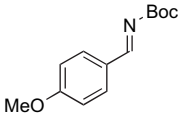
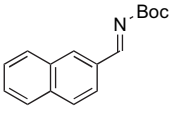
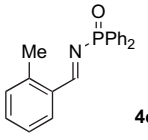
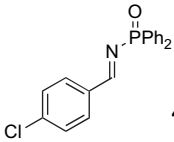
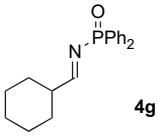
Entry	Aldehyde	3b (x)	DBU (y)	Time (h)	Yield (%)
1	 **1a**	5	5	24	93
2		2.5	2.5	24	91
3	 **1b**	5	5	24	93
4	 **1c**	5	5	24	91
5	 **1d**	5	5	24	82
6	 **1e**	5	5	48	82
7	 **1f**	5	5	24	88
8	 **1g**	5	5	40	92
9	 **1h**	5	5	36	84
10	 **1i**	5	5	48	77
11	 **1j**	5	10	48	82

The present catalytic system was further extended to the addition to imines to provide synthetically useful β-aminonitriles.[18] β-Aminonitrile constitutes a versatile synthon that is readily transformed into β-amino carboxylic acids and 1,3-diamines. Although aziridine opening reactions with cyanide are frequently utilized to access β-amino nitriles,[19] the addition of acetonitrile to imines provides a more straightforward protocol. The optimized reaction conditions were directly applied to the reaction with either *N*-Boc-[20] or *N*-diphenylphosphinoyl(Dpp)[21] imine **4**, affording the desired adducts **5** in high yield (Table 3). No desired product was

Table 3. Direct addition of acetonitrile to imines catalyzed by $CpRu(PPh_3)(CH_3CN)_2PF_6$ (**3b**), DBU, and $NaPF_6$



4 5

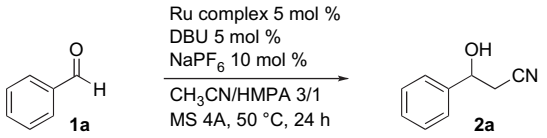
Entry	Imine	Time (h)	Yield (%)
1[a]	 **4a**	24	84
2	 **4b**	12	86
3	 **4c**	24	91
4[a]	 **4d**	48	79
5	 **4e**	48	81
6	 **4f**	48	86
7	 **4g**	24	—

[a] 10 mol % of DBU was used.

isolated in a reaction with aliphatic *N*-Dpp-imine, probably due to the isomerization of imine to the corresponding enamine (entry 7). To the best of our knowledge, this is the first example of a direct catalytic addition of acetonitrile to imines.[11a]

In the present catalytic system, all three catalyst components, Ru complex **3b**, DBU, and $NaPF_6$, work together to render catalytic deprotonative activation of acetonitrile under amine basic conditions. To gain insights into the cooperative catalysis by the catalytic triad, detailed mechanistic investigations were performed. During the course of the reaction at 50 °C, a gradual shift of monophosphine complex **3b** into diphosphine complex **3c** was observed. Thus, the catalytic performance of Ru complexes was reexamined (Table 4). The parent complex **3a** turned out to be virtually ineffective as a catalyst likely due to its instability under the reaction conditions, although a substoichiometric amount of **3a** promoted the reaction to some extent. As the catalytic activity of diphosphine complex **3c** was comparable to that of **3b**, transformation of **3b** into **3c** was not critical to the overall catalytic efficiency. The ^1H and ^{13}C NMR chemical shifts at the methyl terminus of acetonitrile bound to the Ru center of **3b** and **3c** exhibited a downfield shift, compared with those of unbound acetonitrile (Fig. 1). In addition, ESI-MS and NMR studies indicated that benzaldehyde (**1a**) and HMPA barely coordinated to Ru, suggesting that the Ru complex works as a chemoselective soft Lewis acid to make acetonitrile susceptible to deprotonation.[22] A plausible catalytic cycle in the absence of $NaPF_6$ is depicted in Scheme 3. The acidity of the Ru-bound acetonitrile would be sufficiently enhanced to be deprotonated by free DBU to afford Ru complex **6** bearing a metalated acetonitrile.[23] The initial rate kinetics revealed that there was a first-order rate dependency on the Ru complex and DBU, whereas the concentration of aldehyde had no impact on the reaction.[24] Along with the substantial kinetic isotope effect (k_H/k_D=5.6) observed in the attempted reaction with

Table 4. Direct addition of acetonitrile to benzaldehyde (**1a**) catalyzed by CpRu complexes **3a**–**3c**



Entry	CpRu complex	Yield (%)
1	$CpRu(CH_3CN)_3PF_6$ **3a**	0
2	$CpRu(PPh_3)(CH_3CN)_2PF_6$ **3b**	93
3	$CpRu(PPh_3)_2(CH_3CN)PF_6$ **3c**	91

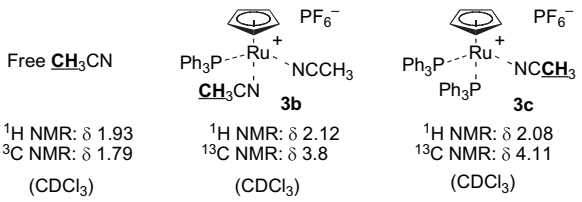
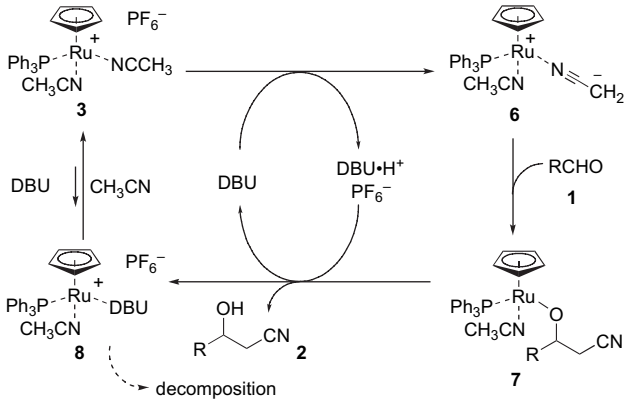


Figure 1. Chemical shifts of methyl terminus of acetonitrile on ^1H and ^{13}C NMR spectroscopy.



Scheme 3. Proposed catalytic cycle without $NaPF_6$.

