JOC The Journal of Organic Chemistry

Note

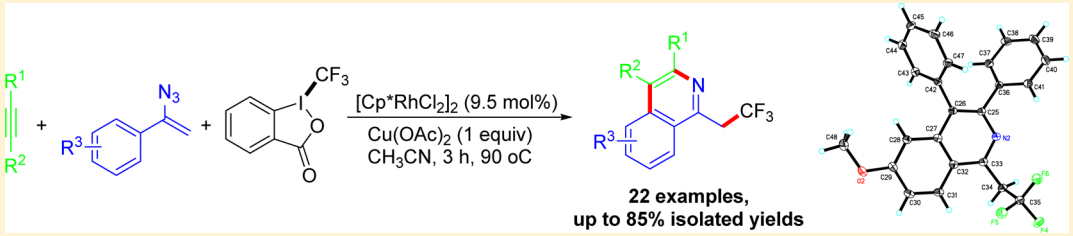
pubs.acs.org/joc

Multicomponent Cascade Synthesis of Trifluoroethyl Isoquinolines from Alkynes and Vinyl Azides

Kai Liu, Shuang Chen, Xing Guang Li, and Pei Nian Liu*

Shanghai Key Laboratory of Functional Materials Chemistry, Key Lab for Advanced Materials and Institute of Fine Chemicals, East China University of Science and Technology, Meilong Road 130, Shanghai, 200237, China

Supporting Information



ABSTRACT: A multicomponent cascade reaction is described that provides concise access to the trifluoroethyl isoquinolines using a Rh(III)−Cu(II) bimetallic system and readily available Togni's reagent. The system tolerates various vinyl azides and internal alkynes. Experimental results suggest that Togni's reagent might act as a CF_3 radical supplier.

The trifluoromethyl group stands out among fluorine functional groups because of its remarkable potential for modulating a molecule's chemical, physical, and biochemical properties.[1] It has been incorporated into many pharmaceuticals and agrochemicals,[1a] and diverse trifluoromethylating reagents have been developed.[2−7] Togni's reagent is a particularly appealing trifluoromethylating reagent because of its easy preparation, versatile reactivity, and shelf stability.[6] Togni's reagent has been used to smoothly trifluoromethylate various compounds, usually in the presence of Cu salts as the catalysts. These compounds include arenes and heteroarenes,[8a,b] alkenes,[8c,d] allenes,[8e] alkynes,[8f,g] alcohols,[8h] thiols,[8i] and phosphines.[8j]

Apart from direct trifluoromethylation, Togni's reagent has also been used in multicomponent reactions, though these have been limited primarily to alkene difunctionalization. In 2012, Li et al. reported the trifluoromethylaminoxylation of alkenes in the absence of transition metals.[9a] In the following year, Ilchenko et al. and Liang et al. reported Cu-catalyzed cyanotrifluoromethylation of styrenes in a three-component reaction.[9b,c] More recently, He et al. described the three-component Cu-catalyzed intermolecular cyanotrifluoromethylation of alkenes and the cyanotrifluoromethylation/azidotrifluoromethylation of 1,6-enynes.[9d,e] Wang et al. and Liang et al. reported three-component Cu-catalyzed intermolecular trifluoromethylarylation, trifluoromethylazidation, and trifluoromethlithiocyanation of alkenes.[9f−h] Despite these advances, we are unaware of reports using Togni's reagent in a multicomponent cascade reaction in which trifluoromethylation is combined with C−H activation catalyzed by $[Cp^*RhCl_2]_2$.

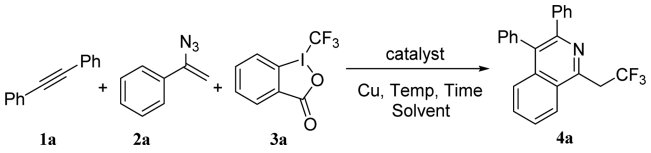
This is an important area to investigate because direct C−H activation/cyclization catalyzed by $[Cp^*RhCl_2]_2$ has emerged as a powerful and promising tool for constructing diverse heterocyclic systems in organic synthesis.[10] Therefore, as part of our continuing studies of heterocycle construction,[11] we report here a new three-component cascade reaction involving α-phenyl vinyl azides, internal alkynes, and Togni's reagent in the presence of a Rh−Cu bimetallic catalytic system. We demonstrate that this trifluoromethylation/C−H activation reaction provides facile access to complex structures of trifluoroethyl isoquinolines.

