ORGANOMETALLICS

Article

pubs.acs.org/Organometallics

New Entry to the Synthesis of α-Iminonitriles by Lewis Acid Mediated Isomerization of Cyano-Substituted Iminoisobenzofurans Prepared by Palladium-Catalyzed Three-Component Coupling of Arynes, Isocyanides, and Cyanoformates

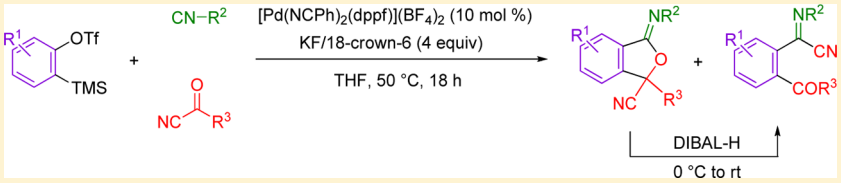
Jing Li,[†] Shintaro Noyori,[†] Kiyohiko Nakajima,[‡] and Yasushi Nishihara*[,†,§]

[†]Division of Earth, Life, and Molecular Sciences, Graduate School of Natural Science and Technology, Okayama University, 3-1-1 Tsushimanaka, Kita-ku, Okayama 700-8530, Japan

[‡]Department of Chemistry, Faculty of Education, Aichi University of Education, 1 Hirosawa, Igaya, Kariya, Aichi 448-8542, Japan

[§]ACT-C, Japan Science and Technology Agency, 4-1-8 Honcho, Kawaguchi, Saitama 332-0012, Japan

Supporting Information



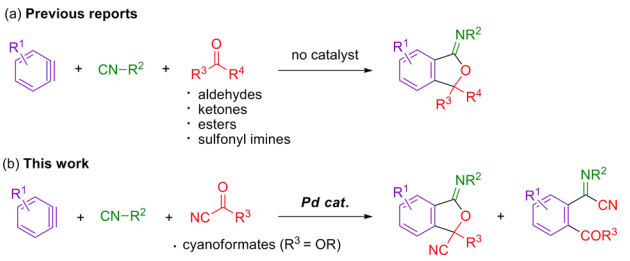
ABSTRACT: A variety of α-iminonitriles were formed as the minor products of three-component coupling reactions of arynes, isocyanides, and cyanoformates in the presence of the cationic palladium complex $[Pd(NCPh)_2(dppf)](BF_4)_2$ as the catalyst, along with cyano-substituted iminoisobenzofurans as the major products. α-Iminonitriles obtained from this process are hardly accessible by conventional methods. In addition, when the isolated iminoisobenzofurans were treated with diisobutylaluminum hydride (DIBAL-H) or $AlMe_3$, the transformation of cyano-substituted iminoisobenzofurans into α-iminonitriles was observed.

INTRODUCTION

α-Iminonitriles, known as imidoyl cyanides, are important compounds for the synthesis of α-keto acids,[1] ketene imines,[2] amides,[3] α-amino acids,[4] imidoylnitriles,[5] β-nitroenamines, amidines, glyoxalic acids,[6] and nitrogen-containing heterocyclic compounds.[7] Although there have been a large number of synthetic methods of α-iminonitriles,[8] the reported procedures are not preparatively satisfactory, owing to the need for a tedious multistep synthesis. No examples to date include an ester group.

On the other hand, arynes have been recognized as highly reactive chemical species, which have played a significant role in synthetic organic chemistry.[9] 2-(Trimethylsilyl)phenyl triflate has been utilized as a common benzyne precursor, which has enabled various carbon−carbon bond-forming processes via addition of nucleophiles to arynes to produce zwitterionic species, followed by trapping with electrophiles.[10] Recently, this feature has been successfully explored by the research groups of Yoshida[11] and Stoltz[12] in three-component coupling reactions of arynes with isocyanides, aldehydes, ketones, sulfonyl imines, or phenyl esters for the direct synthesis of benzoannulated iminofurans under metal-free conditions (Scheme 1a). We felt that added opportunities might accrue from the introduction of transition metals to these reactions with cyanoformates, and indeed this proved the case (Scheme 1b).[13] Despite the large number of related processes now known, our work constitutes the first report of palladium-catalyzed three-component coupling reactions based on activation of electrophiles, insertion of the resulting organo-palladium species into zwitterions, and intramolecular cyclization to afford benzoannulated heterocyclic compounds.

Scheme 1. (a) Metal-Free Synthesis of Iminoisobenzofurans via Three-Component Couplings and (b) Palladium-Assisted Synthesis of Cyano-Substituted Iminoisobenzofurans and α-Iminonitriles



A vast number of functional groups can be installed via coupling of nucleophiles with arynes. The versatility of this transformation can be enhanced, however, by use of novel coupling partners such as cyanoformates.[14] Here we describe the palladium-catalyzed three-component assembly of various arynes, isocyanides, and cyanoformates, which gives access to

Received: April 17, 2014

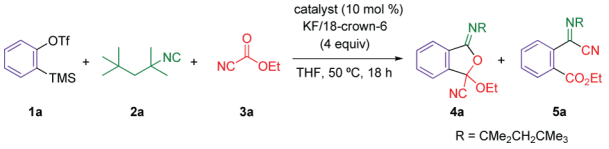
   dx.doi.org/10.1021/om500408h | *Organometallics* XXXX, XXX, XXX−XXX

structurally diverse cyano-substituted iminoisobenzofurans, as well as unexpected α-iminonitriles (Scheme 1b).[15] The latter species are formed via an interesting skeletal rearrangement, involving ring opening of the five-membered iminoisobenzofurans following isolation and treatment of DIBAL-H or $AlMe_3$. This novel reaction, in which α-iminonitriles are formed from three components, formally involves three C−C bond formations and one C−C bond cleavage, accompanied by migration of a cyano group.

RESULTS AND DISCUSSION

We initially optimized the catalyst system used to effect the three-component transformations. Benzyne was prepared in situ from 2-(trimethylsilyl)phenyl triflate (**1a**) and a naked fluoride ion (KF/18-crown-6)[16] and treated with 1,1,3,3-tetramethylbutyl isocyanide (**2a**: $CNCMe_2CH_2CMe_3$) and ethyl cyanoformate (**3a**) at 50 °C for 18 h. The results are summarized in Table 1. When $PdCl_2(NCPh)_2$ was employed as the catalyst, a set of three-component coupled products were obtained (Table 1, entry 1). In our earlier communication,[15] we reported that cyano-substituted iminoisobenzofuran **4a** was formed in 56% yield, but we were unable to characterize a coproduct that was invariably present, formed in up to 33% yield. We are now able to unambiguously assign this species. On the basis of spectroscopic data and single crystal X-ray diffraction (vide infra), we identify this species as α-iminonitrile **5a**, thought to be generated through not only ring opening via C−O bond cleavage but also a CN group migration via C−C bond cleavage in the five-membered heterocyclic ring.

Table 1. Optimization of Three-Component Coupling of the Benzyne Precursor 1a, 1,1,3,3-Tetramethylbutyl Isocyanide (2a), and Ethyl Cyanoformate (3a)[a]



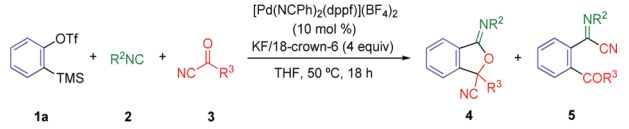
		yield/%[b]	
entry	catalyst	**4a**	**5a**
1	$PdCl_2(NCPh)_2$	56	33
2[d]	$PdCl_2(NCPh)_2$	26	16
3	$Pd_2(dba)_3{\cdot}CHCl_3$	41	26
4	$PdCl_2(PPh_3)_2$	23	14
5	$PdCl_2$(bipy)	26	12
6	$PdCl_2$/2 Py	14	9
7	**$[Pd(NCPh)_2(dppf)](BF_4)_2$**	**68 (44)[c]**	**26 (25)[c]**
8[e]	$[Pd(NCPh)_2(dppf)](BF_4)_2$	59	26
9[f]	$[Pd(NCPh)_2(dppf)](BF_4)_2$	52	28
10	$[Pd(\eta\text{-}C_3H_5)(cod)]BF_4$	52	16
11	$[Rh(cod)_2]BF_4$	45	26
12	$[Cp^*Rh(NCMe)_3](PF_6)_2$	47	24
13	none	0	0

[a]The reaction was carried out using **1a** (0.15 mmol), **2a** (0.15 mmol), **3a** (0.075 mmol), KF (0.3 mmol), 18-crown-6 (0.3 mmol), and a catalyst (10 mol %) in a solvent (0.5 mL) at 50 °C for 18 h. Tf = trifluoromethanesulfonyl, TMS = trimethylsilyl. [b]Yields were determined by GC using tetradecane as an internal standard, based on cyanoformate **3a**. [c]Isolated yields are shown in parentheses. [d]The reaction was carried out at room temperature. [e]The reaction was carried out using $BF_3{\cdot}Et_2O$ (20 mol %) as the additive. [f]The reaction was carried out using $B(C_6F_5)_3$ (20 mol %) as the additive.