$CpRu(PPh_3)(CD_3CN)_2PF_6$ (**3b**-d_6) in CD_3CN/HMPA (Fig. 2),[24] the deprotonation stage is most likely the rate-determining step. The subsequent addition of metalated acetonitrile to aldehyde afforded Ru–alkoxide **7**. In the absence of $NaPF_6$, a proton exchange between **7** and $DBU\cdot H^+PF_6^-$ liberated product **2** and the following ligand exchange from Ru–DBU complex **8** to **3b** completed the catalytic cycle.

To clarify the beneficial effect of $NaPF_6$, the reaction profile was traced under three different conditions; (i) without $NaPF_6$, (ii) with 10 mol % of $NaPF_6$, and (iii) with 10 mol % of Me_4NPF_6 (Fig. 3). With 10 mol % of $NaPF_6$, the reaction reached completion in approximately 24 h, whereas without $NaPF_6$ the reaction deteriorated significantly at an early stage. The ineffectiveness of Me_4NPF_6 clearly showed that Na cation was responsible for the high catalytic efficiency. Of particular note is that the difference in the initial rate of these three conditions was relatively small, implying that $NaPF_6$ served to increase the catalyst longevity rather than the reaction rate. This is consistent with the observation that the yellow reaction mixture turned quickly to dark brown in the absence of $NaPF_6$, which was likely due to decomposition of the Ru complex accompanied by the formation of $Ph_3P{=}O$.[25] ESI-MS and NMR analyses of the mixture of the Ru–monophosphine complex **3b** and DBU in CH_3CN without aldehyde and $NaPF_6$ indicated that DBU coordinates to the Ru center to give Ru–DBU complex **8**, although equilibrium strongly favored **3b** rather than **8** (Scheme 3).[22] On the other hand, the formation of **8** was significantly facilitated in the presence of aldehyde **1a** without $NaPF_6$.[26] Assuming that the dissociated pathway is predominant for the ligand exchange of the CpRu complex, the protonation of Ru–alkoxide **7** with $DBU\cdot H^+PF_6^-$ was accompanied by ligand exchange to preferentially afford Ru–DBU complex **8** (Scheme 3).[27] Considering the so-called piano-stool type coordination mode of the CpRu complex, coordinated DBU is positioned too far away to effect deprotonation intramolecularly. Therefore, the accumulation of Ru–DBU complex **8** decreased the effective concentration of free DBU available for deprotonation. In addition, **8** was relatively unstable and thereby decomposed with the concomitant formation of Ru black and $Ph_3P{=}O$,[25] resulting in low catalyst efficiency (Table 1, entry 12). In contrast, ^{31}P NMR study revealed that the presence of $NaPF_6$ significantly suppressed the formation of Ru–DBU complex **8** during the reaction and the yellow color of the

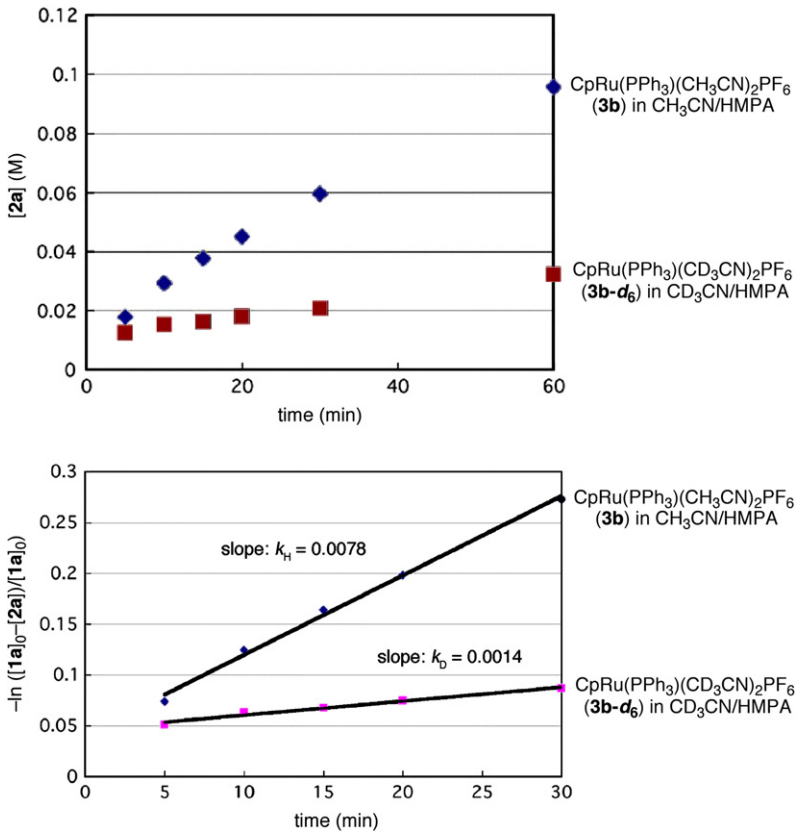


Figure 2. *Top*: reaction profile at an early stage of the reaction using **3b** in CH_3CN/HMPA or **3b**-d_6 in CD_3CN/HMPA. *Bottom*: plot of $-\ln([\mathbf{1a}]_0-[\mathbf{2a}])/[\mathbf{1a}]_0)$ versus reaction time, where $[\mathbf{1a}]_0$ and [**2a**] are the initial concentration of **1a** and the concentration of **2a**, respectively.