We began investigating this multicomponent reaction using α-phenyl vinyl azide **2a**, Togni's reagent **3**, and diphenylacetylene **1a** as model substrates in the presence of Rh (5 mol %) and $Cu(OAc)_2$ (1 equiv) at 90 °C under N_2 (Table 1). The target product was obtained in 38% yield in *N*-methyl-2-pyrrolidone (NMP) (entry 1). Screening numerous solvents showed that CH_3CN performed better, generating the desired product in 55% yield (entries 2−4). Other Cu salts, including CuI and $CuBr_2$, also promoted the reaction, albeit with low yields (entries 5 and 6). Decreasing the $Cu(OAc)_2$ load to 0.2 equiv led to a poor yield (entry 7). To our delight, increasing the load of the Rh catalyst to 9.5 mol % improved the yield to 69% and allowed a shorter reaction time of 3 h (entries 8−10). We were able to further improve the yield to 82% by adding 2 equiv of **2a** and 1.8 equiv of **3a** to the system (entries 11 and 12). $[Cp^*Rh(OAc)_2]$ proved to be less efficient than $[Cp^*RhCl_2]_2$ (entry 13). Changing the temperature resulted in lower yields (entries 14 and 15). Eventually, the optimal conditions were identified as **1a** (1 equiv), **2a** (2 equiv), **3a** (1.8 equiv), $Cu(OAc)_2$ (1 equiv), and $[Cp^*RhCl_2]_2$ (9.5 mol %) in CH_3CN at 90 °C under N_2.

Received: August 26, 2015
Published: December 5, 2015

DOI: 10.1021/acs.joc.5b01995
J. Org. Chem. 2016, 81, 265−270

Table 1. Screening of Optimal Conditions[a]

