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Efficient α-Alkylation of Arylacetonitriles with Secondary Alcohols Catalyzed by a Phosphine-Free Air-Stable Iridium(III) Complex

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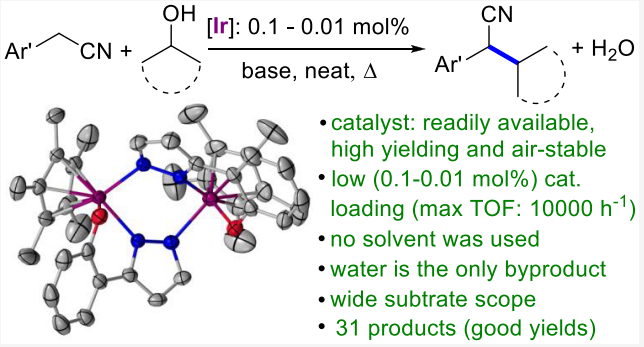
ABSTRACT: A well-defined and readily available air-stable dimeric iridium(III) complex catalyzed α-alkylation of arylacetonitriles using secondary alcohols with the liberation of water as the only byproduct is reported. The α-alkylations were efficiently performed at 120 °C under solvent-free conditions with very low (0.1−0.01 mol %) catalyst loading. Various secondary alcohols including cyclic and acyclic alcohols and a wide variety of arylacetonitriles bearing different functional groups were converted into the corresponding α-alkylated products in good yields. Mechanistic study revealed that the reaction proceeds via alcohol activation by metal−ligand cooperation with the formation of reactive iridium-hydride species.



INTRODUCTION

In organic synthesis, the importance of α-alkylation of nitriles is enormous as α-alkylated nitriles are versatile building blocks for the synthesis of varieties of compounds such as ketones, carboxylic acids, amines, amides, and heterocycles.[1] Conventional α-alkylation of nitrile involves the reaction of nitrile with a stoichiometric or excess amount of base to generate the nitrile anion, which further reacts with toxic alkyl halide.[2] Thus, traditional α-alkylation of nitriles produces a stoichiometric amount of salt waste, and the probable formation of dialkylated byproducts is another major disadvantage.[3] Catalytic alkylations provide a better alternative in which alcohols are utilized as alkylating reagents. Direct catalytic alkylation with alcohols is a highly atom-economic protocol and offers a green alternative as water is the only byproduct. Catalytic alkylation of carbonyls with alcohols is an active field of research. A large number of metal complexes have been reported with primary alcohols.[4] However, the use of secondary alcohols is limited.[5] Catalytic α-alkylation of nitriles is also gaining significant attention. In the early 80s, the pioneering work on catalytic α-alkylation of arylacetonitriles by primary alcohols (methanol, ethanol, and benzyl alcohol) was reported by utilizing ruthenium- and rhodium-phosphine complexes.[6] $RuH_2(PPh_3)_4$ showed the highest catalytic activity. The α-alkylation of nitriles involves oxidation of alcohols to carbonyls followed by the condensation of the resultant carbonyls with nitriles to form α,β-unsaturated nitriles and finally the reduction of α,β-unsaturated nitriles by liberated hydrogen from the oxidation of alcohols. In this tandem process, metal catalysts play a key role in the first and third steps, i.e., dehydrogenation and hydrogenation reactions. Catalytically generated hydrogen from the oxidation of alcohols is later utilized in the hydrogenation of unsaturated intermediates; this is often referred to as the hydrogen autotransfer or borrowing hydrogen method.[7] Only the first two steps, i.e., dehydrogenation of alcohols followed by condensation of the resultant carbonyls with nitriles, are necessary for α-olefination of nitriles with hydrogen and water as byproducts. Thus, α-olefination can be considered as less atom-economic with the loss of valuable hydrogen.

Utilizing the hydrogen autotransfer or borrowing hydrogen method, various transition-metal catalysts were employed for α-alkylation of nitriles using mostly primary alcohols (Scheme 1). Lin and Lau et al. reported cationic aminocyclopentadienyl ruthenium complexes ($[(\eta^5\text{-}C_5H_4NMe_2)Ru(PPh_3)_2(MeCN)][BF_4]$ and $[(\eta^5\text{-}C_5H_4NEt_2)Ru(PPh_3)_2(MeCN)][BF_4]$) as weak to moderately active catalysts for α-alkylation/olefination of arylacetonitriles with primary alcohols giving a mixture of saturated (minor) and unsaturated (major) nitriles.[8a] Later, α-alkylation of acetonitrile by primary alcohols was gracefully done by $[RuHCl(CO)(PPh_3)_3]$.[8b] Recently, Ru−POP,[8c] Ru−PNP,[8d] and Ru−NNN[8e] pincer complexes were employed as very effective catalysts for α-alkylation of arylacetonitriles with primary alcohols. Ru-grafted hydrotalcite[9] and palladium on MgO[10] as heterogeneous catalysts were also utilized. The cationic half-sandwich Os−*N*-heterocyclic carbene (NHC)

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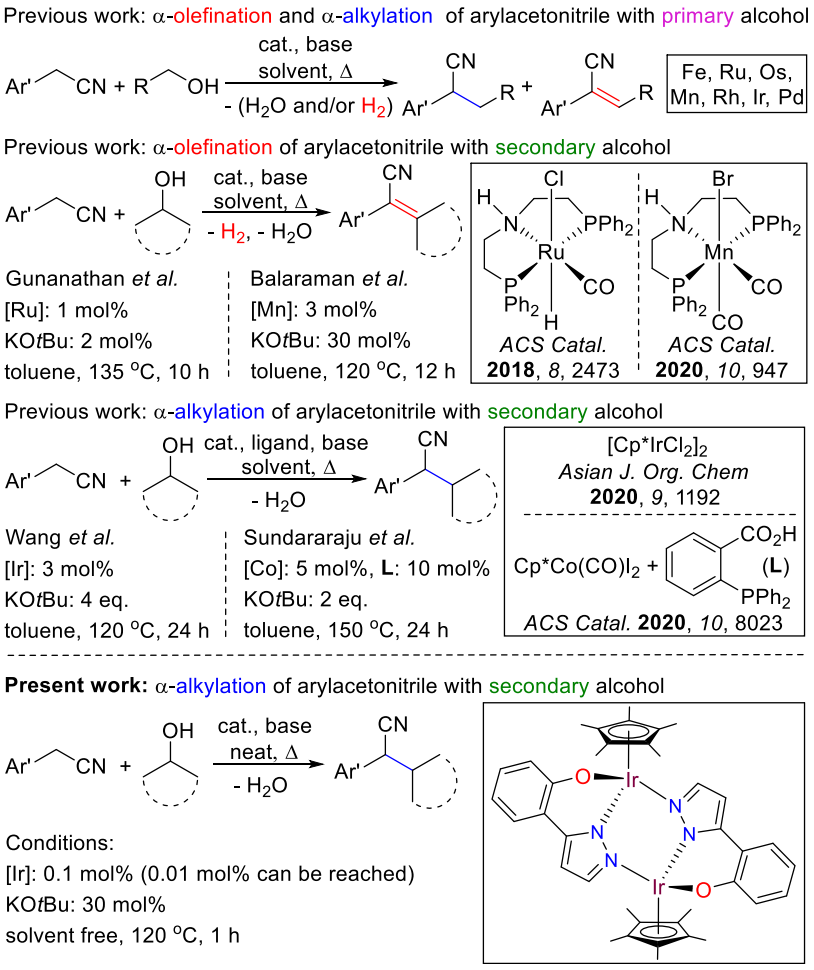
Scheme 1. α-Alkylation and α-Olefination of Nitriles



complex ([Os(η^6-*p*-cymene)(OH)(IPr)][triflate (OTf)])[11] and Fe–PNP pincer complexes[12] were also used effectively. Rhodium complexes were also utilized for the same purpose. By changing the reaction environment, selective α-alkylation or α-olefination of arylacetonitriles with primary alcohols was reported using cationic binuclear Rh-species.[13] Rhodium catalysts were also employed for similar reactions such as synthesis of α-alkylated arylacetamides from arylacetonitriles and primary alcohols[14a] and allylic alkylation of allyl benzoate with α-substituted benzyl nitrile.[14b] Few iridium complexes are known to show catalytic activity for α-alkylation of nitriles.[15] In 2006 and 2007, $[IrCp^*Cl_2]_2$ and $[IrCl(COD)]_2$ with phosphine ligands were used for the α-alkylation of arylacetonitriles and alkyl cyanoacetates, respectively, with primary alcohols in the presence of a base at high temperatures (100–130 °C).[15a,b] Intramolecular alkylation of nitriles has also been reported with $[IrCp^*Cl_2]_2$ and $[IrCl(COD)]_2$ with PPh_3.[15c] A few years later, two research groups independently reported Ir(I)-catalyzed ($[Ir(OH)(COD)]_2/PPh_3$ and $[IrCl(COD)]_2$) α-alkylation of acetonitrile using primary alcohols under microwave irradiation (130–180 °C).[15d,e] The α-alkylation of acetonitrile using secondary alcohols required prolonged (7–36 h) heating at 200 °C.[15c] The number of reports on α-alkylation/olefination of nitriles with secondary alcohols is extremely rare. Recently, Ru–PNP[16] and Mn–PNP[17] pincer complexes were employed as very efficient catalysts for the α-olefination of arylacetonitriles with various secondary alcohols (Scheme 1). Manganese complexes were also used as effective catalysts for α-olefination of arylacetonitriles with primary alcohols.[18] During our study, two groups independently reported catalytic α-alkylation of arylacetonitriles with secondary alcohols.[19] Wang et al. used $[Cp^*IrCl_2]_2$ as the catalyst,[19a] and Sundararaju et al. utilized $Cp^*Co(CO)I_2$ in the presence of 2-(diphenylphosphino)benzoic acid as the ligand (Scheme 1).[19b] To the best of our knowledge, these are the only two reports on the α-alkylation of arylacetonitriles with secondary alcohols. However, the catalyst loading is rather high ([Ir]: 3 mol %; [Co]: 5 mol %; ligand: 10 mol %), as are the amount of base (2–4 equiv), reaction temperature (150 °C for Co catalyst), and reaction time (24 h). It is worth mentioning that the low substrate-to-catalyst (S/C) ratio (Ir: 33, Co: 20) may limit possible applications. Moreover, in recent years, developing phosphine-free stable metal catalysts is gaining significant attention for obvious reasons.[20] Herein, we address the use of a readily available phosphine-free air-stable Ir(III) complex with a commercially available pyrazol-based ligand as a very effective catalyst (maximum turnover frequency (TOF): 10 000 h^{-1}) for the α-alkylation of a large number of arylacetonitriles with varieties of secondary alcohols under solvent-free conditions and at low catalyst loadings (S/C ratio of 10 000 can be achieved).