Yields suffer when the reaction temperature is decreased from 50 °C to room temperature (Table 1, entry 2). Screening of the palladium catalysts $Pd_2(dba)_3{\cdot}CHCl_3$, $PdCl_2(PPh_3)_2$, $PdCl_2$(bipy), and $PdCl_2$/2Py likewise gave poorer results (Table 1, entries 3−6). In contrast, use of the cationic complex $[Pd(NCPh)_2(dppf)](BF_4)_2$[17] afforded **4a** in 68% yield, accompanied by 26% of **5a** (Table 1, entry 7). However, employment of boron-containing Lewis acids ($BF_3{\cdot}Et_2O$ and $B(C_6F_5)_3$) as the additive had minimal impact on the yields and ratios of **4a** and **5a** (Table 1, entries 8 and 9). As shown in Table 1, entries 10−12, the cationic complexes $[Pd(\eta\text{-}C_3H_5)(cod)]BF_4$, $[Rh(cod)_2]BF_4$, and $[Cp^*Rh(NCMe)_3](PF_6)_2$ afforded **4a** and **5a** in moderate combined yields, suggesting that the cationic character of the catalyst gave better results. Interestingly, this reaction failed in the absence of the catalyst (Table 1, entry 13), in sharp contrast with the transition-metal-free three-component coupling reactions reported by Yoshida and Stoltz, in which iminoisobenzofuran derivatives were obtained.[11,12] We also investigated the use of other solvents: lower yields of the products were obtained in di-*n*-butyl ether and benzonitrile. The reaction did not proceed at all in 1,4-dioxane.

The generality of the three-component coupling reactions was shown first by employing a variety of isocyanides **2** and cyanoformates **3** under the optimized reaction conditions. As shown in Table 2, the three-component coupling reactions proceeded smoothly to form the corresponding cyano-substituted iminoisobenzofurans **4a−h** and α-iminonitrile **5a−h**. A series of aliphatic cyanoformates **3b−f** bearing Me, ^{n}Pr, ^{i}Pr, ^{n}Bu, and Bn substituents reacted efficiently to afford the corresponding products **4b−f** and **5b−f** in moderate to good yields (Table 2, entries 2−6). The structure of **4a** was unambiguously confirmed through careful NMR spectroscopy as well as X-ray diffraction analysis. As shown in Figure S1 (Supporting Information), the imine moiety in **4a** was determined to have the *Z* configuration. Unfortunately, neither **4g** nor **5g** was generated from aromatic cyanoformate **3g**

Table 2. Scope of Pd-Catalyzed Three-Component Coupling of 1a, Isocyanides 2, and Cyanoformates 3[a]



				yield/%[b]	
entry	R^2; isocyanide **2**	R^3; cyanoformate **3**	products	**4a**	**5a**
1	$CMe_2CH_2CMe_3$; **2a**	OEt; **3a**	**4a/5a**	44	25
2[d]	**2a**	OMe; **3b**	**4b/5b**	47	25
3	**2a**	O^{n}Pr; **3c**	**4c/5c**	44	20
4	**2a**	O^{i}Pr; **3d**	**4d/5d**	46	25
5	**2a**	O^{n}Bu; **3e**	**4e/5e**	40	19
6	**2a**	OBn; **3f**	**4f/5f**	51	21
7	**2a**	OPh; **3g**	**4g/5g**	0	0
8	^{t}Bu; **2b**	**3a**	**4h/5h**	42	15

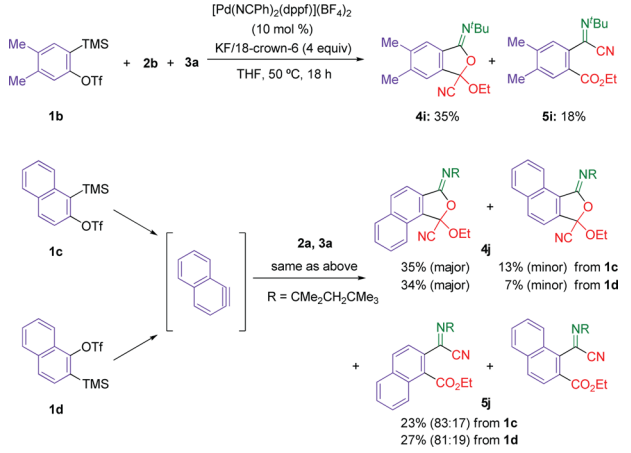
[a]The reactions were carried out using **1a** (1 mmol), **2** (1 mmol), **3** (0.5 mmol), KF (2 mmol), 18-crown-6 (2 mmol), and Pd catalyst (10 mol %) in THF (3.3 mL) at 50 °C for 18 h. [b]Isolated yields, based on cyanoformates **3**.

dx.doi.org/10.1021/om500408h | *Organometallics* XXXX, XXX, XXX−XXX

because diphenyl carbonate as the byproduct was detected (Table 2, entry 7).[14c] In addition to **2a**, other aliphatic substituted isocyanides such as *tert*-butyl isocyanide (**2b**) could participate in the three-component coupling reaction to afford **4h** in 42% yield and **5h** in 15% yield , respectively (Table 2, entry 8).

To understand the effect of substituents on the benzyne moiety in the present reaction, we next employed substituted benzyne precursors **1b–d** as the coupling partners (Scheme 2).

Scheme 2. Three-Component Coupling with Various Substituted Arynes

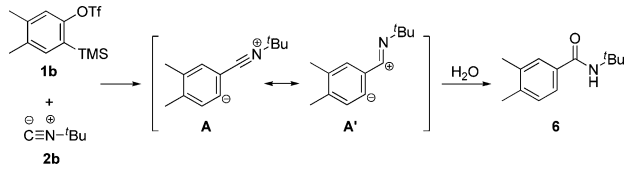


4,5-Dimethyl aryne **1b** reacted smoothly with **2b** and **3a** to give the three-component coupled products **4i** and **5i** in 35% and 18% yields, respectively. Furthermore, the three-component coupling of unsymmetrical aryne was carried out in order to clarify the regioselectivities. 1-(Trimethylsilyl)naphth-2-yl triflate (**1c**) could also be applied to the reaction, leading to the isolation of **4j** in 35% (major) and 13% (minor) yields, respectively, and a isomeric mixture of α-iminonitrile **5j** in 23% combined yield with a 83:17 isomeric ratio. In a similar manner, the reaction of another 1,2-naphthalyne precursor, 2-(trimethylsilyl)naphth-1-yl triflate (**1d**), also took place to give two regioisomers **4j** in 34% and 7% isolated yields, respectively, and an 81:19 ratio of isomers **5j** in 27% combined yield, which indicates that both reactions proceeded through the same 1,2-naphthalyne intermediate. The structure of one of the isomers **5j** was unambiguously confirmed by X-ray diffraction analysis, as depicted in Figure 1.

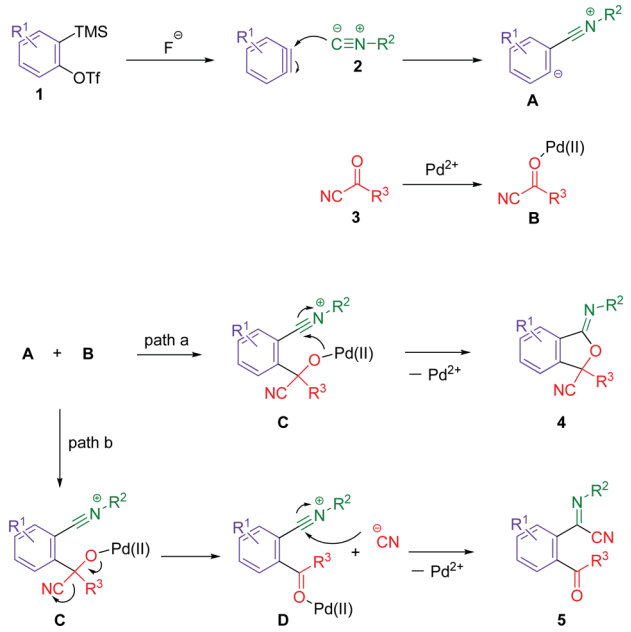
We thus propose the reaction mechanism depicted in Scheme 4. First, zwitterionic species **A** is generated by nucleophilic attack of the carbon atom of isocyanide **2** on the aryne derived from **1** and fluoride ion. Meanwhile, a cationic palladium(II) complex activates cyanoformate **3** to generate active species **B**. Zwitterion **A** then adds to **B** to afford **C**, following which intramolecular cyclization furnishes iminoisobenzofurans **4** (path a). Alternatively, **C** can eliminate a cyano group as the leaving group to form **D**, leading to the formation of **5** (path b). We suspect that the cationic palladium catalyst may interact with cyanoformates **3** to enhance the electrophilicity of the latter.