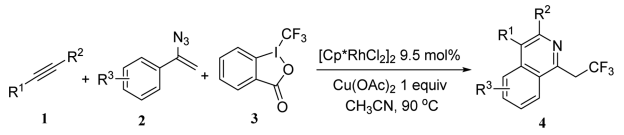


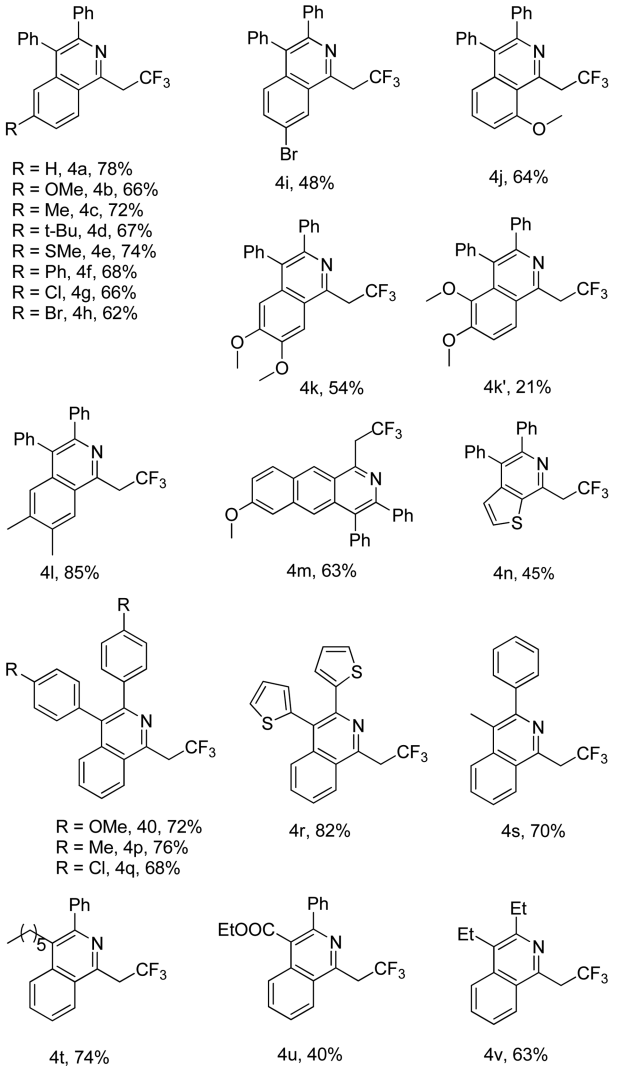
entry	catalyst/(mol %)	additive	time (h)	solvent	yield (%)[b]
1	$[Cp^*RhCl_2]_2$/5	$Cu(OAc)_2$	5	NMP	38
2	$[Cp^*RhCl_2]_2$/5	$Cu(OAc)_2$	5	*t*-BuOH	11
3	$[Cp^*RhCl_2]_2$/5	$Cu(OAc)_2$	5	DMF	46
4	$[Cp^*RhCl_2]_2$/5	$Cu(OAc)_2$	5	CH_3CN	55
5	$[Cp^*RhCl_2]_2$/5	CuI	5	CH_3CN	10
6	$[Cp^*RhCl_2]_2$/5	$CuBr_2$	5	CH_3CN	15
7[c]	$[Cp^*RhCl_2]_2$/5	$Cu(OAc)_2$	5	CH_3CN	26
8	$[Cp^*RhCl_2]_2$/2.5	$Cu(OAc)_2$	5	CH_3CN	40
9	$[Cp^*RhCl_2]_2$/7.5	$Cu(OAc)_2$	3	CH_3CN	67
10	$[Cp^*RhCl_2]_2$/9.5	$Cu(OAc)_2$	3	CH_3CN	69
11[d]	$[Cp^*RhCl_2]_2$/9.5	$Cu(OAc)_2$	3	CH_3CN	72
12[d,e]	$[Cp^*RhCl_2]_2$/9.5	$Cu(OAc)_2$	3	CH_3CN	82
13[d,e]	$Cp^*Rh(OAc)_2$/9.5	$Cu(OAc)_2$	3	CH_3CN	60
14[d,e,f]	$[Cp^*RhCl_2]_2$/9.5	$Cu(OAc)_2$	3	CH_3CN	80
15[d,e,g]	$[Cp^*RhCl_2]_2$/9.5	$Cu(OAc)_2$	3	CH_3CN	78
16[d,e,h]	$[Cp^*RhCl_2]_2$/9.5	$Cu(OAc)_2$	3	CH_3CN	78

[a]Reactions were performed in sealed tubes containing **1a** (0.2 mmol), **2a** (0.3 mmol), Togni's reagent **3** (0.3 mmol), additive, Rh catalyst, and solvent (1 mL) under N_2. [b]Determined by ^1H NMR using $PhSiMe_3$ as internal standard. [c]$Cu(OAc)_2$ (0.04 mmol) was used. [d]Togni's reagent **3a** (0.36 mmol) was used. [e]Vinyl azide **2a** (0.4 mmol) was used. [f]At 80 °C. [g]At 100 °C. [h]Solvent was CH_3CN (0.75 mL).