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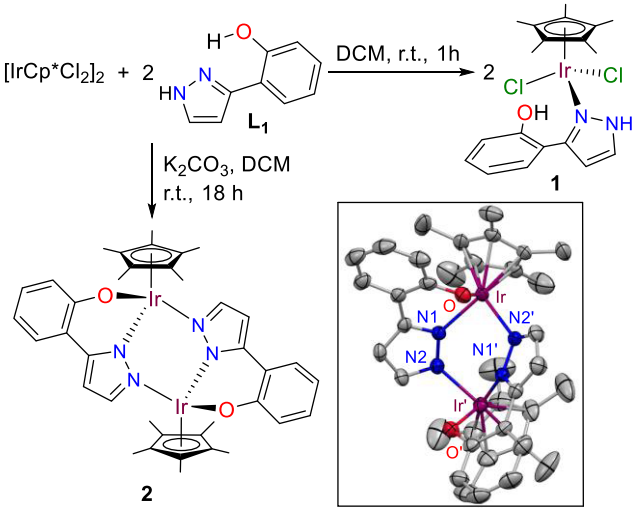
RESULTS AND DISCUSSION

Metal−ligand bifunctional activation of substrates plays a key role in molecular catalysis. Deprotonation−protonation of the ligand attached to the metal is a common strategy employed in these systems such as the Noyori−Ikariya catalyst,[21] the Shvo catalyst,[22] and Milstein's pincer complexes.[23] Very recently, Maji et al. utilized this strategy in manganese-catalyzed α-alkylation of ketones with secondary alcohols.[24] Ligands having a protic NH-group is a common feature in these complexes.[21−24] On the same line of thought, we have selected a pyrazole-based ligand $\mathbf{L_1}$ with a pendant phenol arm (Scheme 2). Facile coordination of the ligand with $[IrCp^*Cl_2]_2$ gave complex **1** in excellent yield. The OH and NH protons appeared as broad resonances (10.97 and 13.20 ppm) in the ^{1}H nuclear magnetic resonance (NMR) spectrum of **1**. Upon reaction of $\mathbf{L_1}$ and $[IrCp^*Cl_2]_2$ in the presence of a base, smooth dehydrochlorination resulted in the formation of complex **2** as a yellow solid in almost quantitative yield (Scheme 2). Complex **2** is air-stable and was characterized by ^{1}H and ^{13}C NMR spectroscopies and mass analysis. As expected, the OH and NH resonances are absent in the ^{1}H NMR spectrum of species **2**. Complex **2** was further characterized by single-crystal X-ray analysis, which revealed a pyrazolato-bridged dinuclear structure. The bond distances and bond angles are consistent with similar iridium complexes utilized as catalysts for intramolecular hydroamination of aminoalkene.[25]

Scheme 2. Synthesis of Complexes 1 and 2 with the Molecular Structure of 2 Showing 50% Ellipsoids[a]

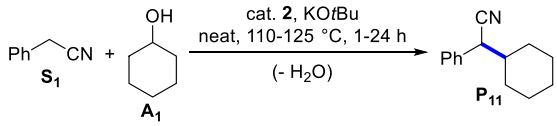


[a]Hydrogen atoms are omitted for clarity.

With the air-stable complex **2** in hand, we set out to investigate the α-alkylation of phenylacetonitrile ($\mathbf{S_1}$) as a standard substrate with cyclohexanol ($\mathbf{A_1}$) as a secondary alcohol (Table 1).

Upon heating a mixture of $\mathbf{S_1}$ and $\mathbf{A_1}$ (2.5 equiv) in the presence of 30 mol % KO*t*Bu and 3 mol % [Ir], a complete conversion of $\mathbf{S_1}$ to 2-cyclohexyl-2-phenylacetonitrile ($\mathbf{P_{11}}$) was observed in 24 h (entry 1). Gradually decreasing the reaction time to 6 h also gave full conversion of $\mathbf{S_1}$ to $\mathbf{P_{11}}$ (entry 1). Reducing the catalyst loading to 2 mol % yielded full conversion of $\mathbf{S_1}$ in 6 h with more than 70% isolated yield of $\mathbf{P_{11}}$ (entry 2). Further reduction of catalyst loading to 1 (entry 3), 0.5 (entry 4: 71% isolated yield of $\mathbf{P_{11}}$), and 0.1 mol % (entry 5: 80% isolated yield of $\mathbf{P_{11}}$) also gave full conversion of $\mathbf{S_1}$ in just 1 h. The reaction did not proceed in the absence of either complex **2** (entry 6) or base (entry 7). Thereafter, we performed two reactions with less amount of base (entry 8: 20 mol % KO*t*Bu) and at lower temperatures (entry 9: 110 °C). In both cases, we observed approximately 95% yield of the product. Reaction at 120 °C with 2 equiv of $\mathbf{A_1}$ gave full conversion with 80% isolated yield (entry 10). Encouraging

Table 1. Catalytic Performance of Complex 2 for the α-Alkylation of Phenylacetonitrile with Cyclohexanol[a]



en.	[Ir] (mol %)	KO*t*Bu (mol %)	$\mathbf{A_1}$ (equiv)	temp. (°C)	time (h)	yield[f] (%)
1[a]	**3**	30	2.5	125	24/18/ 12/8/6	>99
2[a]	**2**	30	2.5	125	6	>99 (72)[g]
3[a]	**1**	30	2.5	125	6/4/2/1	>99
4[a]	**0.5**	30	2.5	125	1	>99 (71)[g]
5[b]	**0.1**	30	2.5	125	1	>99 (80)[g]
6[b]	**no**	30	2.5	125	1	0
7[b]	0.1	**no**	2.5	125	1	0
8[b]	0.1	**20**	2.5	125	1	94
9[b]	0.1	30	2.5	**110**	1	96
10[b]	0.1	30	**2.0**	120	1	>99 (80)[g]
11[b,c]	0.1	30	2.0	120	1	63
12[d]	0.1	30	**1.1**	120	1	92
13[d]	0.1	30	**1.1**	120	**1.5**	>99
14[e]	0.1	30	2.0	120	1	81[g]

[a]Reactions conducted in a pressure tube (10 mL) with 0.5 mmol $\mathbf{S_1}$, 1.25 mmol $\mathbf{A_1}$, and 3/2/1/0.5 mol % [Ir]; [b]with 5.0 mmol $\mathbf{S_1}$, 12.5/10.0 mmol $\mathbf{A_1}$, and 0.1 mol % [Ir]; [c]In 1 mL of toluene; [d]with 5.0 mmol $\mathbf{S_1}$, 5.5 mmol $\mathbf{A_1}$, and 0.1 mol % [Ir]. [e]Gram-scale reaction with 10.0 mmol (1.17 g) $\mathbf{S_1}$, 20.0 mmol $\mathbf{S_2}$, and 0.1 mol % [Ir]. [f]Yields of $\mathbf{P_1}$ were determined by GC using *p*-xylene as the internal standard. [g]Isolated yields of $\mathbf{P_1}$; key parameters for each entry are indicated in bold.