When the reaction was quenched with water, amides were detected in some cases. For example, when the 4,5-dimethyl aryne precursor **1b** was used as the substrate of the reaction of **2b**, amide **6** was isolated in 31% yield (Scheme 3). From this result, we infer that the reaction of **A** with **B** may be the rate-determining step in Scheme 4.

Scheme 3. Capture of Intermediate A Generated from 1b and 2b



Scheme 4. Plausible Mechanism of the Palladium-Catalyzed Three-Component Coupling Reactions



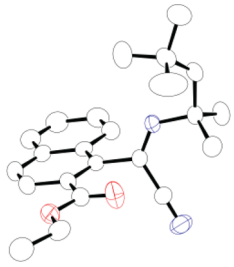
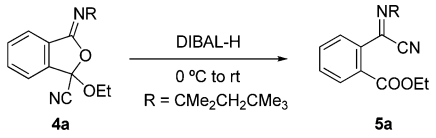


Figure 1. Thermal ellipsoid plot (30% probability) giving the structure of **5j**-minor determined by X-ray crystallography. Hydrogen atoms are omitted for simplicity.

DIBAL-H is a unique and versatile organometallic hydride, widely used as a reducing agent for the reduction of nitriles to the corresponding aldehydes (in conjunction with aqueous workup) or completely to the amines. According to the literature reports,[18] treating **4a** with 1 equiv of DIBAL-H is expected to yield the corresponding aldehyde. To our surprise, however, ring opening via C–O bond cleavage occurred, accompanied by migration of the CN group via C–C bond cleavage, resulting in the transformation of **4a** to **5a** in 18% NMR yield (Scheme 5). When the amount of DIBAL-H was increased to 2.5 equiv, the yield of **5a** increased to 31%; on use of 10 equiv of DIBAL-H and prolonging the reaction time to 24

dx.doi.org/10.1021/om500408h | *Organometallics* XXXX, XXX, XXX–XXX

Scheme 5. Transformation of 4a to 5a with DIBAL-H

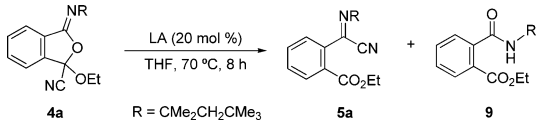


h, **5a** was isolated in 83% yield. However, other metal hydrides such as LiH, NaH, $NaBH_4$, $LiAlH_4$, and $Cp_2Zr(H)Cl$ did not produce **5a** at all. Although numerous examples of the reductive cleavage of acetals,[19] aminals,[20] and ethers[21] by DIBAL-H have been reported, to the best of our knowledge, no applications of DIBAL-H for the cleavage of the C−O bond of iminoisobenzofurans have been reported.

With the optimized reaction conditions in hand, we employed a variety of aryne precursors **1**, isocyanides **2**, and cyanoformates **3** (and benzoyl cyanide **7**) to establish the scope of this transformation. As shown in Table 3, the three-component coupling reactions proceeded smoothly to form mixtures of **4** and **5**. After workup, but without further purification, treatment of the crude mixture with 10 equiv of DIBAL-H in hexane from 0 °C to room temperature for 24 h gave the desired products **5a−j** in moderate to good yields (Table 3, entries 1−9). However, the transformation to the corresponding **8** was not observed for **7** as the substrate (Table 3, entry 10). This transformation provides a novel route to selective synthesis of α-iminonitriles **5**.

To clarify the role of DIBAL-H in this transformation, we explored the use of various alternative Lewis acids. The results are shown in Table 4. Of note, use of the Lewis acids $InCl_3$ and $Hf(OTf)_4$ resulted in lower yields of α-iminonitrile **5a**, due to the formation of amide **9** (Table 4, entries 1 and 2). Reaction in the presence of 20 mol % of $Sc(OTf)_3$ furnished **5a** in 36% yield (Table 4, entry 3). A series of aluminum-based Lewis acids were also tested. Exclusive formation of **5a** was observed on use of equimolar amounts of $AlMe_3$, Al^iBu_3, or $AlEt_2Cl$ (Table 4, entries 4−6), while no reaction occurred when $AlCl_3$ was employed (Table 4, entry 7).

Table 4. Transformation of 4a to 5a with Lewis Acids[a]



entry	Lewis acid (LA)	yield/%[b] 5a	9
1	$InCl_3$	4	38
2	$Hf(OTf)_4$	<1	42
3	$Sc(OTf)_3$	36	<1
4[c]	$AlMe_3$	94	0
5[c]	Al^iBu_3	63	0
6[c]	$AlEt_2Cl$	65	0
7	$AlCl_3$	0	0

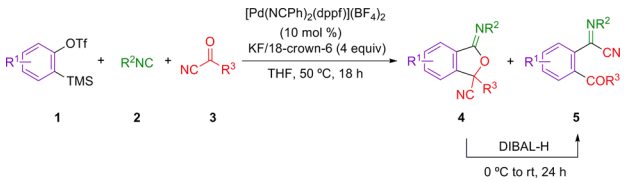
[a]Reactions were carried out using **4a** (0.1 mmol) and Lewis acid (20 mol %) in THF (0.5 mL) at 70 °C for 8 h. [b]Determined by ^1H NMR spectra using CH_2Br_2 as an internal standard. [c]An equimolar amount of Al reagent was used, and the reactions were carried out at room temperature..

Several additional experiments were carried out to gain insight into the reaction mechanism of this transformation. Treatment of **4a** with 0.1 equiv of DIBAL-H and an equimolar amount of KCN afforded the product **5a** in 41% yield. Additionally, when *N*-benzylidene-*tert*-butylamine was treated with KCN, no reaction was observed, and the substrate remained unreacted. On the basis of these results, it is reasonable to hypothesize that DIBAL-H functions as a Lewis acid. We propose that reaction of **4** with DIBAL-H occurs via the mechanism presented in Scheme 6. Thus, DIBAL-H acts as a Lewis acid to promote the cleavage of the C−O bond and release of cyanide ion, which then attacks the iminyl carbon to produce **5**.

CONCLUSION

In summary, we have developed a useful method for the synthesis of α-iminonitriles via a three-component coupling

Table 3. Three-Component Couplings of Aryl Triflates 1, Isocyanides 2, and Cyanoformates 3, Followed by Treatment of DIBAL-H: Exclusive Synthesis of α-Iminonitriles 5[a]

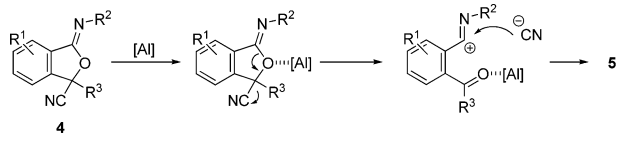


entry	aryne precursors	R^2; isocyanide **2**	R^3; cyanoformate **3**	products	yield/%[b]
1	**1a**	$CMe_2CH_2CMe_3$; **2a**	OEt; **3a**	**5a**	62
2	**1a**	**2a**	OMe; **3b**	**5b**	67
3	**1a**	**2a**	O^{n}Pr; **3c**	**5c**	53
4	**1a**	**2a**	O^{i}Pr; **3d**	**5d**	58
5	**1a**	**2a**	O^{n}Bu; **3e**	**5e**	54
6	**1a**	**2a**	OBn; **3f**	**5f**	57
7	**1a**	^{t}Bu; **2b**	**3a**	**5h**	50
8	**1b**	**2b**	**3a**	**5i**	41
9	**1c**	**2a**	**3a**	**5j**	54
10	**1a**	**2a**	Ph; **7**	**8**	0

[a]The reactions were carried out using **1** (0.5 mmol), **2** (0.5 mmol), **3** (0.25 mmol), KF (1 mmol), 18-crown-6 (1 mmol), and Pd catalyst (10 mol %) in THF (1.6 mL) at 50 °C for 18 h. After workup, the crude products were treated with 10 equiv of DIBAL-H in hexane from 0 °C to room temperature for 24 h. [b]Isolated yields, based on cyanoformates **3**.

dx.doi.org/10.1021/om500408h | *Organometallics* XXXX, XXX, XXX−XXX

Scheme 6. Proposed Mechanism for Transformation of 4 to 5



reaction of arynes, isocyanides, and cyanoformates. A cationic palladium catalyst was found to play a crucial role in promoting this transformation. Isomerization of cyano-substituted iminoisobenzofurans to α-iminonitriles was effectively triggered by treatment with aluminum-based Lewis acids. Studies aimed at elucidating further transformations of the resulting iminoisobenzofurans and α-iminonitriles are in progress in our laboratory and will be reported in due course.