Using these optimized conditions, we explored the substrate scope of the multicomponent cascade reaction of vinyl azides with Togni's reagent and internal alkynes (Table 2). Various *α*-phenyl vinyl azides reacted with diphenylacetylene to give the corresponding products **4a**–**4n** in moderate to good yields. Vinyl azides substituted at the *para* position with electron-donating substituents (−OMe, −Me, *t*-Bu, −SMe) reacted smoothly to afford the desired products **4b**–**4e** in 66–74% yields. Additionally, the molecular structure of **4b** was unambiguously confirmed by X-ray diffraction analysis (Figure 1). In contrast, substrates with conjugated phenyl or electron-withdrawing groups (−Cl, −Br) at the same position slightly inhibited the reaction, affording products **4f**–**4h** in 62–68% yields. Interestingly, *meta*-bromo-substituted vinyl azide reacted exclusively at the less sterically hindered position on the phenyl ring, generating **4i** in 48% yield. *Ortho*-methoxy-substituted vinyl azide provided the desired product **4j** in good yield. Dimethoxy-substituted vinyl azides showed a preference to react with **1a** at the less sterically hindered position to generate **4k** in 54% yield, although the **4k′** isomer was also isolated in 21% yield (see Supporting Information). Interestingly, dimethyl-substituted vinyl azide reacted with **1a** regioselectively to afford product **4l** in 85% yield, due to the hindrance effect of methyl group. We attributed the generation of **4k′** to the stronger electron-donating effect of the methoxy group rather than the methyl group, which might activate the C−H bond at the *ortho*-position of the methoxyl group to generate **4k′**. Both naphthalene-based vinyl azide and thiophene-based vinyl azide worked in the reaction, affording the desired products in respective yields of 63% and 45%.

Table 2. Reaction of Various Vinyl Azides and Internal Alkynes[a,b]





[a]Reaction conditions: **1** (0.2 mmol), **2** (0.4 mmol), **3** (0.36 mmol), $[Cp^*RhCl_2]_2$ (9.5 mol %), $Cu(OAc)_2$ (0.2 mmol), CH_3CN (1 mL), 90 °C, 3 h, under N_2. [b]Isolated yield.

Next we examined the substrate scope of various internal alkynes. Symmetric diarylacetylenes reacted smoothly with vinyl azide **2a** and delivered the desired isoquinolines **4o**–**4q** in 68–72% yields. Dithiophenylacetylene reacted smoothly under the standard conditions and afforded the target **4r** in excellent 82% yield. Interestingly, the nonsymmetrical alkynes reacted regioselectively to form, respectively, **4s** in 70% yield or **4t** in 74% yield. Ethyl 3-phenylpropiolate reacted in a similar manner with **1g** giving the regioselective product **4u** in 40% yield. Dialkyl-substituted alkyne also performed well in this system to afford the product **4v** in 63% yield.

To gain insight into the mechanism of this multicomponent reaction, we conducted several controlled experiments (Scheme 1). Adding the radical scavenger 2,2,6,6-tetramethyl-1-piper-

DOI: 10.1021/acs.joc.5b01995
J. Org. Chem. 2016, 81, 265−270

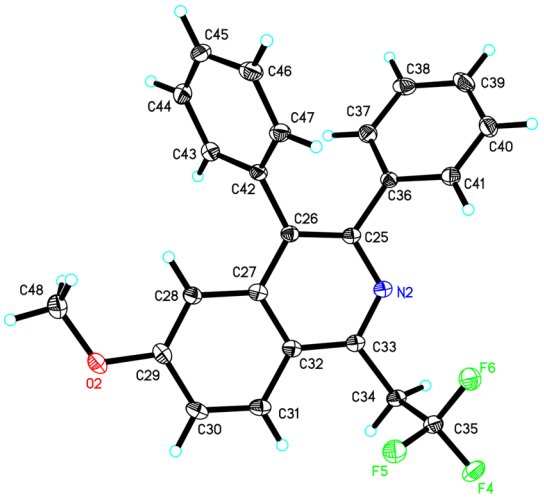
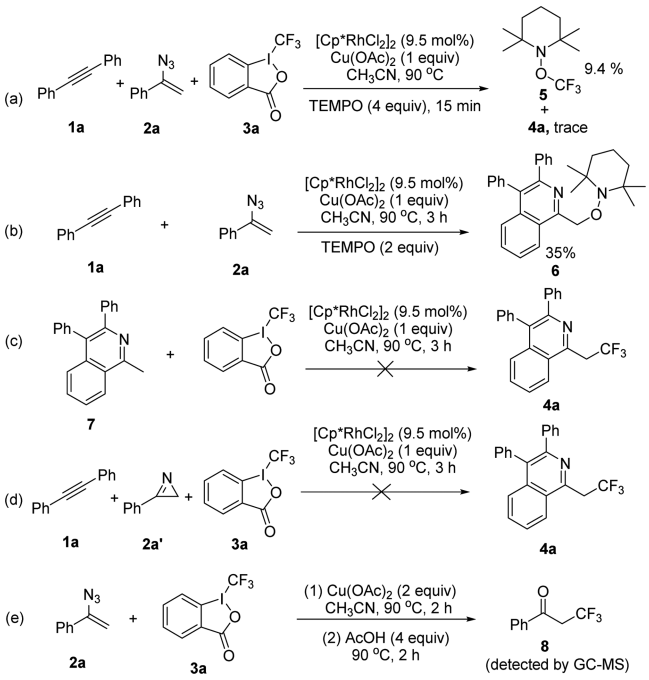