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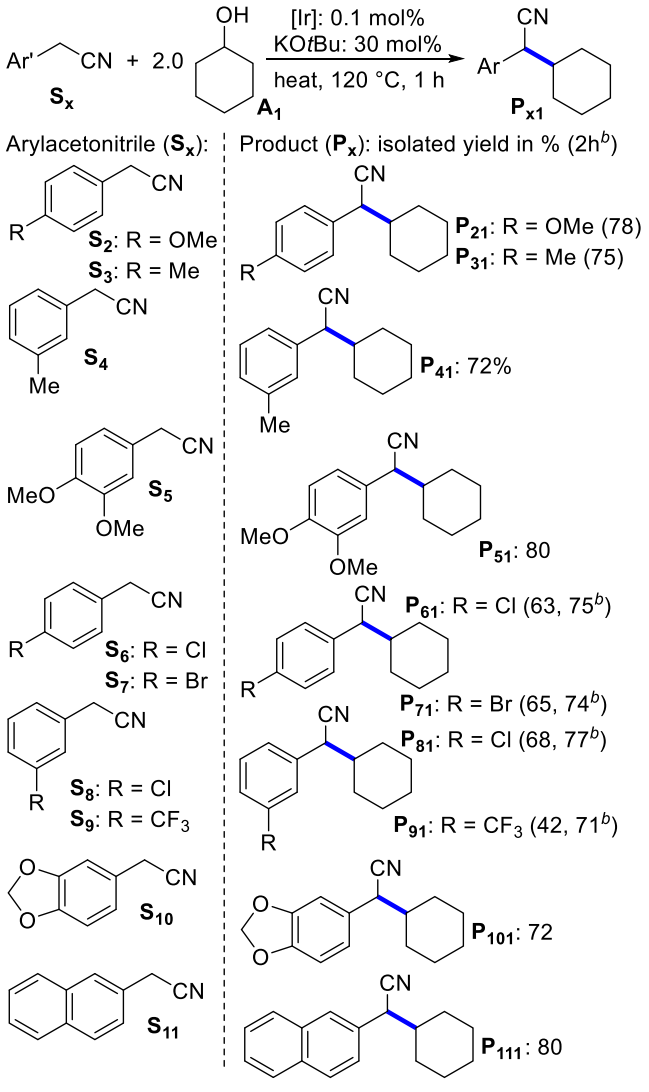
result was not obtained in the presence of 1 mL of toluene as the solvent (entry 11); unreacted starting material was observed. If the reaction is performed with 1.1 equiv of alcohol, less than 10% unreacted starting material was observed (entry 12); however, complete conversion was observed in 1.5 h (entry 13). Thus, it is not necessary to use a large excess of cyclohexanol, which might act as a solvent. To test the robustness of the present catalytic system, a gram-scale reaction was performed with 10.0 mmol (1.17 g) of $\mathbf{S_1}$ with 2 equiv of $\mathbf{A_1}$, 30 mol % base, 0.1 mol % [Ir] at 120 °C for 1 h (entry 14), and 1.62 g of $\mathbf{P_{11}}$ was isolated (81%).

Having established the optimized reaction condition (0.1 mol % [Ir], 30 mol % KO*t*Bu, 2 equiv of secondary alcohol, 120 °C, 1 h, solvent-free), we thereafter examined various other arylacetonitriles to expand the substrate scope. Catalytic α-alkylation of various arylacetonitriles using cyclohexanol as the secondary alcohol was performed (Scheme 3).

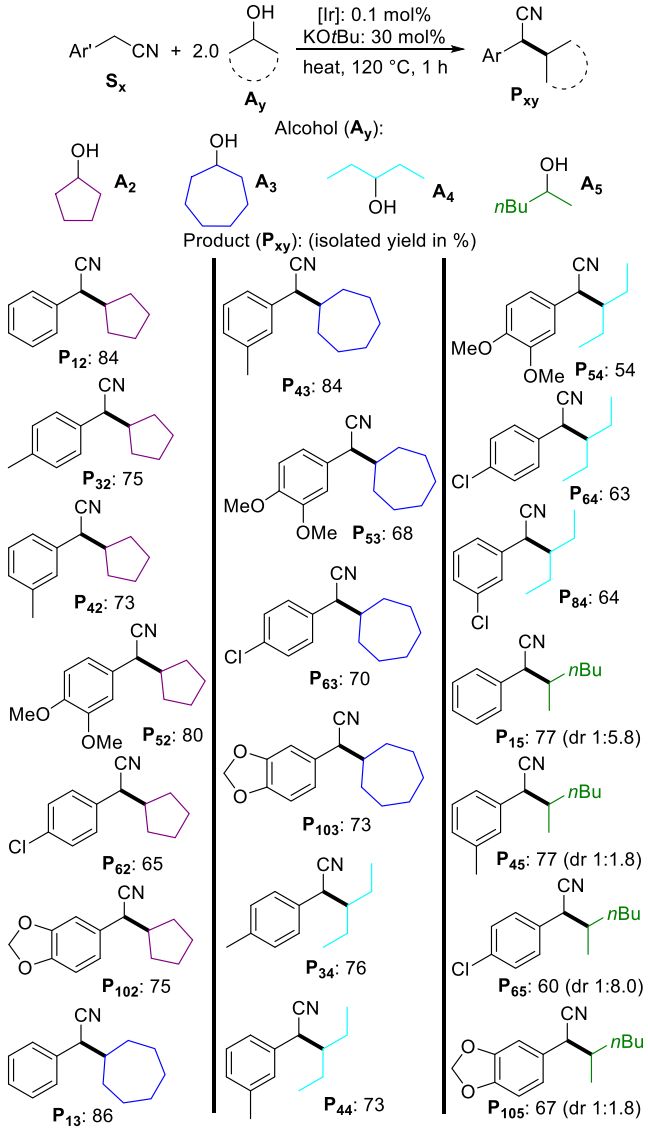
Upon reaction with cyclohexanol, 4-methoxyphenylacetonitrile ($\mathbf{S_2}$) gave 2-cyclohexyl-2-(4-methoxyphenyl)acetonitrile ($\mathbf{P_{21}}$) in good yield (78%). A similar result ($\mathbf{P_{31}}$: 75%; $\mathbf{P_{41}}$: 72%) was obtained for the electron-donating methyl group at the *para* ($\mathbf{S_3}$) and *meta* ($\mathbf{S_4}$) positions of phenylacetonitrile. Substrates with two methoxy groups ($\mathbf{S_5}$) also gave good yield of the α-alkylated product ($\mathbf{P_{51}}$: 80%). Substrates with mild electron-withdrawing groups like halogens at either para ($\mathbf{S_6}$, $\mathbf{S_7}$) or meta ($\mathbf{S_8}$) positions gave decent yields ($\mathbf{P_{61}}$: 63%; $\mathbf{P_{71}}$: 65%; $\mathbf{P_{81}}$: 68%). A much diminished yield of the product ($\mathbf{P_{91}}$: 42%) was obtained for arylacetonitrile with a strong electron-withdrawing CF_3 group ($\mathbf{S_9}$). In the case of substrates with an electron-withdrawing group, we also observed acronitrile intermediates along with a small amount of unreacted starting materials. However, prolonged heating for 2 h gave complete conversion with better isolated yields ($\mathbf{P_{61}}$: 75%; $\mathbf{P_{71}}$: 74%; $\mathbf{P_{81}}$: 77%; $\mathbf{P_{91}}$: 71%). Therefore, the nature of substituents on the aryl moiety has a prominent effect on the outcome of the α-alkylation of arylacetonitriles. As expected, 3,4-methylenedioxy substituents on phenylacetonitrile ($\mathbf{S_{10}}$) gave good yield of the product ($\mathbf{P_{101}}$: 72%). Similarly, 2-napthylacetonitrile was reacted with cyclohexanol to give the corresponding β-branched product ($\mathbf{P_{111}}$: 80%) in good yield.

Thereafter, we explored the scope of this catalytic protocol with respect to various cyclic and acyclic secondary alcohols under standard reaction conditions (Scheme 4). When