EXPERIMENTAL SECTION

General Considerations. All reactions were carried out under an argon atmosphere using standard Schlenk techniques. Glassware was dried in an oven (130 °C) and heated under reduced pressure before use. NMR spectra (^{1}H, ^{13}C{^{1}H}) were recorded on Mercury-300 (300 MHz) and Varian INOVA-600 (600 MHz) spectrometers. All ^{1}H NMR chemical shifts are reported in ppm relative to the proton resonance in $CDCl_3$ at δ 7.26. All ^{13}C{^{1}H} NMR chemical shifts are reported in ppm relative to the carbon resonance in $CDCl_3$ at δ 77.0. Preparatory HPLC was carried out using a Model LC-9204R/U recycling preparative HPLC using UV and RI as detectors with chloroform as the eluent. Infrared spectra were recorded on a Shimadzu IRPrestige-21 spectrophotometer. Elemental analyses were carried out with a Perkin-Elmer 2400 CHN elemental analyzer at Okayama University. High-resolution mass spectra (HRMS) were obtained by fast atom bombardment (FAB) using a double-focusing magnetic sector mass spectrometer.

Each single crystal of **4a** (CCDC-886033) and **5j** (CCDC-968718) was glued to the top of a glass fiber with epoxy resin, and X-ray diffraction data were obtained at ambient temperature using a Rigaku SCXmini CCD diffractometer with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). The data were collected and processed using the CrystalClear software package[22] for both complexes, and numerical absorption corrections were applied.[23] The structures were solved by direct methods (SHELXS97[24]) and refined by a full-matrix least-squares method on F^2 using the SHELXL97 software package.[24] All non-hydrogen atoms were refined anisotropically, and hydrogen atoms were placed at idealized positions by using riding models. All calculations were performed with the CrystalStructure crystallographic software package.[25]

General Procedure for the Synthesis of *N*-[3-Cyano-3-ethoxy-1(3*H*)-isobenzofuranylidene]-2,4,4-trimethyl-2-pentanamine (4a). A flame-dried 25 mL Schlenk flask with a magnetic stir bar was charged with KF (116 mg, 2.0 mmol), 18-crown-6 (529 mg, 2.0 mmol), and $[Pd(PhCN)_2(dppf)](BF_4)_2$ (52 mg, 0.05 mmol, 10 mol %) in THF (3.3 mL) under argon. To this solution were added 2-(trimethylsilyl)phenyl triflate (**1a**; 233 μL, 1.0 mmol), 1,1,3,3-tetramethylbutyl isocyanide (**2a**; 175 μL, 1.0 mmol), and ethyl cyanoformate (**3a**; 51 μL, 0.5 mmol) sequentially via syringe. The reaction mixture was heated to 50 °C for 18 h and then cooled to ambient temperature, quenched with water, and extracted with diethyl ether (20 mL × 3). The combined extracts were washed with brine and dried over anhydrous sodium sulfate. The volatiles were removed under reduced pressure to give crude products, which were purified by silica gel column chromatography (eluent hexane/ethyl acetate, 19/1). Further purification with HPLC (eluent chloroform) gave **4a** (69 mg, 0.22 mmol, 44%) as a yellow solid. IR (KBr, cm^{-1}): 2239 (w, C≡N), 1715 (s, C═N). ^{1}H NMR (300 MHz, $CDCl_3$, room temperature): δ 1.01 (s, 9H), 1.34 (t, $^3J_{HH}$ = 7.2 Hz, 3H), 1.46 (s, 6H), 1.76 (m, 2H), 4.01 (m, 2H), 7.55−7.62 (m, 3H), 7.76−7.79 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 14.9, 30.4, 30.5, 31.7 (×3), 32.0, 55.3, 58.4, 63.6, 98.8, 114.8, 122.5 (×2), 123.9, 131.7, 132.1, 139.2, 147.6. MS (EI, *m*/*z* (relative intensity)): 314 (M$^+$, 2), 299 (71), 253 (28), 243 (86), 197 (54), 159 (31), 158 (100), 157 (67), 148 (31), 130 (71), 102 (43). Anal. Calcd for $C_{19}H_{26}N_2O_2$: C, 72.58; H, 8.33; N, 8.91. Found: C, 72.22; H, 8.42; N, 8.75.

*N-[3-Cyano-3-methoxy-1(3H)-isobenzofuranylidene]-2,4,4-trimethyl-2-pentanamine (**4b**).* Isolated in 47% yield (71 mg, 0.24 mmol) as a pale yellow oil. IR (KBr, cm^{-1}): 2239 (w, C≡N), 1724 (s, C═N). ^{1}H NMR (300 MHz, $CDCl_3$, room temperature): δ 1.02 (s, 9H), 1.45 (s, 3H), 1.46 (s, 3H), 1.76 (m, 2H), 3.68 (s, 3H), 7.58−7.61 (m, 3H), 7.74−7.77 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 30.4, 30.5, 31.7 (×3), 32.0, 54.3, 55.4, 58.4, 99.2, 114.4, 122.5 (×2), 123.9, 131.8, 132.1, 138.8, 147.4. MS (EI, *m*/*z* (relative intensity)): 300 (M$^+$, 2), 285 (59), 253 (15), 230 (15), 229 (100), 202 (16), 197 (38), 173 (17), 162 (16), 158 (34), 157 (47), 130 (92), 102 (40). Anal. Calcd for $C_{18}H_{24}N_2O_2$: C, 71.97; H, 8.05; N, 9.33. Found: C, 71.79; H, 8.43; N, 9.06.

*N-[3-Cyano-3-propoxy-1(3H)-isobenzofuranylidene]-2,4,4-trimethyl-2-pentanamine (**4c**).* Isolated in 44% yield (72 mg, 0.22 mmol) as a pale yellow oil. IR (KBr, cm^{-1}): 2239 (w, C≡N), 1721 (s, C═N). ^{1}H NMR (300 MHz, $CDCl_3$, room temperature): δ 0.97 (t, $^3J_{HH}$ = 7.5 Hz, 3H), 1.01 (s, 9H), 1.45 (s, 6H), 1.70 (m, 2H), 1.75 (d, *J* = 4.2 Hz, 2H), 3.88 (m, 2H), 7.55−7.61 (m, 3H), 7.75−7.77 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 10.4, 22.5, 30.45, 30.53, 31.7 (×3), 32.0, 55.3, 58.4, 69.4, 98.9, 114.8, 122.5 (×2), 123.9, 131.7, 132.0, 139.2, 147.7. MS (EI, *m*/*z* (relative intensity)): 328 (M$^+$, 2), 313 (80), 257 (53), 253 (23), 229 (21), 215 (24), 197 (23), 188 (22), 158 (100), 148 (47), 130 (97), 102 (48). Anal. Calcd for $C_{20}H_{28}N_2O_2$: C, 73.14; H, 8.59; N, 8.53. Found: C, 73.29; H, 8.76; N, 8.36.

*N-[3-Cyano-3-(1-methyethoxy)-1(3H)-isobenzofuranylidene]-2,4,4-trimethyl-2-pentanamine (**4d**).* Isolated in 46% yield (75 mg, 0.23 mmol) as a yellow solid. IR (KBr, cm^{-1}): 2237 (w, C≡N), 1715 (s, C═N). ^{1}H NMR (300 MHz, $CDCl_3$, room temperature): δ 1.02 (s, 9H), 1.33 (d, $^3J_{HH}$ = 6.3 Hz, 3H), 1.40 (d, *J* = 6.3 Hz, 3H), 1.45 (s, 3H), 1.46 (s, 3H), 1.74 (m, 2H), 4.49 (sep, *J* = 6.3 Hz, 1H), 7.54−7.60 (m, 3H), 7.74−7.77 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 23.1, 23.7, 30.6, 31.8 (×3), 32.0, 55.5, 58.2, 72.9, 98.9, 115.2, 122.5, 123.9, 131.6, 132.0, 139.5, 147.7. MS (EI, *m*/*z* (relative intensity)): 328 (M$^+$, 1), 313 (50), 285 (20), 215 (51), 188 (31), 159 (27), 158 (100), 157 (22), 130 (60), 102 (31). Anal. Calcd for $C_{20}H_{28}N_2O_2$: C, 73.14; H, 8.59; N, 8.53. Found: C, 72.97; H, 8.58; N, 8.30.

*N-[3-Buthoxy-3-cyano-1(3H)-isobenzofuranylidene]-2,4,4-trimethyl-2-pentanamine (**4e**).* Isolated in 40% yield (68 mg, 0.20 mmol) as a yellow oil. IR (KBr, cm^{-1}): 2237 (w, C≡N), 1719 (s, C═N). ^{1}H NMR (300 MHz, $CDCl_3$, room temperature): δ 0.93 (t, $^3J_{HH}$ = 7.2 Hz, 3H), 1.01 (s, 9H), 1.42 (m, 2H), 1.45 (s, 3H), 1.46 (s, 3H), 1.67 (m, 2H), 1.75 (m, 2H), 3.92 (m, 2H), 7.56−7.60 (m, 3H), 7.75−7.69 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 13.7, 19.1, 30.4, 30.5, 31.2 (×3), 31.7, 32.0, 55.3, 58.3, 67.6, 98.9, 114.8, 122.5, 123.9, 131.7, 132.0, 139.2, 147.6. MS (EI, *m*/*z* (relative intensity)): 342 (M$^+$, 4), 327 (100), 271 (41), 215 (25), 188 (23), 159 (23), 158 (81), 157 (37), 148 (48), 130 (94), 102 (38). Anal. Calcd for $C_{21}H_{30}N_2O_2$: C, 73.65; H, 8.83; N, 8.18. Found: C, 73.37; H, 9.13; N, 7.93.