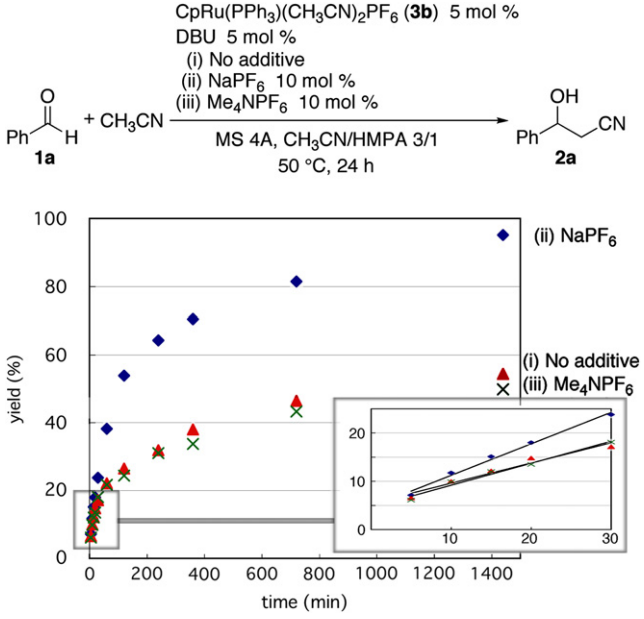
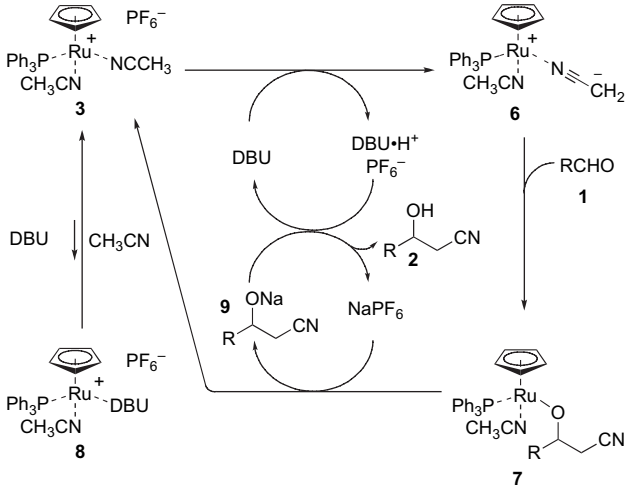


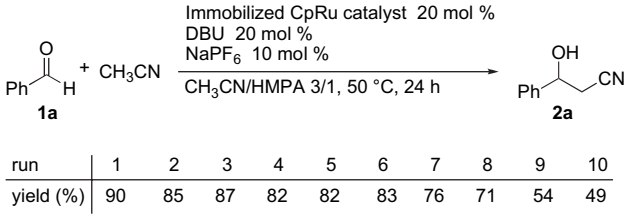
Figure 3. Direct addition of acetonitrile to **1a** under three different conditions; (i) without additive, (ii) with 10 mol % of $NaPF_6$, and (iii) with 10 mol % Me_4NPF_6. (a) Reaction profile: 0–24 h. (b) Reaction profile: 0–30 min.



Scheme 4. Proposed catalytic cycle with $NaPF_6$.

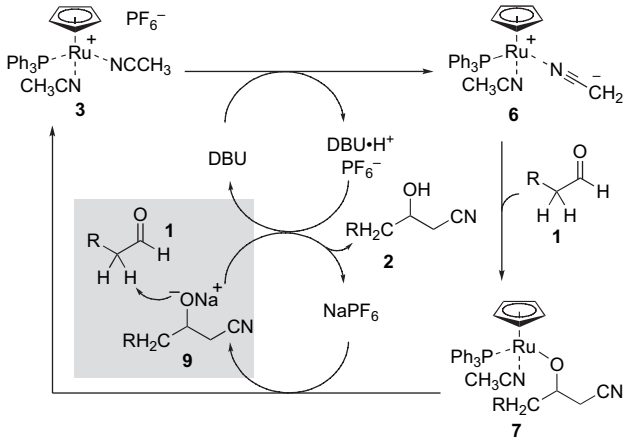
catalyst was maintained for a much longer time. The following bypassing pathway would be in accordance with the observed beneficial effect of $NaPF_6$ (Scheme 4). An obvious soft–hard mismatch between a soft Ru Lewis acid and a hard alkoxide would induce a rapid cation exchange between Ru–alkoxide **7** and $NaPF_6$ to give initial complex **3b** and Na alkoxide **9**, avoiding the formation of **8**. Na alkoxide **9** would eventually afford the product via proton exchange with $DBU{\cdot}H^+PF_6^-$. All three components of the catalytic triad of the Ru complex, DBU, and $NaPF_6$ work cooperatively to efficiently activate acetonitrile and exhibit a high catalytic turnover, allowing the reaction to complete with 5 mol % catalyst loading.

A logical extension of the present catalyst system is immobilization of the Ru complex on a solid support. Immobilization leads to both stabilization and reuse of the Ru complex, which is the most vulnerable and expensive among the catalyst components. Solid supports elaborated with a phosphine functionality are readily available. Among the solid supports initially screened, *JandaJel*™ with PPh_2 emerged as a nearly ideal polymer.[28] Addition of the colorless *JandaJel*™-PPh_2 (100 mg, 0.2–0.3 P/mmol) in yellow CH_2Cl_2 solution of $CpRu(CH_3CN)_3PF_6$ and 30 min of shaking at room temperature afforded a colorless solution and a yellow polymer, which was collected by filtration and washed with CH_3CN. Mass balance after drying indicated almost complete loading of the Ru complex on the solid support. The thus obtained polymer-supported Ru catalyst was evaluated in a reaction with benzaldehyde (**1a**). Because MS 4 Å, which was essential to reduce the catalyst loading, was not compatible with these particular reaction conditions, 20 mol % of the polymer-supported catalyst, 20 mol % of DBU, and $NaPF_6$ were employed in a CH_3CN/HMPA mixed solvent system. The reaction under vigorous shaking at 50 °C for 24 h afforded the product **2a** in 90% yield and the Ru catalyst was recovered by simple filtration. The recovered catalyst exhibited comparable catalytic activity for at least six cycles (Scheme 5).



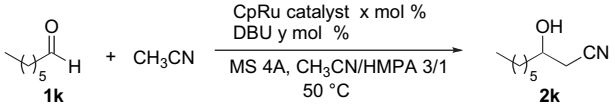
Scheme 5. Direct addition of acetonitrile with immobilized Ru catalyst.