Scheme 3. α-Alkylation with Cyclohexanol



Scheme 4. α-Alkylation of Arylacetonitriles with Various Secondary Alcohols



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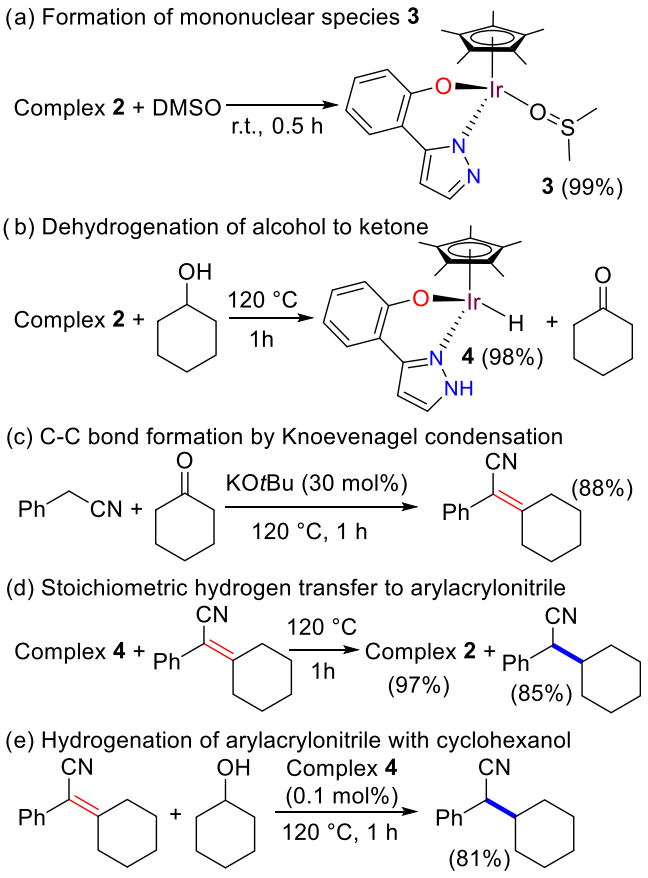
cyclopentanol was reacted with phenylacetonitrile, the corresponding α-alkylated product 2-cyclopentyl-2-phenylacetonitrile ($\mathbf{P_{12}}$) was isolated in 84% yield. Substituting phenylacetonitrile with electron-donating groups such as methyl and methoxy at *o*-, *p*-, and *m*-positions gave the corresponding products in 75−80% yield. As expected, lesser yield ($\mathbf{P_{62}}$: 65%) was obtained when cyclopentanol was reacted with 4-chlorophenylacetonitrile. Another cyclic alcohol, cycloheptanol, also provided similar yields of desired products ($\mathbf{P_{13}}$: 86%; $\mathbf{P_{43}}$: 84%; $\mathbf{P_{53}}$: 68%; $\mathbf{P_{63}}$: 70%; $\mathbf{P_{103}}$: 73%) with substituted phenylacetonitriles under standard reaction conditions. We also tested acyclic secondary alcohols, both symmetric and asymmetric. We were pleased to see that 3-pentanol as a symmetric acyclic secondary alcohol yielded the corresponding α-alkylated products ($\mathbf{P_{34}}$: 76%; $\mathbf{P_{44}}$: 73%; $\mathbf{P_{54}}$: 54%; $\mathbf{P_{64}}$: 63%; $\mathbf{P_{84}}$: 64%) in decent to good yields upon reaction with various arylacetonitriles. Interestingly, we obtained a mixture of two diastereomers in similar yields ($\mathbf{P_{15}}$: 77%; $\mathbf{P_{45}}$: 77%; $\mathbf{P_{65}}$: 60%; $\mathbf{P_{105}}$: 67%) when substituted phenylacetonitriles were reacted with (±)-2-hexanol as an asymmetric alcohol. We also tested aromatic secondary alcohols such as 1-phenylethanol and diphenylmethanol; however, the present catalytic protocol failed to give the desired products. To test the robustness of the present catalyst, α-alkylations of phenylacetonitrile with cyclohexanol were scaled up to a 25 mmol scale (multigrams) with a catalyst loading of 0.005 mol % ([Ir]: 0.01 mol %) for 1 h, and we were pleased to see a complete conversion of the substrate with a good isolated yield of 2-cyclohexyl-2-phenylacetonitrile (4.33 g, 87%). Therefore, a maximum TOF of 10 000 h^{-1} could be achieved. Hence, a simple but highly efficient catalytic protocol is reported for the α-alkylation of a wide range of arylacetonitriles with various secondary alcohols.

Several control experiments were performed to shed light on the reaction mechanism. Complex **2** is a dimer of the coordinatively unsaturated 16-electron pyrazolato complex, and thus it is highly likely that it forms the coordinatively saturated 18-electron mononuclear species during substrate coordination. To test this, complex **2** was reacted with dimethyl sulfoxide (DMSO), and indeed DMSO-coordinated 18-electron mononuclear species **3** was isolated and fully characterized (Scheme 5a). Thereafter, we performed a stoichiometric reaction of complex **2** with cyclohexanol. In the absence of KO*t*Bu, heating a mixture of complex **2** and cyclohexanol at 120 °C for 1 h resulted in the formation of iridium-hydride species **4** and cyclohexanone in excellent isolated yields (Scheme 5b). This clearly shows that the iridium catalyst **2** is able to dehydrogenate alcohol to ketone in the absence of a base. It is known that KO*t*Bu as a base can alone catalyze aldol-type Knoevenagel condensation, and the fact is also supported by theoretical studies.[26] Hence, we performed the reaction of cyclohexanone and phenylacetonitrile in the presence of 30 mol % KO*t*Bu (Scheme 5c). This indeed resulted in the formation of phenylacrylonitrile in excellent yield. Thereafter, a stoichiometric reaction of hydride species **4** with phenylacrylonitrile was carried out (Scheme 5d) to test whether hydrogen could be transferred from the hydride complex **4** to the C=C of unsaturated phenylacrylonitrile. Clean formation of the saturated product $\mathbf{P_{11}}$ suggested a successful hydrogen transfer from the hydride species **4**. We also tested if hydride species **4** could catalyze the hydrogenation of phenylacrylonitrile with cyclohexanol. As expected, the reaction of phenylacrylonitrile with cyclohexanol

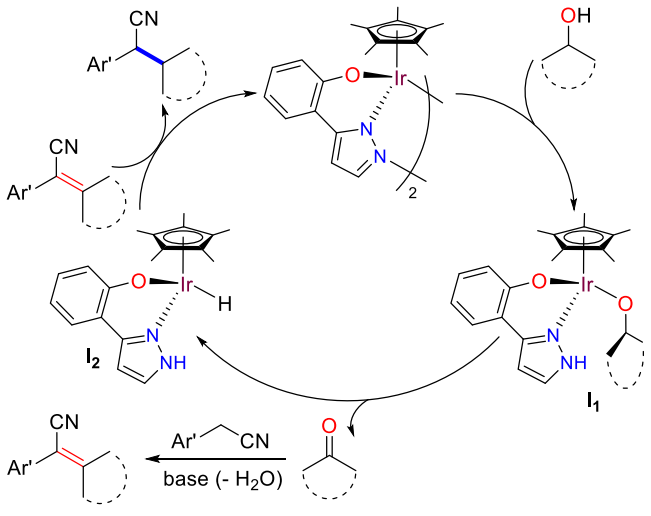
Scheme 5. Control Experiments



in the presence of 0.1 mol % hydride species **4** also yielded $\mathbf{P_{11}}$ (Scheme 5e).

Therefore, we proposed a plausible mechanism based on the experimental evidence and previous reports (Scheme 6).[8,16,17,19] Initially, alcohol interacts with the iridium dimer **2**, and the O−H activation of the alcohol via proton transfer to the pyrazolato moiety yielded an alkoxy intermediate $\mathbf{I_1}$. A similar instance of nitrogen atom in the pyrazolato moiety picking up the hydrogen was reported in the past; a similar

Scheme 6. Plausible Mechanism for Catalytic α-Alkylation of Arylacetonitrile



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iridium−pyrazolato complex activated the N−H bond of tosyl amine via proton transfer to the pyrazolato moiety.[25b] Thereafter, the β-hydride elimination of intermediate $\mathbf{I_1}$ resulted in the formation of ketone and hydride intermediate $\mathbf{I_2}$ (or complex **4**), which was isolated and fully characterized. As β-hydride elimination requires a vacant site at the metal center, this second step might also undergo a Cp ring slippage from η^5 to η^3 coordination. However, the proposed β-hydride elimination in saturated complexes has also been reported.[18,19] Thereafter, ketone and arylnitrile undergo Knoevenagel condensation in the presence of a base to form vinyl nitrile with the elimination of water. Finally, hydrogen transfer from the hydride intermediate $\mathbf{I_2}$ to the vinyl nitrile yielded α-alkylated arylacetonitrile with the regeneration of iridium complex **2**.

CONCLUSIONS

In conclusion, we have developed a readily accessible (single-step synthesis) and air-stable iridium(III) catalyst, which is very efficient for the α-alkylation of arylacetonitriles using challenging secondary alcohols with the liberation of water as a green byproduct. The substrate scope includes a wide range of arylacetonitriles and various secondary alcohols. Compared to the previously reported cobalt ([Co]: 5 mol %; phosphine ligand: 10 mol %) and iridium ([Ir]: 3 mol %) catalysts,[19] we can reach very low (up to 0.01 mol % [Ir]) catalyst loading, which is realistic for possible future applications. Moreover, the present catalytic protocol is operative with a catalytic amount of base (30 mol %) in contrast to the huge amount of base (2−4 equiv) used in other reported catalytic systems. In addition, the present catalytic system is much faster (24 vs 1 h; maximum TOF of 1−2 vs 10 000 h^{-1}) and another advantage of this green catalytic protocol is solvent-free α-alkylation. With the excellent conversion in a very short period of time with attractive catalyst loading, the iridium catalyst has been proven to be an excellent catalyst for the α-alkylation reaction. Based on experimental evidences, the reaction is believed to follow the borrowing hydrogen principle, which involves iridium-catalyzed oxidation of alcohol to ketone followed by base-catalyzed aldol-type condensation of ketone and nitrile to vinyl nitrile and finally reduction of vinyl nitrile to the α-alkylated product. Further investigations will involve the utilization of this catalyst for other catalytic reactions; particularly, the isolation of iridium-hydride intermediates opens the gateway for various hydrofunctionalization reactions.

EXPERIMENTAL SECTION

General Experimental. Syntheses of the iridium complexes **1**, **2**, and **3** were performed in air. All air- and moisture-sensitive experiments such as the synthesis of intermediate iridium-hydride complex **4** and catalytic α-alkylation of nitriles were performed under a dry nitrogen atmosphere using standard Schlenk or glovebox (MBraun) techniques. Catalytic α-alkylation of nitriles was performed in Ace pressure tubes purchased from Sigma-Aldrich. Analysis and purification of the products were carried out in air. For the air-sensitive experiments, solvents dichloromethane (DCM) and diethylether (Et_2O) were distilled, degassed, and stored over 3 Å molecular sieves. Solvents were purchased from Merck and Spectrochem. Deuterated solvents ($CDCl_3$ and DMSO-d_6) were purchased from Sigma-Aldrich. For recording NMR spectra of air- and moisture-sensitive samples, $CDCl_3$ was degassed and stored over 3 Å molecular sieves. 2-(1H-Pyrazol-3-yl)phenol, $[IrCp^*Cl_2]_2$, KO*t*Bu, *p*-xylene, all organic nitriles, and all secondary alcohols were purchased from Sigma Aldrich, Alfa Aesar, and TCI Chemicals and used without further purification.