*N-[3-Cyano-3-(phenylmethoxy)-1(3H)-isobenzofuranylidene]-2,4,4-trimethyl-2-pentanamine (**4f**).* Isolated in 51% yield (96 mg, 0.26 mmol) as a pale yellow oil. IR (KBr, cm^{-1}): 2239 (w, C≡N), 1722 (s, C═N). ^{1}H NMR (300 MHz, $CDCl_3$, room temperature): δ 1.02 (s, 9H), 1.45 (s, 3H), 1.46 (s, 3H), 1.76 (m, 2H), 4.88 (d, $^3J_{HH}$ = 10.5 Hz, 1H), 5.02 (d, $^3J_{HH}$ = 10.5 Hz, 1H), 7.32−7.37 (m, 5H), 7.56−7.64 (m, 3H), 7.75−7.76 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 30.46, 30.51, 31.8 (×3), 32.0, 55.4, 58.4, 69.7, 98.7, 114.7, 122.7, 123.9, 128.3 (×2), 128.5, 128.6 (×2), 131.85, 132.1, 135.3, 138.9, 147.3. MS (EI, *m*/*z* (relative intensity)): 376 (M$^+$, 0.24), 361 (16), 285 (47), 188 (31), 148 (13), 130 (13), 111 (12), 92 (8), 91 (100), 65 (9). Anal. Calcd for $C_{24}H_{28}N_2O_2$: C, 76.56; H, 7.50; N, 7.44. Found: C, 76.36; H, 7.86; N, 7.30.

dx.doi.org/10.1021/om500408h | *Organometallics* XXXX, XXX, XXX−XXX

*N-[3-Cyano-3-ethoxy-1(3H)-isobenzofuranylidene]-2-methyl-2-propanamine (**4h**).* Isolated in 42% yield (54 mg, 0.21 mmol) as a yellow oil. IR (KBr, cm^{-1}): 2239 (w, C≡N), 1721 (s, C═N). ^1H NMR (300 MHz, $CDCl_3$, room temperature): δ 1.33 (t, $^3J_{HH}$ = 7.2 Hz, 3H), 1.42 (s, 9H), 3.98 (m, 2H), 7.56−7.62 (m, 3H), 7.79−7.81 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 14.9, 28.0, 30.1 (×3), 54.8, 63.6, 98.8, 114.7, 122.5, 123.9, 131.7, 132.2, 139.2, 149.3. MS (EI, *m*/*z* (relative intensity)): 258 (M^+, 1), 243 (100), 197 (44), 158 (68), 157 (31), 130 (55), 102 (49). Anal. Calcd for $C_{15}H_{18}N_2O_2$: C, 69.74; H, 7.02; N, 10.84. Found: C, 69.99; H, 7.07; N, 10.53.

*N-[3-Cyano-3-ethoxy-5,6-dimethyl-1(3H)-isobenzofuranylidene]-2,4,4-trimethyl-2-pentanamine (**4i**).* Isolated in 33% yield (47 mg, 0.17 mmol) as a yellow oil. IR (KBr, cm^{-1}): 2212 (w, C≡N), 1715 (s, C═N). ^1H NMR (300 MHz, $CDCl_3$, room temperature): δ 1.31 (t, $^3J_{HH}$ = 7.2 Hz, 3H), 1.41 (s, 9H), 2.33 (s, 3H), 2.36 (s, 3H), 3.98 (m, 2H), 7.37 (s, 1H), 7.58 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 14.9, 20.0, 20.4, 30.1, 54.6, 63.3, 98.7, 115.0, 123.0, 124.2, 129.2, 137.1, 141.2, 142.1, 149.8. MS (EI, *m*/*z* (relative intensity)): 286 (M^+, 6), 271 (100), 225 (58), 201 (24), 186 (67), 158 (78), 103 (41), 77 (26). Anal. Calcd for $C_{17}H_{22}N_2O_2$: C, 71.30; H, 7.74; N, 9.78. Found: C, 71.20; H, 7.81; N, 9.48.

*1-Ethoxy-3-(2,4,4-trimethylpentan-2-ylimino)-1,3-dihydronaphtho[1,2-c]furan-1-carbonitrile (**4j**-major).* Isolated in 35% yield (64 mg, 0.18 mmol) (from **1c**) or 34% yield (62 mg, 0.17 mmol) (from **1d**) as a yellow oil. IR (KBr, cm^{-1}): 2237 (C≡N), 1713 (s, C═N). ^1H NMR (300 MHz, $CDCl_3$, room temperature): δ 1.04 (s, 9H), 1.35 (t, $^3J_{HH}$ = 7.2 Hz, 3H), 1.54 (s, 3H), 1.55 (s, 3H), 1.88 (m, 2H), 4.02 (m, 2H), 7.61−7.73 (m, 3H), 7.95 (d, $^3J_{HH}$ = 7.5 Hz, 1H), 8.06 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 9.34 (d, $^3J_{HH}$ = 8.1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 14.9, 30.8, 30.9, 31.9 (×3), 32.1, 55.2, 59.0, 63.5, 98.3, 114.9, 118.3, 125.1, 126.2, 127.9, 128.3, 128.4, 128.6, 133.4, 135.0, 138.7, 148.4. MS (EI, *m*/*z* (relative intensity)): 364 (M^+, 26), 349 (44), 293 (26), 247 (34), 225 (26), 223 (20), 210 (20), 208 (40), 207 (34), 197 (23), 180 (100), 179 (39), 153 (35), 152 (66), 127 (23), 126 (28), 97 (19). HRMS (FAB^+): *m*/*z* calcd for $C_{23}H_{29}N_2O_2$ $(M + H)^+$ 365.2229, found 365.2251.

*3-Ethoxy-1-(2,4,4-trimethylpentan-2-ylimino)-1,3-dihydronaphtho[2,1-c]furan-3-carbonitrile (**4j**-minor).* Isolated in 13% yield (24 mg, 0.07 mmol) (from **1c**) or 7% yield (13 mg, 0.04 mmol) (from **1d**) as a yellow oil. IR (KBr, cm^{-1}): 2237 (C≡N), 1713 (s, C═N). ^1H NMR (300 MHz, $CDCl_3$, room temperature): δ 1.08 (s, 9H), 1.18 (t, $^3J_{HH}$ = 7.2 Hz, 3H), 1.99 (d, $^3J_{HH}$ = 14.4 Hz, 1H), 2.52 (d, $^3J_{HH}$ = 14.4 Hz, 1H), 3.00 (m, 1H), 3.33 (m, 1H), 7.61−7.73 (m, 3H), 7.95 (d, $^3J_{HH}$ = 7.5 Hz, 1H), 8.13 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 9.14 (d, $^3J_{HH}$ = 8.1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 14.5, 26.7, 28.9, 31.5 (×3), 31.8, 51.0, 58.9, 61.9, 85.3, 117.0, 118.3, 124.3, 126.1, 128.0, 128.5, 129.0, 134.3, 134.8, 139.2, 168.9. MS (EI, *m*/*z* (relative intensity)): 364 (M^+, 9), 349 (71), 293 (20), 247 (35), 225 (29), 223 (25), 208 (46), 207 (42), 180 (100), 153 (29), 152 (73), 126 (21), 97 (20). HRMS (FAB+): *m*/*z* calcd for $C_{23}H_{29}N_2O_2$ $(M + H)^+$ 365.2229, found 365.2236.

*(Z)-Ethyl 2-[Cyano(2,4,4-trimethylpentan-2-ylimino)methyl]-benzoate (**5a**).* Isolated in 25% yield (39 mg, 0.13 mmol) as a pale yellow oil. IR (KBr, cm^{-1}): 2210 (w, C≡N), 1717 (s, C═N), 1614 (s, C═O). ^1H NMR (300 MHz, $CDCl_3$, room temperature): δ 1.01 (s, 9H), 1.40 (t, $^3J_{HH}$ = 7.2 Hz, 3H), 1.61 (s, 6H), 1.90 (s, 2H), 4.40 (q, $^3J_{HH}$ = 7.2 Hz, 2H), 7.50−7.59 (m, 3H), 7.91−7.94 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 14.2, 29.1, 31.8, 32.0, 55.8, 61.7, 63.0, 112.6, 129.3, 130.1, 130.2, 130.3, 132.2, 136.2, 138.2, 166.4. MS (EI, *m*/*z* (relative intensity)): 314 (M^+, 3), 300 (22), 299 (93), 253 (23), 243 (55), 197 (36), 158 (53), 157 (100), 148 (38), 130 (66), 102 (35). Anal. Calcd for $C_{19}H_{26}N_2O_2$: C, 72.58; H, 8.33; N, 8.91. Found: C, 72.83; H, 8.12; N, 8.92.