Our attention was next directed toward the reaction with enolizable α,α-nonsubstituted aldehydes,[11b] which were notoriously highly susceptible to self-condensation under basic conditions. We anticipated that our strategy of chemoselective activation of nitrile with the Ru complex–DBU combination would address this issue to effect the deprotonation of acetonitrile while leaving the more acidic, enolizable aldehyde untouched. In the reaction with heptanal (**1k**) as a representative α,α-nonsubstituted aldehyde, DBU itself promoted neither self-condensation of **1k** nor the desired reaction, indicating the feasibility that chemoselective deprotonation occurs in combination with the Ru complex (Table 5, entry 1). As expected, with 10 mol % of monophosphine Ru complex and 50 mol % of DBU, the desired reaction proceeded through chemoselective activation of acetonitrile to give **2k** in modest yield (54%) with little formation of the self-condensation product (entry 2). As suggested by the mechanistic study, 10 mol % of $NaPF_6$ was employed to bring about a higher catalytic efficiency in entry 3. The yield of desired product **2k**, however, decreased to 34% along with substantial formation of the self-condensation product. We ascribed the inferior effect of $NaPF_6$ to the possibility that the Na alkoxide generated in situ was basic enough to trigger the undesirable deprotonation of the aldehyde **1**, allowing a much higher fraction of aldehyde to undergo self-condensation (Scheme 6). To avoid the self-condensation as well as the formation of the Ru–DBU complex, we focused on the use of diphosphine complex **3c**, which exhibits similar catalytic efficiency as monophosphine complex **3b** (Table 4), and its acquired steric constraint around the Ru center might make the coordination of DBU less likely.[29] In line with this expectation, ESI-MS analysis revealed that the formation of the Ru–DBU complex was much less favorable[22] with the diphosphine complex and yield was improved to 64% with 10 mol % catalyst loading (entry 4). Slow addition of aldehyde to keep the concentration of aldehyde low further improved the chemical yield to 82% (entry 5).[30] The amount of DBU can be reduced to 25 mol % with comparable chemical yield (entry 6).



Scheme 6. Self-condensation of enolizable aldehyde by in situ generated Na alkoxide.

Table 5. Direct addition of acetonitrile to heptanal (**1k**) with CpRu complex **3** and DBU



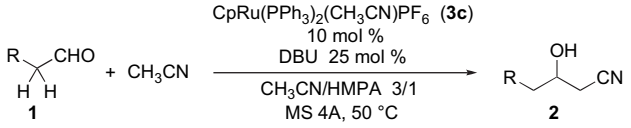
Entry	CpRu complex	CpRu catalyst (*x*)	DBU (*y*)	$NaPF_6$ (mol %)	Time (h)	Yield (%)
1	None	—	50	0	24	0
2	$CpRu(PPh_3)(CH_3CN)_2PF_6$ **3a**	10	50	0	24	54
3	$CpRu(PPh_3)(CH_3CN)_2PF_6$ **3a**	10	50	10	24	38
4	$CpRu(PPh_3)_2(CH_3CN)PF_6$ **3b**	10	50	0	10	64
5[a]	$CpRu(PPh_3)_2(CH_3CN)PF_6$ **3b**	10	50	0	10	82
6[a]	$CpRu(PPh_3)_2(CH_3CN)PF_6$ **3b**	10	25	0	10	76

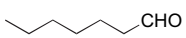
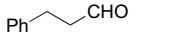
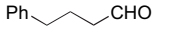
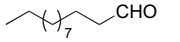
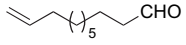
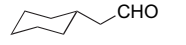
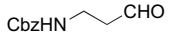
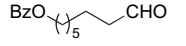
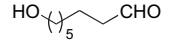
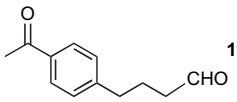
[a] Aldehyde **1k** was added over 7 h via syringe drive.

With suitable reaction conditions for enolizable aldehydes in hand, the reaction was performed with various α,α-nonsubstituted aldehydes (Scheme 6).[31] By using 10 mol % of diphosphine Ru complex **3c** and 25–50 mol % of DBU, modest to good chemical yield was achieved with broad functional group compatibility. In entries 1–6, chemoselective deprotonation of acetonitrile and the subsequent addition to aldehydes **1k**–**1t** proceeded smoothly to give the desired adduct in 63–90% yield. 10-Undecenal (**1o**) afforded only modest yield, possibly due to an unfavorable interaction between the unsaturated bond of **1o** and the Ru catalyst (entry 7). Amide and ester functionalities remained intact to furnish the desired adduct in good yield (entries 8 and 9). The reaction proceeded smoothly with aldehydes bearing a free hydroxyl group, which is not compatible with the reaction using metalated nitriles (entry 10). A methyl ketone moiety of aldehyde **1t** served neither as an electrophile nor as a pronucleophile under the reaction conditions, affording the desired β-hydroxynitrile in 75% yield (entry 11). Treatment of **1m** or **1t** with 10 mol % of KO^{t}Bu at 0 °C gave rise to a complicated reaction mixture, highlighting the highly chemoselective nature of the present catalysis (Table 6).

The use of ketones as electrophiles next prompted our interest, because they afford synthetically useful β-cyano tertiary alcohols. Addition to ketones is often hampered due to their low reactivity, originating from both steric and electronic factors. The unique linear structure of the acetonitrile nucleophile would be advantageous to minimize the steric barrier. Although metalated nitrile or trimethylsilylacetonitrile

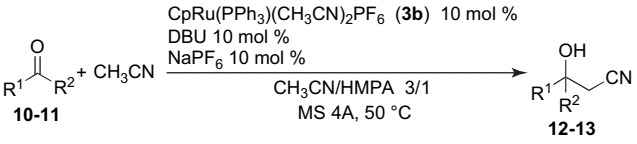
Table 6. Direct addition of acetonitrile to enolizable aldehydes catalyzed by $CpRu(PPh_3)_2(CH_3CN)PF_6$ (**3c**) and DBU[a]

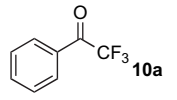
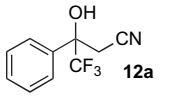
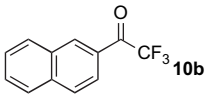
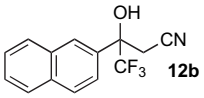
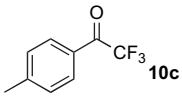
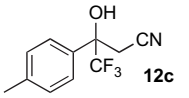
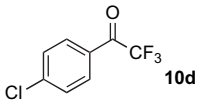
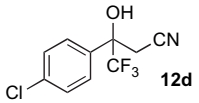
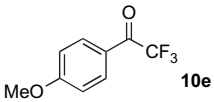
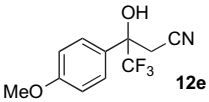
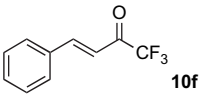
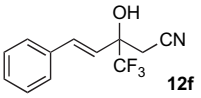
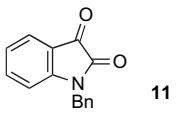
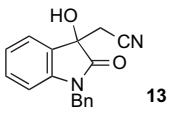