^1H and $^{13}C\{^1H\}$ NMR spectra were recorded at the Bruker AV-400 and JEOL-400 (^1H at 400 MHz and ^{13}C at 101 MHz). ^1H and $^{13}C\{^1H\}$ NMR chemical shifts are referenced in parts per million (ppm) with respect to residual solvent peaks ($CDCl_3$: δ 7.26 and 77.16 ppm; DMSO-d_6: 2.50 and 39.52 ppm). The coupling constants (J) are reported in hertz (Hz). The following abbreviations are used to describe multiplicity: s, singlet; bs, broad signal; d, doublet; t, triplet; q, quadtrate, m, multiplate. High-resolution mass spectra (HRMS) were recorded on a Bruker microTOF-Q II spectrometer. Elemental analysis was carried out on a EuroEA Elemental Analyser.

Synthesis of Complex 1. A solution of 2-(1H-pyrazol-3-yl)phenol (0.032 g, 0.20 mmol) in DCM (2.5 mL) was added dropwise to a solution of $[IrCp^*Cl_2]_2$ (0.080 g, 0.10 mmol) in DCM (2.5 mL) at r.t. A yellow precipitate formed instantly. The reaction mixture was stirred at r.t. for 1 h. The liquid was decanted off, and the yellow solid was washed with DCM (2 × 2.5 mL). The yellow solid was dried under a high vacuum to give complex **1** (0.110 g, 98%) as a pure compound. ^1H NMR (DMSO-d_6): δ 13.20 (bs, 1H), 10.97 (bs, 1H), 7.71 (d, J = 7 Hz, 1H), 7.16 (t, J = 7 Hz, 1H), 7.00−6.72 (m, 3H), 1.60 (s, 15H). $^{13}C\{^1H\}$ NMR (DMSO-d_6): δ 155.1, 128.8, 126.8, 119.3, 117.1, 116.4, 102.1, 92.1, 8.3. HRMS (electrospray ionization-time-of-flight (ESI-TOF)) m/z: $[M]^+$ calcd for $C_{19}H_{23}Cl_2IrN_2O$ 558.0817; found 558.0821. Anal. calcd for $C_{19}H_{23}Cl_2IrN_2O$ (558.52): C, 40.86; H, 4.15; N, 5.02; found: C, 40.83; H, 4.18; N, 5.11.

Synthesis of Complex 2. DCM (20 mL) and three to four drops of water were added to a solid mixture of 2-(1*H*-pyrazol-3-yl)phenol (0.032 g, 0.20 mmol), $[IrCp^*Cl_2]_2$ (0.080 g, 0.10 mmol), and K_2CO_3 (0.031 g, 0.22 mmol) at r.t. The reaction mixture was stirred at r.t. for 16 h, resulting in an orange-yellow solution with a white precipitate. The solid was filtered off, and the orange-yellow solution was dried under a high vacuum. The crude product was dissolved in DCM (2 mL), and the solution was added dropwise to Et_2O while stirring vigorously. This resulted in an orange-yellow solid with a very pale-yellow solution. The solid was collected after filtration and dried under a high vacuum to give complex **2** (0.096 g, 99%) as a pure compound. ^1H NMR ($CDCl_3$): δ 7.80 (d, J = 2 Hz, 1H), 7.31 (d, J = 7 Hz, 1H), 6.85 (t, J = 7 Hz, 1H), 6.69 (d, J = 7 Hz, 1H), 6.47 (d, J = 2 Hz, 1H), 6.44 (t, J = 7 Hz, 1H), 1.41 (s, 15H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 164.2, 150.7, 146.6, 127.2, 126.9, 126.1, 122.0, 115.8, 103.4, 84.9, 9.6. HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{38}H_{42}Ir_2N_4O_2$ 972.2523; found 972.2549. Anal. calcd for $C_{38}H_{42}Ir_2N_4O_2$ (971.21): C, 46.99; H, 4.36; N, 5.77; found: C, 47.13; H, 4.37; N, 5.85.

Synthesis of Complex 3. All manipulations were performed in air using commercially available solvents without further drying. DMSO (2 mL) was added to solid complex **2** (0.097 g, 0.1 mmol). The resulting yellow solution was stirred at r.t. for 30 min. The solution was dried under high vacuum at 80 °C in an oil bath for 6 h to give a yellow solid as pure complex **3** (0.112 g, 99%) as a pure compound. ^1H NMR (DMSO-d_6): δ 7.36 (d, J = 2 Hz, 1H), 7.30 (d, J = 7 Hz, 1H), 6.86 (t, J = 7 Hz, 1H), 6.77 (d, J = 7 Hz, 1H), 6.49 (t, J = 7 Hz, 1H), 6.42 (d, J = 2 Hz, 1H), 2.54 (s, 3H), 1.49 (s, 15H). $^{13}C\{^1H\}$ NMR (DMSO-d_6): δ 159.6, 143.0, 141.8, 126.5, 126.4, 122.5, 121.0, 116.1, 99.2, 91.0, 40.4, 8.1. Anal. calcd for $C_{21}H_{27}IrN_2O_2S$ (563.74): C, 44.74; H, 4.83; N, 4.97; S, 5.69; found: C, 44.68; H, 4.79; N, 5.01; S, 5.71.

Synthesis of Complex 4. All manipulations were performed in a glovebox under a N_2 atmosphere using dry and degassed solvents. Excess cyclohexanol (1.0 mL, 10 mmol) was added to solid complex **2** (98 mg, 0.1 mmol). The resulting mixture was stirred at 120 °C in an oil bath for 1 h, resulting in a dark-red solution. The solution was cooled down to r.t., and it was added dropwise to Et_2O while stirring vigorously. This resulted in a black-red precipitate and a pale-red solution. The liquid was decanted off (pale-red was kept for further analysis), and the solid was dried to get the pure complex **4** (96 mg, 98%). ^1H NMR ($CDCl_3$): δ 13.76 (bs, 1H), 7.46 (d, J = 7 Hz, 1H), 7.00 (t, J = 7 Hz, 1H), 6.93 (d, J = 7 Hz, 1H), 6.86 (s, 1H), 6.76 (t, J

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= 7 Hz, 1H), 6.26 (s, 1H), 1.83 (s, 15H), −13.20 (s, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 156.9, 152.1, 139.1, 126.1, 125.0, 120.1, 118.1, 116.3, 99.4, 91.6, 86.9, 11.5. HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{19}H_{23}IrN_2O$ 488.1522; found 488.1556. Anal. calcd for $C_{19}H_{23}IrN_2O$ (487.62): C, 46.88; H, 4.75; N, 5.75; S, 5.69; found: C, 46.80; H, 4.75; N, 5.74.

Note: The pale-red solution was analyzed by GC, which clearly shows the formation of cyclohexanone.

Synthesis of 2-Cyclohexylidene-2-phenylacetonitrile (P_{11}'). A mixture of 2-phenylacetonitrile (0.586 g, 5.0 mmol), cyclohexanone (0.491 g, 5.0 mmol), and KO*t*Bu (0.168 g, 1.5 mmol) was stirred in a pressure tube at 120 °C using an oil bath for 1 h under a N_2 atmosphere. The mixture was cooled down to r.t., and the following workup was performed in air. From the reaction mixture, 2-cyclohexylidene-2-phenylacetonitrile (0.868 g, 88%) was purified by column chromatography (using silica as the stationary phase and a mixture of hexanes and ethylacetate (9.5:0.5) as the eluent). ^1H NMR ($CDCl_3$): δ 7.43−7.25 (m, 5H), 2.73−2.63 (m, 4H), 2.36−2.27 (m, 2H), 1.82−1.70 (m, 2H), 1.69−1.53 (m, 4H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 161.9, 133.9, 129.3, 128.7, 128.2, 118.7, 107.8, 35.4, 31.3, 28.1, 27.9, 25.9.

Synthesis of P_{11} by Stoichiometric Reaction of Complex 4 and 2-Cyclohexylidene-2-phenylacetonitrile. A mixture of complex **4** (49 mg, 0.1 mmol) and 2-cyclohexylidene-2-phenylacetonitrile (20 mg, 0.1 mmol) was stirred in a narrow pressure tube (2 mL) at 120 °C using an oil bath for 1 h under a N_2 atmosphere. The mixture was cooled down to r.t., and the following workup was performed in air. From the reaction mixture, $\mathbf{P_{11}}$ (17 mg, 85%) was extracted in Et_2O (2 × 5 mL) and it was purified by column chromatography using silica as the stationary phase and a mixture of hexanes and ethylacetate (9.5:0.5) as the eluent. The yellow solid insoluble in Et_2O was found to be complex **2** (47 mg, 97%).