*(Z)-Methyl 2-[Cyano(2,4,4-trimethylpentan-2-ylimino)methyl]-benzoate (**5b**).* Isolated in 25% yield (38 mg, 0.13 mmol) as a pale yellow oil. IR (KBr, cm^{-1}): 2210 (w, C≡N), 1728 (s, C═N), 1614 (s, C═O). ^1H NMR (300 MHz, $CDCl_3$, room temperature): δ 1.01 (s, 9H), 1.60 (s, 6H), 1.90 (s, 2H), 3.92 (s, 3H), 7.49−7.62 (m, 3H), 7.89−7.92 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 25.2, 27.8, 28.0, 48.4, 51.8, 59.0, 108.6, 125.3, 125.8, 126.3, 126.4, 128.4, 132.2, 134.2, 163.0. MS (EI, *m*/*z* (relative intensity)): 300 (M^+, 3), 286 (20), 285 (100), 229 (64), 197 (30), 162 (16), 158 (17), 157 (51), 130 (88), 102 (31). Anal. Calcd for $C_{18}H_{24}N_2O_2$: C, 71.97; H, 8.05; N, 9.33. Found: C, 71.72; H, 8.31; N, 9.01.

*(Z)-Propyl 2-[Cyano(2,4,4-trimethylpentan-2-ylimino)methyl]-benzoate (**5c**).* Isolated in 20% yield as(33 mg, 0.10 mmol) as a pale yellow oil. IR (KBr, cm^{-1}): 2210 (w, C≡N), 1714 (s, C═N), 1616 (s, C═O). ^1H NMR (300 MHz, $CDCl_3$, room temperature): δ 1.01 (t, $^3J_{HH}$ = 7.5 Hz, 12H), 1.61 (s, 6H), 1.80 (m, 2H), 1.89 (s, 2H), 4.30 (t, *J* = 6.9 Hz, 2H), 7.50−7.59 (m, 3H), 7.91−7.94 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 10.4, 22.0, 29.1, 31.7 (overlapped), 32.0, 55.8, 63.0, 67.2, 112.6, 129.3, 130.2, 130.3, 132.2, 136.2, 138.3, 166.5. MS (EI, *m*/*z* (relative intensity)): 328 (M^+, 4), 314 (22), 313 (100), 257 (29), 197 (20), 158 (39), 157 (45), 148 (34), 130 (58), 102 (16). Anal. Calcd for $C_{20}H_{28}N_2O_2$: C, 73.14; H, 8.59; N, 8.53. Found: C, 73.34; H, 8.74; N, 8.23.

*(Z)-Isopropyl 2-[Cyano(2,4,4-trimethylpentan-2-ylimino)methyl]-benzoate (**5d**).* Isolated in 25% yield (41 mg, 0.13 mmol) as a yellow solid. IR (KBr, cm^{-1}): 2210 (w, C≡N), 1716 (s, C═N), 1618 (s, C═O). ^1H NMR (300 MHz, $CDCl_3$, room temperature): δ 1.02 (s, 9H), 1.39 (d, $^3J_{HH}$ = 6.3 Hz, 6H), 1.62 (s, 6H), 1.90 (s, 2H), 5.28 (seq, $^3J_{HH}$ = 6.3 Hz, 1H), 7.47−7.58 (m, 3H), 7.91−7.94 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 21.9, 29.1, 31.8, 32.0, 55.9, 63.0, 69.5, 112.8, 129.4, 130.0, 130.3, 130.4, 132.2, 136.4, 138.6, 165.8. MS (EI, *m*/*z* (relative intensity)): 328 (M^+, 4), 314 (22), 313 (100), 285 (27), 271 (29), 215 (64), 188 (21), 175 (22), 158 (59), 157 (50), 148 (41), 130 (71), 111 (20), 102 (20). Anal. Calcd for $C_{20}H_{28}N_2O_2$: C, 73.14; H, 8.59; N, 8.53. Found: C, 72.77; H, 8.97; N, 8.14.

*(Z)-Butyl 2-[Cyano(2,4,4-trimethylpentan-2-ylimino)methyl]-benzoate (**5e**).* Isolated in 19% yield (32 mg, 0.10 mmol) as a yellow oil. IR (KBr, cm^{-1}): 2210 (w, C≡N), 1718 (s, C═N), 1620 (s, C═O). ^1H NMR (300 MHz, $CDCl_3$, room temperature): δ 0.97 (t, $^3J_{HH}$ = 7.2 Hz, 3H), 1.01 (s, 9H), 1.45 (m, 2H), 1.61 (s, 6H), 1.75 (m, 2H), 1.89 (s, 2H), 4.34 (t, $^3J_{HH}$ = 6.6 Hz, 2H), 7.49−7.61 (m, 3H), 7.90−7.93 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 13.7, 19.2, 29.1, 30.6, 31.7 (overlapped), 32.0, 55.8, 63.0, 65.5, 112.6, 129.3, 130.2, 130.3, 132.2, 136.2, 138.3, 166.5. MS (EI, *m*/*z* (relative intensity)): 342 (M^+, 4), 328 (24), 327 (100), 271 (26), 158 (39), 157 (38), 148 (35), 130 (60), 102 (19). Anal. Calcd for $C_{21}H_{30}N_2O_2$: C, 73.65; H, 8.83; N, 8.18. Found: C, 73.25; H, 8.69; N, 7.94.

*(Z)-Benzyl 2-[Cyano(2,4,4-trimethylpentan-2-ylimino)methyl]-benzoate (**5f**).* Isolated in 21% yield (39 mg, 0.11 mmol) as a pale yellow oil. IR (KBr, cm^{-1}): 2212 (w, C≡N), 1717 (s, C═N), 1614 (s, C═O). ^1H NMR (300 MHz, $CDCl_3$, room temperature): δ 0.99 (s, 9H), 1.53 (s, 6H), 1.86 (s, 2H), 5.37 (s, 2H), 7.36−7.42 (m, 5H), 7.51−7.59 (m, 3H), 7.93−7.95 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 29.0, 31.7, 31.9, 55.8, 63.0, 67.4, 112.6, 128.4, 128.5, 128.6, 129.4, 129.7, 130.2, 130.5, 132.4, 135.3, 136.0, 138.4, 166.3. MS (EI, *m*/*z* (relative intensity)): 376 (M^+, 0.31), 361 (17), 285 (50), 188 (33), 148 (13), 130 (13), 111 (12), 91 (100), 65 (15). Anal. Calcd for $C_{24}H_{28}N_2O_2$: C, 76.56; H, 7.50; N, 7.44. Found: C, 76.17; H, 7.58; N, 7.30.

*(Z)-Ethyl 2-[(tert-Butylimino)(cyano)methyl]benzoate (**5h**).* Isolated in 15% yield (19 mg, 0.08 mmol) as a yellow oil. IR (KBr, cm^{-1}): 2212 (w, C≡N), 1717 (s, C═N), 1622 (s, C═O). ^1H NMR (300 MHz, $CDCl_3$, room temperature): δ 1.40 (t, $^3J_{HH}$ = 7.2 Hz, 3H), 1.55 (s, 9H), 4.40 (q, $^3J_{HH}$ = 7.2 Hz, 2H), 7.51−7.60 (m, 3H), 7.90−7.92 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 14.2, 29.1, 59.0, 61.7, 112.2, 129.6, 130.2, 130.3, 130.4, 132.2, 137.7, 137.8, 166.5. MS (EI, *m*/*z* (relative intensity)): 258 (M^+, 5), 243 (64), 229 (27), 202 (38), 197 (29), 173 (26), 158 (51), 157 (92), 156 (35), 130 (100), 104 (21), 103 (27), 102 (51). Anal. Calcd for $C_{15}H_{18}N_2O_2$: C, 69.74; H, 7.02; N, 10.84. Found: C, 69.78; H, 7.03; N, 10.56.

*(Z)-Ethyl 2-[(tert-Butylimino)(cyano)methyl]-4,5-dimethylbenzoate (**5i**).* Isolated in 18% yield (26 mg, 0.09 mmol) as a yellow oil. IR (KBr, cm^{-1}): 2214 (w, C≡N), 1714 (s, C═N), 1607 (s, C═O). ^1H NMR (300 MHz, $CDCl_3$, room temperature): δ 1.39 (t, $^3J_{HH}$ = 6.9 Hz, 3H), 1.54 (s, 9H), 2.32 (s, 3H), 2.32 (s, 3H), 4.37 (q, $^3J_{HH}$ =

dx.doi.org/10.1021/om500408h | *Organometallics* XXXX, XXX, XXX−XXX

7.5 Hz, 2H), 7.23 (s, 1H), 7.69 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 14.2, 19.5, 19.7, 29.2, 58.7, 61.4, 112.4, 127.3, 130.7, 131.5, 135.6, 138.2, 139.4, 141.7, 166.6. MS (EI, *m*/*z* (relative intensity)): 286 (M^+, 14), 271 (54), 257 (25), 230 (48), 225 (38), 201 (53), 186 (42), 185 (86), 184 (100), 158 (87), 132 (37), 131 (20), 130 (19), 103 (31), 77 (19). Anal. Calcd for $C_{17}H_{22}N_2O_2$: C, 71.30; H, 7.74; N, 9.78. Found: C, 71.37; H, 7.81; N, 9.45.