Entry	Aldehyde		Product	Time (h)	Yield (%)
1		**1k**	**2k**	10	76
2[b]			**2k**	10	82
3[b]		**1l**	**2l**	10	77
4		**1m**	**2m**	10	86
5[c]		**1n**	**2n**	16	85
6		**1o**	**2o**	24	63
7		**1p**	**2p**	14	90
8		**1q**	**2q**	10	74
9		**1r**	**2r**	14	82
10[d]		**1s**	**2s**	12	87
11		**1t**	**2t**	10	75

[a] Aldehyde was added over 7 h via syringe drive.
[b] 50 mol % of DBU was used.
[c] Aldehyde was added over 12 h via syringe drive.
[d] Aldehyde was added as HMPA solution.

Table 7. Direct addition of acetonitrile to trifluoromethylketones **10** and *N*-Bn isatin **11** catalyzed by $CpRu(PPh_3)(CH_3CN)_2PF_6$ (**3b**), DBU, and $NaPF_6$



Entry	Ketone	Product	Time (h)	Yield (%)
1	 **10a**	 **12a**	48	68
2	 **10b**	 **12b**	48	74
3	 **10c**	 **12c**	36	77
4	 **10d**	 **12d**	48	63
5	 **10e**	 **12e**	48	81
6	 **10f**	 **12f**	48	71
7	 **11**	 **13**	48	75

enables addition to ketones,[10a,32] the direct catalytic addition of alkylnitrile is not well investigated and is still a formidable challenge.[33] Recently, compounds bearing a CF_3 group have been the subject of growing interest from both chemical and biological community for their characteristic chemical properties and medicinal use.[34] Thus, we conducted the reaction with various trifluoromethylketones under the optimized conditions with $NaPF_6$.[35] Using 10 mol % each of Ru, DBU, and $NaPF_6$, the desired reaction proceeded smoothly to furnish α-trifluoromethyl-β-cyano tertiary alcohols in modest to good yield (Table 7).[36] Both aromatic ketones with an electron-withdrawing and -donating group provided the desired tertiary alcohol **12** (entries 4 and 5). Exclusive 1,2-addition was observed in the reaction with α,β-unsaturated ketone **10f** (entry 6). *N*-Bn isatin **11** was also found to be a suitable substrate for the present catalysis to give tertiary alcohols with an oxindole skeleton **13** (entry 7).

3. Conclusion

In summary, we developed a direct catalytic addition reaction of acetonitrile to carbonyl compounds and imines through chemoselective, nucleophilic activation of nitrile

functionality by the catalytic triad of cationic Ru complex, DBU, and $NaPF_6$. Mechanistic studies disclosed that the three catalyst components work together to achieve deprotonation of the α-hydrogen of nitrile under mild amine basic conditions with a high catalytic efficiency. The high chemoselectivity of the present catalysis is illustrated by the broad functional group tolerance of electrophiles. Facile reuse of the polymer-supported Ru catalyst is of significant importance from a practical point of view. This work holds considerable potential toward the development of an enantioselective variant with a rationally elaborated chiral Ru catalyst, which will be addressed in due course.

4. Experimental

4.1. General remarks

Infrared (IR) spectra were recorded on a JASCO FTIR 410 Fourier transform infrared spectrophotometer. NMR spectra were recorded on a JEOL JNM-LA500 spectrometer, operating at 500 MHz for ^1H NMR, 125.65 MHz for ^{13}C NMR, and 470.65 MHz for ^{19}F NMR. Chemical shifts in $CDCl_3$ were reported downfield from TMS (=0) or in the scale relative to $CHCl_3$ (7.24 ppm) for ^1H NMR. For ^{13}C NMR, chemical shifts were reported in the scale relative to $CHCl_3$ (77.0 ppm for ^{13}C NMR) as an internal reference. Chemical shifts in CD_3CN were reported in the scale relative to CH_3CN (1.93 ppm) for ^1H NMR. For ^{13}C NMR, chemical shifts were reported in the scale relative to CH_3CN (1.3 ppm for ^{13}C NMR) as an internal reference. Chemical shifts for ^{31}P NMR were reported in the scale relative to 85% phosphoric acid as an external standard. FAB mass spectra were measured on JEOL JMS-MS700V. ESI mass spectra were measured on Waters-ZQ4000. Column chromatography was performed with silica gel Merck 60 (230–400 mesh ASTM). Acetonitrile was distilled from CaH_2. $Cu(CH_3CN)_4PF_6$, $Pd(CH_3CN)_4(BF_4)_2$, $Ag(CH_3CN)_4BF_4$, and *JandaJel*™–PPh_3 were purchased from Aldrich and used as received. $CpRu(CH_3CN)_3PF_6$ was prepared as reported in the literature (Ref. 15c). Alternatively, $CpRu(CH_3CN)_3PF_6$ is commercially available from Strem Chemicals, Inc. (Cat. No. 44-7870) and used as received. The activity difference between prepared complex and purchased one is negligible. Aldehydes were distilled by usual method. *N*-Dpp- and *N*-Boc-protected imines were prepared as reported in the literature (Ref. 20 and 21a).

4.1.1. Preparation of acetonitrile solution of $CpRu(PPh_3)(CH_3CN)_2PF_6$ (3b).

4.1.1.1. $CpRu(PPh_3)(CH_3CN)_2PF_6$ (3b). A flame-dried flask was charged with $CpRu(CH_3CN)_3PF_6$ (**3a**) (21.7 mg, 0.05 mmol) and PPh_3 (13.1 mg, 0.05 mmol) under Ar. To the flask was added dry acetonitrile (833 μL) and stirred for 1 h at room temperature. The resulting 0.06 M CH_3CN solution of $CpRu(PPh_3)(CH_3CN)_2PF_6$ (**3b**) was used as catalyst.