Synthesis of P_{11} by Reaction of 2-Cyclohexylidene-2-phenylacetonitrile and A_1 Catalyzed by Complex 4. A mixture of complex **4** (2.4 mg, 0.005 mmol), 2-cyclohexylidene-2-phenylacetonitrile (99 mg, 0.50 mmol), and $\mathbf{A_1}$ (56 mg, 0.55 mmol) was stirred in a pressure tube at 120 °C using an oil bath for 1 h under a N_2 atmosphere. The mixture was cooled down to r.t., and the following workup was performed in air. From the reaction mixture, $\mathbf{P_{11}}$ (82 mg, 82%) was purified by column chromatography using silica as the stationary phase and a mixture of hexanes and ethylacetate (9.5:0.5) as the eluent.

General Conditions for Reaction Optimization (Procedure A). Inside a glovebox, an appropriate amount of phenylacetonitrile ($\mathbf{S_1}$), cyclohexanol ($\mathbf{A_1}$), KO*t*Bu, *p*-xylene (as the internal standard), and complex **2** were transferred into a pressure tube fitted with a magnetic stir-bar. The reaction mixture was heated at an appropriate temperature in a preheated oil bath for an appropriate time. Thereafter, the reaction mixture was cooled down to r.t. and the product mixture was analyzed by GC. Occasionally, the crude product was purified by column chromatography using silica as the stationary phase and a mixture of hexanes and ethylacetate (9.5:0.5) as the eluent.

Note: The mercury drop test was performed, and no decreased catalytic activity was observed.

General Condition for Gram-Scale Synthesis of P_{11} (Procedure B). Inside a glovebox, a mixture of phenylacetonitrile (1.17 g, 10.0 mmol), cyclohexanol (2.00 g, 20.0 mmol), KO*t*Bu (0.34 g, 0.30 mmol), and complex **2** (4.8 mg, 5 × 10^{-3} mmol) was transferred into a pressure tube fitted with a magnetic stir-bar. The reaction mixture was heated at 120 °C in a preheated oil bath for 1 h. Thereafter, the reaction mixture was cooled down to r.t., and the crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and ethylacetate (9.5:0.5) as the eluent) to give a colorless oil as a product (1.62 g, 81%).

A total of 4.33 g of $\mathbf{P_{11}}$ (87%) was obtained by heating a mixture of phenylacetonitrile (2.93 g, 25.0 mmol), cyclohexanol (5.00 g, 50.0 mmol), KO*t*Bu (0.85 g, 0.75 mmol), and complex **2** (1.2 mg, 1.25 × 10^{-3} mmol).

General Condition for Substrate Screening (Procedure C). Inside a glovebox, a mixture of organic nitrile (5.0 mmol), secondary alcohol (1.00 g, 10.0 mmol), KO*t*Bu (0.17 g, 0.15 mmol), and complex **2** (2.4 mg, 2.5 × 10^{-3} mmol) was transferred into a pressure tube fitted with a magnetic stir-bar. The reaction mixture was heated at 120 °C in a preheated oil bath for 1 h (occasionally 2 h). Thereafter, the reaction mixture was cooled down to r.t. and the crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and ethylacetate or hexane and Et_2O as the eluent) to give the pure product.

Following known compounds are characterized by ^1H and $^{13}C\{^1H\}$ NMR spectroscopies, and new compounds are characterized by ^1H and $^{13}C\{^1H\}$ NMR spectroscopies and HRMS.

2-Cyclohexyl-2-phenylacetonitrile (P_{11}).[27] The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and ethylacetate (9.5:0.5) as the eluent) to give pure product $\mathbf{P_{11}}$ as a colorless oil (0.798 g, 80%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.42−7.27 (m, 5H), 3.63 (d, *J* = 7 Hz, 1H), 1.95−1.56 (m, 6H), 1.35−1.04 (m, 5H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 134.7, 128.8, 128.0, 127.9, 120.1, 44.4, 42.8, 31.2, 29.6, 26.0, 25.9, 25.8.

2-Cyclohexyl-2-(4-methoxylphenyl)acetonitrile (P_{21}).[19a] The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and ethylacetate (9.5:0.5) as the eluent) to give pure product $\mathbf{P_{21}}$ as a colorless oil (0.894 g, 78%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.20 (d, *J* = 8 Hz, 2H), 6.89 (d, *J* = 8 Hz, 2H), 3.81 (s, 3H), 3.56 (d, *J* = 7 Hz, 1H), 1.90−1.53 (m, 6H), 1.26−1.00 (m, 5H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 159.3, 129.2, 126.8, 120.5, 114.3, 55.5, 43.7, 42.9, 31.2, 29.8, 26.1, 26.0, 25.9.

2-Cyclohexyl-2-(4-methylphenyl)acetonitrile (P_{31}).[27] The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and ethylacetate (9.5:0.5) as the eluent) to give pure product $\mathbf{P_{31}}$ as a colorless oil (0.798 g, 75%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.21−7.12 (m, 4H), 3.59 (d, *J* = 7 Hz, 1H), 2.34 (s, 3H), 1.92−1.58 (m, 6H), 1.27−1.05 (m, 5H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 137.6, 131.7, 129.4, 127.8, 120.3, 43.9, 42.7, 31.2, 29.6, 25.9, 25.9, 25.8, 21.0.

2-Cyclohexyl-2-(3-methylphenyl)acetonitrile (P_{41}).[27] The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and Et_2O (9.8:0.2) as the eluent) to give pure product $\mathbf{P_{41}}$ as a colorless oil (0.768 g, 72%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.31−7.23 (m, 1H), 7.16−7.03 (m, 3H), 3.63 (d, *J* = 7 Hz, 1H), 2.39 (s, 3H), 1.97−1.60 (m, 6H), 1.34−1.06 (m, 5H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 138.5, 134.6, 128.6, 125.0, 120.2, 44.2, 42.7, 31.2, 29.6, 25.9, 25.8, 25.8, 21.3.

2-Cyclohexyl-2-(3,4-dimethoxyphenyl)acetonitrile (P_{51}).[19a] The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and Et_2O (9.8:0.2) as the eluent) to give pure product $\mathbf{P_{51}}$ as a colorless oil (1.038 g, 80%). ^1H NMR (400 MHz, $CDCl_3$): δ 6.89−6.71 (m, 3H), 3.89 (s, 3H), 3.87 (s, 3H), 3.55 (d, *J* = 7 Hz, 1H), 1.88−1.56 (m, 6H), 1.31−1.06 (m, 5H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 149.3, 148.8, 127.2, 120.5, 111.3, 111.0, 56.1, 44.1, 42.9, 31.3, 29.8, 26.0, 22.8, 14.2.

2-Cyclohexyl-2-(4-chlorophenyl)acetonitrile (P_{61}).[27] The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and Et_2O (9.8:0.2) as the eluent) to give pure product $\mathbf{P_{61}}$ as a colorless oil (0.733 g, 63%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.27 (d, *J* = 8 Hz, 2H), 7.15 (d, *J* = 8 Hz, 2H), 3.54 (d, *J* = 7 Hz, 1H), 1.84−1.49 (m, 6H), 1.29−0.96 (m, 5H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 134.0, 133.3, 129.4, 129.1, 119.8, 43.8, 42.8, 31.2, 29.6, 26.0, 25.9, 25.8.

2-Cyclohexyl-2-(4-bromophenyl)acetonitrile (P_{71}). The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and Et_2O (9.8:0.2) as the eluent) to give pure product $\mathbf{P_{71}}$ as a colorless oil (0.904 g, 65%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, *J* = 8 Hz, 2H), 7.16 (d, *J* = 8 Hz, 2H), 3.59 (d, *J* = 7 Hz, 1H), 1.85−1.49 (m, 6H), 1.30−0.98 (m, 5H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 133.9, 132.1, 132.0, 131.0, 129.8, 122.2, 119.7, 44.0, 42.9, 31.3, 29.8, 29.7, 26.0, 25.9, 25.9.

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HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{14}H_{16}BrNNa$ 300.0358; found 300.0309.

*2-Cyclohexyl-2-(3-chlorophenyl)acetonitrile (**P$_{81}$**).*[27] The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and Et2O (9.8:0.2) as the eluent) to give pure product **P$_{81}$** as a white solid (0.793 g, 68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27−7.17 (m, 3H), 7.15−7.04 (m, 1H), 3.54 (d, J = 7 Hz, 1H), 1.84−1.48 (m, 6H), 1.28−0.97 (m, 5H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 136.7, 134.8, 130.1, 128.3, 126.3, 119.6, 44.0, 42.8, 31.3, 29.5, 25.9, 25.8, 25.8.

*2-Cyclohexyl-2-(3-trifluromethylphenyl)acetonitrile (**P$_{91}$**).*[27] Compound P91 was synthesized according to the general procedure C. The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and Et_2O (9.5:0.5) as the eluent) to give the pure product as a colorless oil (0.560 g, 42%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71−7.37 (m, 4H), 3.71 (d, J = 7 Hz, 1H), 1.91−1.60 (m, 6H), 1.27−1.05 (m, 5H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 135.9, 131.5, 129.5, 125.0, 124.9, 119.5, 44.3, 42.9, 31.3, 29.5, 26.0, 25.8, 25.8.