Compound ***5j***. Isolated in 23% (major:minor = 83:17) combined yield (42 mg, 0.12 mmol) (from **1c**) or 27% (major:minor = 81:19) combined yield (49 mg, 0.14 mmol) (from **1d**) as a yellow solid. IR (KBr, cm^{-1}): 2210 (w, C≡N), 1715 (s, C═N), 1622 (s, C═O). HRMS (FAB^+): *m*/*z* calcd for $C_{23}H_{29}N_2O_2$ $(M + H)^+$ 365.2229, found 365.2205.

*(Z)-Ethyl 2-[Cyano(2,4,4-trimethylpentan-2-ylimino)methyl]-1-naphthoate (****5j****-major).* ^{1}H NMR (300 MHz, $CDCl_3$, room temperature): δ 0.98 (s, 9H), 1.43 (t, $^3J_{HH}$ = 7.2 Hz, 3H), 1.77 (s, 6H), 1.84 (s, 2H), 4.43 (q, $^3J_{HH}$ = 7.2 Hz, 2H), 7.60−7.64 (m, 2H), 7.91−8.05 (m, 3H), 8.05−8.08 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 14.3, 28.3, 31.5, 31.9, 56.9, 61.7, 63.6, 112.9, 125.4, 125.6, 127.7, 128.3, 128.4, 129.8, 130.2, 130.5, 134.3, 135.5, 137.1, 166.0. MS (EI, *m*/*z* (relative intensity)): 364 (M^+, 55), 350 (23), 349 (93), 308 (23), 293 (51), 253 (27), 252 (25), 247 (69), 238 (22), 223 (32), 220 (31), 210 (39), 208 (61), 207 (60), 198 (23), 180 (100), 179 (62), 153 (25), 152 (59), 127 (23), 126 (24), 97 (16).

*(Z)-Ethyl 1-[Cyano(2,4,4-trimethylpentan-2-ylimino)methyl]-2-naphthoate (****5j****-minor).* ^{1}H NMR (300 MHz, $CDCl_3$, room temperature): 1.02 (s, 9H), 1.44 (t, $^3J_{HH}$ = 7.2 Hz, 3H), 1.61 (s, 6H), 1.96 (s, 2H), 4.48 (q, $^3J_{HH}$ = 7.2 Hz, 2H), aromatic signals are overlapped with those of major isomer. ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 14.1, 29.5, 31.7, 31.9, 55.1, 61.5, 63.2, 112.1, 124.5, 125.8, 126.8, 127.7, 128.1, 130.0, 130.5, 130.9, 134.3, 135.0, 137.1, 168.2. MS (EI, *m*/*z* (relative intensity)): 364 (M^+, 11), 350 (25), 349 (100), 318 (25), 303 (26), 293 (31), 247 (56), 223 (38), 221 (21), 220 (31), 210 (23), 208 (58), 207 (63), 198 (19), 180 (66), 153 (21), 152 (47), 126 (18).

*N-tert-Butyl-3,4-dimethylbenzamide (****6****).*[26] Isolated in 31% yield (32 mg, 0.16 mmol) as a yellow solid. IR (KBr, cm^{-1}): 1643 (s, C═O). ^{1}H NMR (300 MHz, $CDCl_3$, room temperature): δ 1.46 (s, 9H), 2.29 (s, 3H), 2.30 (s, 3H), 5.91 (brs, 1H, NH), 7.15 (d, $^3J_{HH}$ = 7.8 Hz, 1H), 7.42 (d, $^3J_{HH}$ = 7.8, 1H), 7.51 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 19.72, 19.73, 28.9 (×3), 51.4, 124.0, 128.0, 129.6, 133.4, 136.8, 140.0, 167.0 (CO).

General Procedure of Transformation of 4 to 5 using DIBAL-H. A flame-dried 25 mL Schlenk with a magnetic stirring bar was charged with KF (58 mg, 1.0 mmol), 18-crown-6 (264 mg, 1.0 mmol), and $[Pd(NCPh)_2(dppf)](BF_4)_2$ (26 mg, 0.025 mmol, 10 mol %) in THF (1.6 mL) under argon. To this solution were added 2-(trimethylsilyl)phenyl triflate (**1a**; 116 μL, 0.5 mmol), 1,1,3,3-tetramethylbutyl isocyanide (**2a**; 88 μL, 0.5 mmol), and ethyl cyanoformate (**3a**; 25 μL, 0.25 mmol) sequentially via syringe. The reaction mixture was heated to 50 °C for 18 h and then cooled to ambient temperature, quenched with water, and extracted with diethyl ether (20 mL × 3). The combined extracts were washed with brine and dried over anhydrous Na_2SO_4. The volatiles were removed under reduced pressure to give a mixture of crude products, which were checked by GC-MS. Then to a stirred solution of the mixture of crude products in hexanes at 0 °C under an atmosphere of nitrogen was added diisopropylaluminum hydride in hexanes (2.5 mL, 2.5 mmol, 10 equiv, 1 M) dropwise. The solution was warmed to room temperature and stirred for 5 h. HCl (10%) was then added to the light yellow solution. The reaction mixture was stirred for 30 min at room temperature. The reaction mixture was extracted with Et_2O (3 × 20 mL). The combined organic layers were washed with saturated $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated. The crude product was purified by column chromatography (eluent hexane/ethyl acetate, 19/1) to afford the colorless liquid **5a** in 62% yield (48.7 mg, 0.16 mmol).

*2-[[(1,1,3,3-Tetramethylbutyl)amino]carbonyl]benzoic Acid Ethyl Ester (****9****).* Isolated in 42% yield (13 mg, 0.04 mmol) as white solid. IR (KBr, cm^{-1}): 1726 (s, C═O), 1634 (s, C═O). ^{1}H NMR (300 MHz, $CDCl_3$, room temperature): δ 1.05 (s, 9H), 1.36 (t, $^3J_{HH}$ = 7.2 Hz, 3H), 1.54 (s, 6H), 1.85 (s, 2H), 4.36 (q, $^3J_{HH}$ = 7.5 Hz, 2H), 5.69 (s, 1H), 7.40−7.49 (m, 3H), 7.79−7.82 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, room temperature): δ 14.2, 28.7, 31.5, 31.7, 52.3, 55.9, 61.4, 127.1, 129.2, 129.86, 129.91, 131.5, 139.1, 167.1, 167.8. MS (EI, *m*/*z* (relative intensity)): 305 (M^+, 0.26), 248 (6.4), 234 (21), 178 (11), 177 (100), 150 (8), 149 (98), 148 (17), 130 (7), 121 (7), 105 (6), 97 (9), 65 (7). Anal. Calcd for $C_{18}H_{27}NO_3$: C, 70.79; H, 8.91; N, 4.59. Found: C, 70.82; H, 8.65; N, 4.69.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Text, figures, tables, and CIF files giving experimental procedures as well as characterization data for all of the compounds prepared and X-ray data for **4a** and **5j**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Y.N.: fax, +81-86-251-7855; e-mail, ynishiha@okayama-u.ac.jp.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was partially supported by a Grant-in-Aid for Scientific Research (KAKENHI) (No. 24550119) from JSPS and the MEXT program for promoting the enhancement of research universities. The authors gratefully thank Dr. Masayuki Iwasaki at Okayama University for the HRMS measurements, Ms. Megumi Kosaka and Mr. Motonari Kobayashi at the Department of Instrumental Analysis, Advanced Science Research Center, Okayama University, for measurements of elemental analyses, and the SC-NMR Laboratory of Okayama University for the NMR spectral measurements.

■ REFERENCES

(1) Jursic, B. S.; Douelle, F.; Bowdy, K.; Stevens, E. D. *Tetrahedron Lett.* **2002**, *43*, 5361.

(2) De Corte, B.; Denis, J. M.; De Kimpe, N. *J. Org. Chem.* **1987**, *52*, 1147.

(3) Gualtierotti, J.-B.; Schumacher, X.; Fontaine, P.; Masson, G.; Wang, Q.; Zhu, J.-P. *Chem. Eur. J.* **2012**, *18*, 14812.

(4) Williams, R. M. *Synthesis of Optically Active α-Amino Acids*; Pergamon Press: Oxford, U.K., 1989; p 208.

(5) Pellissier, H.; Gil, G. *Tetrahedron Lett.* **1989**, *30*, 171.

(6) Roychowdhury, A.; Kumar, V. V.; Bhaduri, A. P. *Synth. Commun.* **2006**, *36*, 715.