4.1.1.2. $CpRu(PPh_3)_2(CH_3CN)PF_6$ (3c). A flame-dried flask was charged with $CpRu(CH_3CN)_3PF_6$ (**3a**) (50 mg, 0.115 mmol) and PPh_3 (60.4 mg, 0.23 mmol) under Ar. To the mixture was added $CDCl_3$ (2.0 mL) and the resulting yellow solution was stirred at 50 °C for 2 h. The formation of diphosphine complex **3c** was confirmed by ^1H NMR analysis of small aliquot of the reaction mixture. The solvent was removed under reduced pressure and dry CH_3CN was refilled to the resulting residue to give 0.06 M CH_3CN solution of **3c**.

4.1.2. Representative procedure for the preparation of β-hydroxynitrile and β-aminonitrile (RP1) (Tables 2 and 3).

A 20 mL test tube was charged with magnetic stirrer bar and MS 4 Å (240 mg) under Ar. MS 4 Å was flame-dried under reduced pressure (~0.7 kPa) for 5 min. After cooling, to the flask were added $NaPF_6$ (150 μL, 0.03 mmol, 0.2 M/CH_3CN), $CpRu(PPh_3)(CH_3CN)_2PF_6$ (**3a**) (250 μL, 0.015 mmol, 0.06 M/CH_3CN), dry CH_3CN (90 μL), and HMPA (200 μL) successively under Ar and stirred at room temperature. To the mixture was added benzaldehyde (**1a**) (30 μL, 0.3 mmol) at the same temperature, and resulting mixture was degassed by three cycles of freeze-pump-thaw process. After warming up to room temperature, DBU (30 μL, 0.015 mmol, 0.5 M/CH_3CN) was added and stirred at 50 °C. After stirring for 24 h, the mixture was quenched with 1 M HCl and extracted with ether. The combined organic layers were washed with satd $NaHCO_3$ aq and brine, and then dried over Na_2SO_4. The organic solvent was evaporated and resulting crude mixture was purified by flash column chromatography (SiO_2, eluent: hexane/ethyl acetate 4:1) to give **2a** (39.2 mg, 0.28 mmol, 93% yield) as a colorless oil.

4.1.3. Representative procedure for the preparation of β-hydroxynitrile from enolizable aldehyde (RP2) (Table 5).

A test tube was charged with magnetic stirrer bar and MS 4 Å (240 mg) under Ar. MS 4 Å was flame-dried under reduced pressure (ca. 0.7 kPa) for 5 min. After cooling, to the flask were added $CpRu(PPh_3)_2(CH_3CN)PF_6$ (**3b**) (500 μL, 0.03 mmol, 0.06 M/CH_3CN), dry CH_3CN (100 μL) and HMPA (200 μL) successively under Ar and stirred at room temperature. To the mixture was added DBU (11.2 μL, 0.075 mmol) at room temperature, and resulting mixture was degassed by three cycles of freeze-pump-thaw process. After warming up to 50 °C, heptanal (**1k**) (42.3 μL, 0.3 mmol) was added over 7 h via syringe drive. After stirring for 24 h at 50 °C, the mixture was quenched with 1 M HCl and extracted with diethyl ether. The combined organic layers were washed with satd $NaHCO_3$ aq and brine, then dried over Na_2SO_4. The organic solvent was evaporated and resulting crude mixture was purified by flash column chromatography (SiO_2, eluent: hexane/ethyl acetate 4:1) to give **2k** (35.3 mg, 0.227 mmol, 76% yield) as a colorless oil.

4.1.4. Representative procedure for the preparation of β-hydroxynitrile from ketone (RP3) (Table 7).

A 20 mL test tube was charged with magnetic stirrer bar and MS 4 Å (400 mg) under Ar. MS 4 Å was flame-dried under reduced pressure (~0.7 kPa) for 5 min. After cooling, to the flask were added $NaPF_6$ (100 μL, 0.05 mmol, 0.5 M/CH_3CN), $CpRu(PPh_3)(CH_3CN)_2PF_6$ (**3b**) (500 μL, 0.05 mmol, 0.1 M/CH_3CN), and HMPA (233 μL) successively under Ar and the resulting mixture was stirred at room temperature. To the mixture was added α,α,α-trifluoroacetophenone (**10a**) (70.2 μL, 0.5 mmol) at the same temperature, and resulting mixture was degassed by three cycles of freeze-pump-thaw process. After warming up to room temperature, DBU (100 μL, 0.05 mmol, 0.5 M/CH_3CN) was added and stirred

at 50 °C. After stirring for 24 h, the mixture was quenched with 1 M HCl and extracted with ether. The combined organic layers were washed with satd $NaHCO_3$ aq and brine, and then dried over Na_2SO_4. The organic solvent was evaporated and resulting crude mixture was purified by flash column chromatography (SiO_2, eluent: hexane/ether 4:1 to 2:1) to give **12a** (73.3 mg, 0.34 mmol, 68% yield) as a colorless solid.

4.1.5. Reaction with immobilized Ru catalyst. To a 20 mL test tube, 100 mg (0.2–0.3 mmol phosphine) of *JandaJel*™-PPh_3(70–90 mesh, 2% cross-linked, 2–3 mmol phosphine/g) was placed under Ar. To the flask, dry CH_2Cl_2 (2.0 mL) was added and the resulting mixture was shaken (around 200 rpm) at room temperature for 1 h to swell the *jel*. At this stage, the white jel was floating in CH_2Cl_2 solvent. To the mixture, $CpRu(CH_3CN)_3PF_6$ (**3a**) (43.4 mg, 0.01 mmol) was added and the resultant yellow solution was shaken (around 200 rpm) at the same temperature. After 30 min of shaking, the CH_2Cl_2 solution became colorless and yellow jel sank to the bottom of the test tube. The mixture was filtered off and washed with dry CH_2Cl_2 twice. The resulting yellow jel was dried under vacuum at room temperature to give 138.9 mg of $CpRu(CH_3CN)_3PF_6$ supported jel. Based on the calculation, 0.1 mmol of **3a**–CH_3CN: 39.3 mg (assuming one phosphine coordinates to one Ru), almost all of the CpRu complex was immobilized on the jel.