*2-Cyclohexyl-2-(3,4-methylenedioxyphenyl)acetonitrile (**P$_{101}$**).* The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and Et_2O (9.5:0.5) as the eluent) to give pure product **P$_{101}$** as a colorless oil (0.876 g, 72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.81−6.67 (m, 3H), 5.98 (s, 2H), 3.51 (d, J = 7 Hz, 1H), 1.92−1.56 (m, 6H), 1.28−1.00 (m, 5H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 148.1, 147.4, 128.4, 121.5, 120.3, 108.4, 108.3, 101.4, 44.0, 42.9, 31.1, 29.8, 26.0, 25.9, 25.9. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{17}NO_2Na$ 266.1157; found 266.1165.

*2-Cyclohexyl-2-(2-napthyl)acetonitrile (**P$_{111}$**).*[19a] The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and ethylacetate (9.8:0.2) as the eluent) to give pure product **P$_{111}$** as a white solid (0.994 g, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90−7.75 (m, 4H), 7.56−7.46 (m, 2H), 7.41−7.34 (m, 1H), 3.81 (d, J = 7 Hz, 1H), 1.97−1.59 (m, 6H), 1.28−1.00 (m, 5H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 133.3, 132.9, 132.1, 128.8, 128.0, 127.8, 127.2, 126.8, 126.5, 125.6, 120.3, 44.6, 42.9, 31.5, 29.9, 29.7, 26.1, 26.0, 25.9.

*2-Cyclopentyl-2-phenylacetonitrile (**P$_{12}$**).*[28] The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and ethylacetate (9.0:1.0) as the eluent) to give pure product **P$_{12}$** as a colorless oil (0.778 g, 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.27 (m, 5H), 3.72 (d, J = 7 Hz, 1H), 2.38−2.24 (m, 1H), 1.91−1.80 (m, 1H), 1.78−1.48 (m, 6H), 1.40−1.29 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 136.0, 129.0, 128.0, 127.7, 120.6, 45.4, 42.6, 31.1, 30.3, 25.0, 24.9.

*2-Cyclopentyl-2-(4-methylphenyl)acetonitrile (**P$_{32}$**).* The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and Et_2O (9.7:0.3) as the eluent) to give pure product **P$_{32}$** as a colorless oil (0.747 g, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27−7.11 (m, 4H), 3.67 (d, J = 7 Hz, 1H), 2.39−2.24 (m, 4H), 1.90−1.79 (m, 1H), 1.77−1.47 (m, 6H), 1.40−1.28 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 137.8, 133.0, 129.7, 127.6, 120.9, 45.4, 42.4, 31.1, 30.4, 25.0, 25.0, 21.2. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{14}H_{17}NNa$ 222.1253; found 222.1250.

*2-Cyclopentyl-2-(3-methylphenyl)acetonitrile (**P$_{42}$**).* The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and ethylacetate (9.8:0.2) as the eluent) to give pure product **P$_{42}$** as a colorless oil (0.727 g, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25−7.20 (m, 1H), 7.16−7.07 (m, 3H), 3.67 (d, J = 7 Hz, 1H), 2.43−2.21 (m, 4H), 1.90−1.79 (m, 1H), 1.75−1.48 (m, 6H), 1.40−1.28 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 138.8, 135.9, 128.9, 128.4, 124.8, 120.8, 45.4, 42.5, 31.1, 30.4, 25.0, 25.0, 21.5. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{14}H_{17}NNa$ 222.1253; found 222.1249.

*2-Cyclopentyl-2-(3,4-dimethoxyphenyl)acetonitrile (**P$_{52}$**).*[28] The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and ethylacetate (8.5:1.5) as the eluent) to give pure product **P$_{52}$** as a colorless oil (0.981 g, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.88−6.74 (m, 3H), 3.89 (s, 3H), 3.87 (s, 3H), 3.63 (d, J = 7 Hz, 1H), 2.37−2.22 (m, 1H), 1.90−1.79 (m, 1H), 1.77−1.47 (m, 6H), 1.40−1.28 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 149.3, 148.8, 128.4, 120.9, 120.0, 111.4, 110.7, 45.4, 42.2, 31.0, 30.4, 25.0, 25.0.

*2-Cyclopentyl-2-(4-chlorophenyl)acetonitrile (**P$_{62}$**).*[29] The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and Et2O (9.8:0.2) as the eluent) to give pure product **P$_{62}$** as a colorless oil (0.714 g, 65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.31 (m, 2H), 7.30−7.22 (m, 2H), 3.70 (d, J = 7 Hz, 1H), 2.36−2.21 (m, 1H), 1.89−1.78 (m, 1H), 1.77−1.48 (m, 6H), 1.38−1.25 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 134.5, 134.0, 129.2, 129.1, 120.2, 45.3, 42.0, 31.0, 30.3, 25.0, 24.9.

*2-Cyclopentyl-2-(3,4-methylenedioxyphenyl)acetonitrile (**P$_{102}$**).* The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and ethylacetate (9.8:0.2) as the eluent) to give pure product **P$_{102}$** as a colorless oil (0.858 g, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.82−6.72 (m, 3H), 5.95 (s, 2H), 3.59 (d, J = 7 Hz, 1H), 2.32−2.18 (m, 1H), 1.90−1.78 (m, 1H), 1.75−1.45 (m, 6H), 1.35−1.22 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 148.1, 147.3, 129.6, 121.1, 120.7, 108.5, 108.0, 101.4, 45.3, 42.1, 30.9, 30.3, 24.9, 24.9. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{14}H_{15}NO_2Na$ 252.0995; found 252.0988.

*2-Cycloheptyl-2-phenylacetonitrile (**P$_{13}$**).* Crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and ethylacetate (9.8:0.2) as the eluent) to give pure product **P$_{13}$** as a colorless oil (0.916 g, 86%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.27 (m, 5H), 3.74 (d, J = 7 Hz, 1H), 2.03−1.90 (m, 1H), 1.84−1.63 (m, 4H), 1.61−1.35 (m, 8H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 135.1, 128.7, 127.9, 127.8, 120.3, 44.6, 44.4, 33.1, 30.6, 27.7, 27.7, 26.1, 25.9. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{19}NNa$ 236.1410; found 236.1414.

*2-Cycloheptyl-2-(3-methylphenyl)acetonitrile (**P$_{43}$**).* The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and ethylacetate (9.8:0.2) as the eluent) to give pure product **P$_{43}$** as a colorless oil (0.954 g, 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32−7.17 (m, 2H), 7.15−7.05 (m, 3H), 3.70 (d, J = 7 Hz, 1H), 2.05−1.88 (m, 1H), 1.86−1.66 (m, 4H), 1.65−1.30 (m, 8H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 138.6, 135.1, 128.7, 128.6, 125.1, 120.5, 44.7, 44.5, 33.2, 30.7, 27.8, 27.8, 26.2, 26.1, 21.4. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{21}NNa$ 250.1566; found 250.1566.

*2-Cycloheptyl-2-(3,4-dimethoxyphenyl)acetonitrile (**P$_{53}$**).* The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and ethylacetate (7.5:2.5) as the eluent) to give pure product **P$_{53}$** as a colorless oil (0.930 g, 68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.88−6.75 (m, 3H), 3.89 (s, 3H), 3.87 (s, 3H), 3.64 (d, J = 7 Hz, 1H), 1.97−1.86 (m, 1H), 1.85−1.65 (m, 4H), 1.61−1.34 (m, 8H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 149.3, 148.8, 127.7, 120.7, 120.5, 111.3, 111.0, 56.1, 56.1, 44.7, 44.5, 33.1, 30.9, 28.0, 27.9, 26.3, 26.3. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{17}H_{23}NO_2Na$ 296.1621; found 296.1627.

*2-Cycloheptyl-2-(4-chlorophenyl)acetonitrile (**P$_{63}$**).* The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and ethylacetate (9.8:0.2) as the eluent) to give pure product **P$_{63}$** as a colorless oil (0.867 g, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.31 (m, 2H), 7.28−7.22 (m, 2H), 3.70 (d, J = 7 Hz, 1H), 1.99−1.87 (m, 1H), 1.81−1.63 (m, 4H), 1.61−1.32 (m, 8H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 134.1, 133.9, 129.4, 129.3, 120.0, 44.7, 44.4, 33.3, 30.8, 27.9, 27.9, 26.3, 26.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{18}ClNNa$ 270.1020; found 270.1023.

*2-Cycloheptyl-2-(3,4-methylenedioxyphenyl)acetonitrile (**P$_{103}$**).* The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and ethylacetate (9.0:1.0) as the eluent) to give pure product **P$_{103}$** as a pale-yellow oil (0.940 g, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.80−6.68 (m, 3H), 5.95 (s, 2H), 3.60 (d, J = 7 Hz, 1H), 1.96−1.83 (m, 1H), 1.83−1.61

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(m, 4H), 1.60−1.30 (m, 8H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 148.1, 147.3, 128.9, 121.4, 120.5, 108.3, 108.2, 101.4, 44.6, 44.4, 32.9, 30.8, 27.8, 27.8, 26.2, 26.0. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{16}H_{19}NO_2Na$ 280.1306; found 280.1311.

*3-Ethyl-2-(4-methylphenyl)pentanenitrile (**P**$_{34}$).*[19a] The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and Et_2O (9.8:0.2) as the eluent) to give pure product **P**$_{34}$ as a colorless oil (0.764 g, 76%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.25−7.10 (m, 4H), 3.87 (d, *J* = 7 Hz, 1H), 2.35 (s, 3H), 1.57−1.34 (m, 5H), 0.95 (t, *J* = 8 Hz, 3H), 0.87 (t, *J* = 8 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 137.7, 132.1, 129.6, 127.9, 120.3, 46.3, 40.4, 23.3, 22.6, 21.2, 11.2, 11.1.