(7) (a) Heintzelman, G. R.; Meigh, I. R.; Mahajan, Y. R.; Weinreb, S. M. *Org. React.* **2005**, *65*, 141. (b) Sisti, N. J.; Zeller, E.; Grierson, D. S.; Fowler, F. W. *J. Org. Chem.* **1997**, *62*, 2093. (c) Motorina, I. A.; Grierson, D. S. *Tetrahedron Lett.* **1999**, *40*, 7215. (d) Amos, D. T.; Renslo, A. R.; Danheiser, R. L. *J. Am. Chem. Soc.* **2003**, *125*, 4970. (e) Tarver, J. E., Jr.; Terranova, K. M.; Joullié, M. M. *Tetrahedron* **2004**, *60*, 10277. (f) Maloney, K. M.; Danheiser, R. L. *Org. Lett.* **2005**, *7*, 3115. (g) Fontaine, P.; Masson, G.; Zhu, J. *Org. Lett.* **2009**, *11*, 1555.

(8) (a) Takahashi, K.; Kimura, S.; Ogawa, Y.; Yamada, K.; Iida, H. *Synthesis* **1978**, 892. (b) Boyer, J. H.; Kooi, J. *J. Am. Chem. Soc.* **1976**, *98*, 1099. (c) De Kimpe, N.; Verhé, R.; De Buyck, L.; Chys, J.; Schamp, N. *Synthesis* **1978**, 895. (d) Smith, J. G.; Irwin, D. C. *Synthesis* **1978**, 894. (e) Pochat, F. *Tetrahedron Lett.* **1981**, *22*, 955. (f) Maruoka, K.; Miyazaki, T.; Ando, M.; Matsumura, Y.; Sakane, S.; Hattori, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1983**, *105*, 2831. (g) Konwar, D.; Goswami, B. N.; Borthakur, N. *J. Chem. Res. Synop.* **1999**, 242. (h) Tobisu, M.; Kitajima, A.; Yoshioka, S.; Hyodo, I.; Oshita, M.;

Chatani, N. *J. Am. Chem. Soc.* **2007**, *129*, 11431. (i) Fontaine, P.; Chiaroni, A.; Masson, G.; Zhu, J. *Org. Lett.* **2008**, *10*, 1509. (j) Gualtierotti, J.-B.; Schmacher, X.; Wang, Q.; Zhu, J. *Synthesis* **2013**, *45*, 1380.

(9) (a) Hoffmann, R. W. *Dehydrobenzene and Cycloalkynes*; Academic Press: New York, 1967. (b) Hart, H. In *The Chemistry of Triple-Bonded Functional Groups, Supplement C2*; Patai, S., Ed.; Wiley: Chichester, U.K., 1994; Chapter 18. (c) Pellissier, H.; Santelli, M. *Tetrahedron* **2003**, *59*, 701. (d) Wenk, H. H.; Winkler, M.; Sander, W. *Angew. Chem., Int. Ed.* **2003**, *42*, 502. (e) Peña, D.; Pérez, D.; Guitián, E. *Angew. Chem., Int. Ed.* **2006**, *45*, 3579. (f) Dyke, A. M.; Hester, A. J.; Lloyd-Jones, G. C. *Synthesis* **2006**, 4093. (g) Tadross, P. M.; Stoltz, B. M. *Chem. Rev.* **2012**, *112*, 3550. (h) Gampe, C. M.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2012**, *51*, 3766. (i) Okuma, K. *Heterocycles* **2012**, *85*, 515.

(10) (a) Kessar, S. V. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Eds.; Pergamon: Oxford, U.K., 1991; Vol. *4*, p 483. (b) Biehl, E. R.; Khanapure, S. P. *Acc. Chem. Res.* **1989**, *22*, 275. (c) Yoshida, H.; Ohshita, J.; Kunai, A. *Bull. Chem. Soc. Jpn.* **2010**, *83*, 199. (d) Wu, C.; Shi, F. *Asian J. Org. Chem.* **2013**, *2*, 116. (e) Dubrovskiy, A. V.; Markina, N. A.; Larock, R. C. *Org. Biomol. Chem.* **2013**, *11*, 191.

(11) (a) Yoshida, H.; Fukushima, H.; Ohshita, J.; Kunai, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 3935. (b) Yoshida, H.; Fukushima, H.; Ohshita, J.; Kunai, A. *Tetrahedron Lett.* **2004**, *45*, 8659. (c) Yoshida, H.; Fukushima, H.; Morishita, T.; Ohshita, J.; Kunai, A. *Tetrahedron* **2007**, *63*, 4793. (d) Yoshida, H.; Takaki, K. *Heterocycles* **2012**, *85*, 1333.

(12) Allan, K. M.; Gilmore, C. D.; Stoltz, B. M. *Angew. Chem., Int. Ed.* **2011**, *50*, 4488.

(13) (a) Ito, Y.; Kato, H.; Saegusa, T. *J. Org. Chem.* **1982**, *47*, 741. (b) Meyers, A. I.; Hanagan, M. A.; Trefonas, L. M.; Baker, R. J. *Tetrahedron* **1983**, *39*, 1991. (c) Nair, V.; Vinod, A. U. *Chem. Commun.* **2000**, 1019. (d) Fayol, A.; Zhu, J. *Angew. Chem., Int. Ed.* **2002**, *41*, 3633. (e) Chatani, N.; Oshita, M.; Tobisu, M.; Ishii, Y.; Murai, S. *J. Am. Chem. Soc.* **2003**, *125*, 7812. (f) Fayol, A.; Zhu, J. *Org. Lett.* **2004**, *6*, 115. (g) Lygin, A. V.; de Meijere, A. *J. Org. Chem.* **2009**, *74*, 4554. (h) Kobayashi, K.; Fujita, S.; Nakai, D.; Fukumoto, S.; Fukamachi, S.; Konishi, H. *Helv. Chim. Acta* **2010**, *93*, 1274. (i) Kobayashi, K.; Shirai, Y.; Fukamachi, S.; Konishi, H. *Synthesis* **2010**, 666. (j) Yan, Z.-Y.; Tan, C.-M.; Wang, X.; Li, F.; Gao, G.-L.; Chen, X.-M.; Wu, W.-S; Wang, J.-J. *Synlett* **2011**, 1863. (k) Chen, D.; Song, G.; Jia, A.; Li, X. *J. Org. Chem.* **2011**, *76*, 8488. (l) Kobayashi, K.; Matsumoto, K.; Konishi, H. *Heterocycles* **2011**, *83*, 99.

(14) (a) Nishihara, Y.; Inoue, Y.; Itazaki, M.; Takagi, K. *Org. Lett.* **2005**, *7*, 2639. (b) Nishihara, Y.; Inoue, Y.; Izawa, S.; Miyasaka, M.; Tanemura, K.; Nakajima, K.; Takagi, K. *Tetrahedron* **2006**, *62*, 9872. (c) Nishihara, Y.; Miyasaka, M.; Inoue, Y.; Yamaguchi, T.; Kojima, M.; Takagi, K. *Organometallics* **2007**, *26*, 4054.

(15) Li, J.; Noyori, S.; Iwasaki, M.; Nakajima, K.; Nishihara, Y. *Heterocycles* **2012**, *86*, 933.

(16) Himeshima, Y.; Sonoda, T.; Kobayashi, H. *Chem. Lett.* **1983**, 1211.

(17) Oi, S.; Kashiwagi, K.; Terada, E.; Ohuchi, K.; lnoue, Y. *Tetrahedron Lett.* **1996**, *37*, 6351.

(18) Liskey, C. W.; Liao, X.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 11389.

(19) (a) Sarpe, V. A.; Kulkarni, S. S. *Org. Biomol. Chem.* **2013**, *11*, 6460. (b) Furman, B.; Thürmer, R.; Kałuża, Z.; Voelter, W.; Chmielewski, M. *Tetrahedron Lett.* **1999**, *40*, 5909. (c) Ishihara, K.; Mori, A.; Yamamoto, H. *Tetrahedron* **1990**, *46*, 4595.

(20) Yamamoto, H.; Maruoka, K. *J. Am. Chem. Soc.* **1981**, *103*, 4186.

(21) Winterfeldt, E. *Synthesis* **1975**, 617.

(22) *CrystalClear*; Rigaku Corp., Akishima, Tokyo, Japan, 1999. *CrystalClear Software User's Guide*; Molecular Structure Corp.: The Woodlands, TX, 2000. Pflugrath, J. W. *Acta Crystallogr., Sect. D* **1999**, *55*, 1718.

(23) Higashi, T. *SHAPE*; Rigaku Corporation, Akishima, Tokyo, Japan, 1999.

(24) Sheldrick, G. M. *Acta Crystallogr., Sect. A* **2008**, *64*, 112.

(25) *CrystalStructure 4.0: Crystal Structure Analysis Package*; Rigaku Corp., Tokyo 196-8666, Japan, 2000−2010.

(26) Calvert, D. J.; O'Conner, C. J. *Aust. J. Chem.* **1979**, *32*, 337.