4.1.5.1. Procedure of the direct addition of acetonitrile with immobilized Ru catalyst. To a 20 mL test tube, CpRu immobilized jel prepared above (138.9 mg, 0.1 mmol CpRu complex) was placed and dried under vacuum for 1 h at room temperature. To the flask, Ar gas was refilled and HMPA (600 μL) was added. The resulting mixture was shaken (around 200 rpm) at room temperature to swell the jel. After 1 h, $NaPF_6$/CH_3CN (250 μL, 0.2 M, 0.05 mmol), CH_3CN (350 μL), benzaldehyde (**1a**) (50 μL, 0.5 mmol), and DBU (15 μL, 0.1 mmol) were successively added to the mixture. The resulting mixture was shaken (around 200 rpm) at 50 °C for 24 h. Then the mixture was diluted with ethyl acetate and filtered off to collect the jel, and the filtrate was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (SiO_2) to give **2a** as a colorless oil in 90% yield (66.1 mg). Further reaction cycles were conducted by analogous procedure using collected jel.

4.1.6. Procedures for initial rate kinetic study.

4.1.6.1. Initial rate kinetics on DBU. A 20 mL test tube was charged with magnetic stirrer bar and MS 4 Å (80 mg) under Ar. MS 4 Å was flame-dried under reduced pressure (~0.7 kPa) for 5 min. After cooling, to the flask were added $NaPF_6$ (50 μL, 0.01 mmol, 0.2 M/CH_3CN), $CpRu(PPh_3)(CH_3CN)_2PF_6$ (**3b**) (83 μL, 0.005 mmol, 0.06 M/CH_3CN), dry CH_3CN (52 μL), and HMPA (200 μL) successively under Ar and stirred at room temperature. To the mixture was added benzaldehyde (**1a**) (10 μL, 0.1 mmol) at the same temperature, and resulting mixture was degassed by three cycles of freeze-pump-thaw process. After warming up to room temperature, a solution of DBU (5 μL, 0.0025 mmol, 0.5 M/CH_3CN, DBU: 2.5 mol % condition) was added and stirred at 50 °C. After stirring for each specified period, the mixture was diluted with 5 mL of hexane/ethyl acetate 1:1 and passed through short pad of silica gel with hexane/ethyl acetate 1:1 as eluent. The organic solvent was evaporated and the resulting residue was analyzed by ^1H NMR spectroscopy to determine chemical yield with $Me_3SiSiMe_3$ as internal standard. Monitoring was performed with four different DBU concentrations (2.5, 5.0, 7.5, and 10.0 mol %). The slope in the plot of ln v versus ln[DBU] is 1.09, suggesting first-order rate dependency on DBU, where v and [DBU] are the reaction rate and the concentration of DBU, respectively.

Initial rate kinetics on Ru complex $CpRu(PPh_3)(CH_3CN)_2PF_6$ (**3a**) was carried in a similar way as described above. Monitoring was performed with three different **3a** concentrations (1.0, 2.5, and 5.0 mol %). The slope in the plot of ln v versus ln[**3a**] is 0.64, suggesting **3a** would be involved in rate-determining step, where v and [**3a**] are the reaction rate and the concentration of **3a**, respectively.

Initial rate kinetics on **1a** was carried in a similar way as described above. Monitoring was performed with four different **1a** concentrations (0.05, 0.075, 0.10, and 0.125 mmol). The slope in the plot of ln v versus ln[**1a**] is 0.04, suggesting **1a** would be hardly involved in rate-determining step.

4.1.7. Kinetic isotope effect.

4.1.7.1. $CpRu(PPh_3)(CD_3CN)_2PF_6$ (3b-d_6). The parent complex **3a** (21.7 mg, 0.05 mmol) was dissolved in CD_3CN (800 μL) and the resulting solution was stirred at room temperature for 8 h, followed by the evaporation of the solvent afforded yellow solid of **3a**-d_9 (22.0 mg) exclusively. Treatment of **3a**-d_9 (22.0 mg, 0.05 mmol) with 1 equiv of PPh_3 (13.1 mg, 0.05 mmol) in CD_3CN (833 μL) at room temperature for 30 min gave the CD_3CN solution of **3b**-d_6. The 0.06 M CD_3CN solution of **3b**-d_6 thus obtained was used as Ru catalyst.

The reaction procedure was similar to that of Section 4.1.5. The reaction profiles of normal and deuterated conditions are shown in Figure 2. For small fractional conversions assuming that we have pseudo-first-order reaction conditions, the rate law for the conversion of **1a** to **2a** can be obtained as $d[\mathbf{1a}]/[\mathbf{1a}]=-k\,dt$, where [**1a**] and k are concentration of **1a** and the rate constant, respectively. Assuming that $[\mathbf{1a}]=([\mathbf{1a}]_0-[\mathbf{2a}])$, the equation above can be expressed as $d([\mathbf{1a}]_0-[\mathbf{2a}])/([\mathbf{1a}]_0-[\mathbf{2a}])=-k\,dt$. After integration, $\ln(([\mathbf{1a}]_0-[\mathbf{2a}])/[\mathbf{1a}]_0)=-kt$ has been obtained, where $[\mathbf{1a}]_0$ and $[\mathbf{2a}]$ are initial concentration of **1a** and the concentration of **2a**, respectively. A plot of $-\ln(([\mathbf{1a}]_0-[\mathbf{2a}])/[\mathbf{1a}]_0)$ versus t (Fig. 2 (bottom)) gives a slope of k, an observed constant. If k_H is the observed constant for the reaction with $CpRu(PPh_3)(CH_3CN)_2PF_6$ (**3b**) in CH_3CN, and k_D is the corresponding constant for the reaction with $CpRu(PPh_3)(CD_3CN)_2PF_6$ (**3b**-d_6) in CD_3CN, the kinetic isotope effect can be calculated as a ratio of k_H/k_D. From Figure 2, $k_H/k_D=0.0078/0.0014=5.6$.

4.1.8. Na cation effect. The reaction profiles under three kinds of reaction conditions ((i) without additive, (ii) with 10 mol % of $NaPF_6$, and (iii) with 10 mol % of Me_4NPF_6) were examined using 5 mol % each of Ru catalyst **3b** and DBU. The procedure is similar to that described in Section 4.1.5. The chemical yield was estimated by ^1H NMR analysis ($Me_3SiSiMe_3$ was used as internal standard) of each reaction mixture, which was quenched at each specified period.