*3-Ethyl-2-(3-methylphenyl)pentanenitrile (**P**$_{44}$).*[27] The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and Et_2O (9.8:0.2) as the eluent) to give pure product **P**$_{44}$ as a colorless oil (0.734 g, 73%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.29−7.22 (m, 1H), 7.17−7.06 (m, 3H), 3.88 (d, *J* = 7 Hz, 1H), 2.37 (s, 3H), 1.73−1.64 (m, 1H), 1.58−1.36 (m, 4H), 0.97 (t, *J* = 8 Hz, 3H), 0.87 (t, *J* = 8 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 138.7, 135.1, 128.8, 128.7, 125.1, 120.2, 46.3, 40.7, 23.3, 22.6, 21.5, 11.2, 11.1.

*3-Ethyl-2-(3,4-dimethoxyphenyl)pentanenitrile (**P**$_{54}$).*[19a] The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and Et_2O (9.0:1.0) as the eluent) to give pure product **P**$_{54}$ as a colorless oil (0.667 g, 54%). ^1H NMR (400 MHz, $CDCl_3$): δ 6.89−6.72 (m, 3H), 3.89 (s, 3H), 3.88 (s, 3H), 3.63 (d, *J* = 7 Hz, 1H), 1.59−1.34 (m, 5H), 0.94 (t, *J* = 8 Hz, 3H), 0.87 (t, *J* = 8 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 149.3, 148.4, 127.6, 120.5, 111.4, 111.0, 56.2, 56.1, 46.3, 40.5, 29.8, 23.2, 22.7, 11.2, 11.1.

*3-Ethyl-2-(4-chlorophenyl)pentanenitrile (**P**$_{64}$).*[19a] The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and Et_2O (9.8:0.2) as the eluent) to give pure product **P**$_{64}$ as a colorless oil (0.698 g, 63%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.42−7.17 (m, 4H), 3.89 (d, *J* = 7 Hz, 1H), 1.71−1.60 (m, 1H), 1.54−1.34 (m, 4H), 0.96 (t, *J* = 8 Hz, 3H), 0.86 (t, *J* = 8 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 134.0, 133.7, 129.4, 129.2, 119.7, 46.4, 40.3, 23.3, 22.6, 11.2, 11.1.

*3-Ethyl-2-(3-chlorophenyl)pentanenitrile (**P**$_{84}$).* The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and Et_2O (9.0:1.0) as the eluent) to give pure product **P**$_{84}$ as a colorless oil (0.709 g, 64%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.35−7.28 (m, 3H), 7.25−7.18 (m, 1H), 3.89 (d, *J* = 7 Hz, 1H), 1.72−1.62 (m, 1H), 1.57−1.35 (m, 4H), 0.97 (t, *J* = 8 Hz, 3H), 0.87 (t, *J* = 8 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 137.2, 135.0, 130.3, 128.3, 126.3, 119.5, 46.4, 40.6, 23.4, 22.7, 11.2, 11.1. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{13}H_{16}ClNNa$ 244.0863; found 244.0861.

*3-Methyl-2-phenylheptanenitrile (**P**$_{15}$).* The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and Et_2O (9.8:0.2) as the eluent) to give pure product **P**$_{15}$ (mixture of two diastereomers) as a colorless oil (0.775 g, 77%). ^1H NMR (400 MHz, $CDCl_3$) (m_j, major isomer; m_n, minor isomer): δ 7.60−7.27 (m, 5H), 3.86 (m_j), 3.69 (m_n), (two d, *J* = 8 Hz, 1H), 2.01−1.85 (m, 1H), 1.57−1.25 (m, 6H), 1.00 (m_n), 0.96 (m_j), (two d, *J* = 8 Hz, 3H), 0.91 (m_j), 0.84 (m_n), (two t, *J* = 8 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 135.2, 134.8, 128.9, 128.2, 127.9, 127.9, 119.6, 44.3, 43.6, 38.8, 34.8, 29.3, 22.7, 17.6, 15.8, 14.1. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{14}H_{19}NNa$ 224.1410; found 224.1416.

*3-Methyl-2-(3-methylphenyl)heptanenitrile (**P**$_{45}$).* The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and Et_2O (9.8:0.2) as the eluent) to give pure product **P**$_{45}$ (mixture of two diastereomers) as a colorless oil (0.829 g, 77%). ^1H NMR (400 MHz, $CDCl_3$) (m_j, major isomer; m_n, minor isomer): δ 7.33−7.05 (m, 4H), 3.84 (m_j), 3.67 (m_n), (two d, *J* = 8 Hz, 1H), 2.04−1.88 (m, 1H), 1.59−1.26 (m, 6H), 1.02 (m_n), 0.99 (m_j), (two d, *J* = 8 Hz, 3H), 0.95 (m_j), 0.90 (m_n), (two t, *J* = 8 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 137.8, 137.7, 132.1, 131.7, 129.6, 129.5, 129.3, 129.2, 128.0, 127.7, 120.6, 119.8, 43.9, 43.2,38.7, 38.3, 34.8, 32.7, 29.3, 22.7, 21.1, 17.5, 15.8, 14.1, 14.1. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{15}H_{21}NNa$ 238.1566; found 238.1575.

*3-Methyl-2-(4-chlorophenyl)heptanenitrile (**P**$_{65}$).* The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and Et_2O (9.8:0.2) as the eluent) to give pure product **P**$_{65}$ (mixture of two diastereomers) as a colorless oil (0.707 g, 60%). ^1H NMR (400 MHz, $CDCl_3$) (m_j, major isomer; m_n, minor isomer): δ 7.47−7.29 (m, 2H), 7.28−7.11 (m, 2H), 3.83 (m_n), 3.67 (m_j), (two d, *J* = 8 Hz, 1H), 2.01−1.83 (m, 1H), 1.40−1.15 (m, 6H), 0.99 (m_j), 0.95 (m_n), (two d, *J* = 8 Hz, 3H), 0.90 (m_n), 0.86 (m_j), (two t, *J* = 8 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 134.1, 133.3, 129.5, 129.2, 129.1, 120.0, 43.8, 43.1, 38.8, 38.4, 34.8, 32.6, 29.8, 29.3, 29.1, 22.7, 17.6, 15.8, 14.1. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{14}H_{18}ClNNa$ 258.1025; found 258.1020.

*3-Methyl-2-(3,4-methylenedioxyphenyl)heptanenitrile (**P**$_{105}$).* The crude product was purified by column chromatography (silica as the stationary phase and a mixture of hexanes and Et_2O (9.8:0.2) as the eluent) to give pure product **P**$_{105}$ (mixture of two diastereomers) as a colorless oil (0.821 g, 67%). ^1H NMR (400 MHz, $CDCl_3$) (m_j, major isomer; m_n, minor isomer): δ 7.47−7.29 (m, 2H), 7.28−7.11 (m, 2H), 6.01 (m_n), 5.95 (m_j), (two s, 1H), 3.73 (m_j), 3.57 (m_n), (two d, *J* = 8 Hz, 1H), 1.95−1.78 (m, 1H), 1.40−1.16 (m, 6H), 0.95 (two d, *J* = 8 Hz, 3H), 0.89 (m_j), 0.86 (m_n), (two t, *J* = 8 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 148.1, 147.4, 147.3, 129.5, 128.8, 128.4, 121.6, 121.2, 120.4, 119.7, 108.4, 108.4, 108.1, 101.4, 43.9, 43.2, 38.7, 38.3, 34.5, 32.7, 29.2, 29.0, 22.7, 17.4, 15.8, 14.0. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{15}H_{19}NO_2Na$ 268.1313; found 268.1310.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02400.

^1H and ^{13}C NMR spectra of complexes **1**, **2**, **3**, **4**, and 2-cyclohexylidene-2-phenylacetonitrile (**P**$_{11}$′); ^1H and ^{13}C NMR spectra of products; and crystal data of complex (**2**) (PDF)

FAIR Data is available as a Supporting Information for Publication and includes the primary NMR FID files for compounds 2-cyclohexylidene-2-phenylacetonitrile (**P**$_{11}$′), complexes **1**−**4**, **P**$_{11}$−**P**$_{15}$, **P**$_{21}$, **P**$_{31}$−**P**$_{34}$, **P**$_{41}$−**P**$_{45}$, **P**$_{51}$−**P**$_{54}$, **P**$_{61}$−**P**$_{65}$, **P**$_{71}$, **P**$_{81}$, **P**$_{84}$, **P**$_{91}$, **P**$_{101}$−**P**$_{105}$, **P**$_{111}$ (ZIP)

Accession Codes

CCDC 2025918 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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■ ABBREVIATIONS

MeCN, acetonitrile; NHC, *N*-heterocyclic carbene; Cp*, 1,2,3,4,5-pentamethylcyclopentadienyl; COD, cyclooctadiene; OTf, triflate; TOF, turnover frequency; NMR, nuclear magnetic resonance; DMSO, dimethylsulfoxide; DCM, dichloromethane; Et_2O, diethylether

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