4.1.9. Spectral data.

4.1.9.1. 3-Hydroxy-3-(2-naphthyl)-3-(trifluoromethyl)-propanenitrile (12b). Colorless solid; IR (KBr) ν 3294, 2278; ^{1}H NMR ($CDCl_3$) δ 3.19 (d, J=17.2 Hz, 1H), 3.25 (d, J=17.2 Hz, 1H), 3.81 (s, 1H), 7.50–7.58 (m, 3H), 7.84–7.90 (m, 3H), 8.06 (s, 1H); ^{13}C NMR δ 27.0, 75.4 (q, $^2J_{C-F}$=30.0 Hz), 114.8, 122.5, 124.3 (q, $^1J_{C-F}$=286.4 Hz), 126.2, 126.8, 127.4, 127.6, 128.6, 131.6, 132.7, 133.5; ^{19}F NMR ($CDCl_3$) δ −80.0; ESI-MS m/z 288 [M+Na]$^+$; HRMS (FAB$^+$) calcd for $C_{14}H_{10}F_3NOCs$ m/z 397.9769 [M+Cs]$^+$, found 397.9773.

4.1.9.2. 3-Hydroxy-3-(*p*-tolyl)-3-(trifluoromethyl)propanenitrile (12c). Colorless solid; IR (KBr) ν 3349, 2278; ^{1}H NMR ($CDCl_3$) δ 2.35 (s, 3H), 3.11 (d, J=16.8 Hz, 1H), 3.15 (d, J=16.8 Hz, 1H), 3.42 (s, 1H), 7.23 (d, J=8.0 Hz, 2H), 7.39 (d, J=8.0 Hz, 2H); ^{13}C NMR δ 21.0, 26.9, 75.3 (q, $^2J_{C-F}$=30.0 Hz), 114.9, 124.2 (q, $^1J_{C-F}$=286.4 Hz), 125.8, 129.6, 131.4, 140.0; ^{19}F NMR ($CDCl_3$) δ −80.5; ESI-MS m/z 252 [M+Na]$^+$; HRMS (FAB$^+$) calcd for $C_{11}H_{10}F_3NOCs$ m/z 361.9769 [M+Cs]$^+$, found 361.9762.

4.1.9.3. 3-(*p*-Chlorophenyl)-3-hydroxy-3-(trifluoromethyl)propanenitrile (12d). Colorless solid; IR (KBr) ν 3342, 2278; ^{1}H NMR ($CDCl_3$) δ 3.16 (s, 2H), 3.32 (s, 1H), 7.43 (d, J=8.6 Hz, 2H), 7.49 (d, J=8.0 Hz, 2H); ^{13}C NMR δ 27.1, 75.0 (q, $^2J_{C-F}$=30.0 Hz), 114.4, 124.0 (q, $^1J_{C-F}$= 288.7 Hz), 127.5, 129.2, 132.7, 136.3; ^{19}F NMR ($CDCl_3$) δ −80.5; ESI-MS m/z 272 [M+Na]$^+$; HRMS (FAB$^+$) calcd for $C_{10}H_7ClF_3NOCs$ m/z 381.9223 [M+Cs]$^+$, found 381.9219.

4.1.9.4. 3-(*p*-Anisoyl)-3-hydroxy-3-(trifluoromethyl)-propanenitrile (12e). Colorless solid; IR (KBr) ν 3344, 2278; ^{1}H NMR ($CDCl_3$) δ 3.01 (d, J=17.2 Hz, 1H), 3.16 (d, J=17.2 Hz, 1H), 3.58 (s, 1H), 3.81 (s, 3H), 6.94 (d, J= 8.8 Hz, 2H), 7.44 (d, J=8.8 Hz, 2H); ^{13}C NMR δ 26.9, 55.3, 75.0 (q, $^2J_{C-F}$=30.0 Hz), 114.2, 114.9, 124.2 (q, $^1J_{C-F}$= 286.4 Hz), 126.3, 127.4, 160.5; ^{19}F NMR ($CDCl_3$) δ −80.6; ESI-MS m/z 268 [M+Na]$^+$; HRMS (FAB$^+$) calcd for $C_{11}H_{10}F_3NO_2Cs$ m/z 377.9718 [M+Cs]$^+$, found 377.9713.

4.1.9.5. (*E*)-3-Hydroxy-5-phenyl-3-(trifluoromethyl)-pent-4-ene-nitrile (12f). Colorless solid; IR (KBr) ν 3419, 2272; ^{1}H NMR ($CDCl_3$) δ 2.88 (d, J=16.8 Hz, 1H), 2.99 (d, J=16.8 Hz, 1H), 6.26 (d, J=16.1 Hz, 1H), 7.03 (d, J=16.1 Hz, 1H), 7.30–7.38 (m, 3H), 7.40–7.44 (m, 2H); ^{13}C NMR δ 26.0, 74.1 (q, $^2J_{C-F}$=30.1 Hz), 114.4, 123.3 (q, $^1J_{C-F}$=288.7 Hz), 127.2, 128.8, 129.3, 134.4, 135.6; ^{19}F NMR ($CDCl_3$) δ −81.9; ESI-MS m/z 264 [M+Na]$^+$; HRMS (FAB$^+$) calcd for $C_{12}H_{10}F_3NOCs$ m/z 373.9769 [M+Cs]$^+$, found 373.9768.

4.1.9.6. 1-Benzyl-3-cyanomethyl-3-hydroxy-oxindole (13). Colorless solid; IR (KBr) ν 3345, 2256, 1721; ^{1}H NMR ($CDCl_3$) δ 2.75 (d, J=16.5 Hz, 1H), 3.07 (d, J=16.5 Hz, 1H), 4.13 (s, 1H), 4.77 (d, J=15.5 Hz, 1H), 4.92 (d, J=15.5 Hz, 1H), 6.74 (d, J=7.6 Hz, 1H), 7.11 (d, J=7.6, 7.6 Hz, 1H), 7.24–7.31 (m, 6H), 7.61 (d, J=7.4 Hz, 1H); ^{13}C NMR δ 27.5, 44.2, 72.7, 110.2, 115.2, 124.0, 124.3, 127.2, 127.5, 128.0, 129.0, 130.9, 134.6, 142.0, 175.7; ESI-MS m/z 301 [M+Na]$^+$; HRMS (FAB$^+$) calcd for $C_{17}H_{14}N_2O_2Cs$ m/z 411.0110 [M+Cs]$^+$, found 411.0109.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.04.051.

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