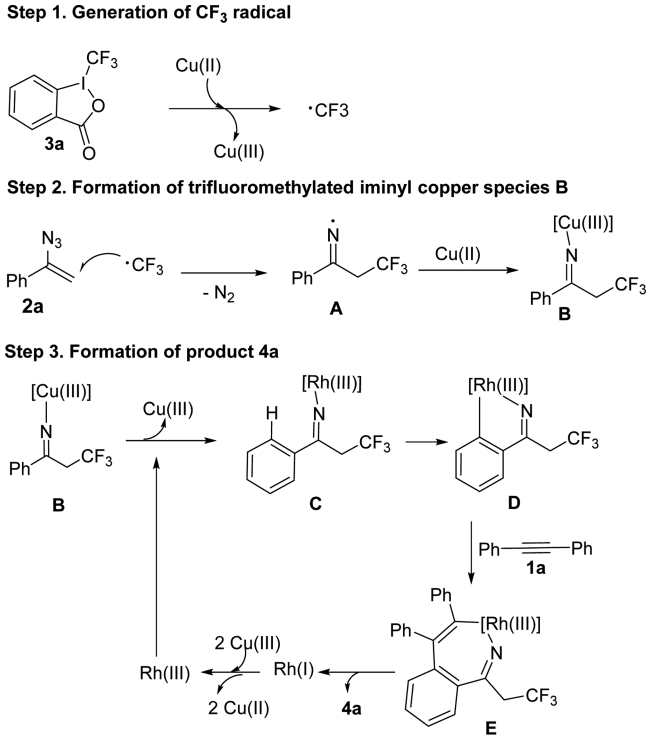
Figure 1. ORTEP diagram of **4b** with ellipsoids shown at the 30% probability level.

Scheme 1. Investigation of the Reaction Mechanism



idinyloxyl (TEMPO) to the reaction under standard conditions led to only trace amounts of the desired product **4a**. Instead, compound **5** was detected by ^{19}F NMR (Scheme 1a).[8g] Using TEMPO instead of Togni's reagent led to compound **6** in 35% yield (Scheme 1b). These results suggest that a CF_3 radical may be generated in the system and added to the C−C double bond of the azide. Using compound **7** could not produce product **4a** (Scheme 1c). The result suggested that trifluoromethylation might occur prior to isoquinoline assembly. Consistent with this idea, we were able to rule out 2*H*-azirine **2a′** as a possible intermediate because it did not give the desired product under standard conditions (Scheme 1d). In addition, in the control experiment of **2a** and **3a** with $Cu(OAc)_2$ (2 equiv) but without $[Cp^*RhCl_2]_2$, compound **8** was detected after addition of AcOH (4 equiv) and an additional 2 h of reaction (Scheme 1e). The result indicated that intermediate **B** in Scheme 2 might be generated in the reaction although the imine intermediate could not detected due to its instability.

Scheme 2. Plausible Mechanism for the Cascade Reaction



Based on the experimental results and the literature,[8g,12] the reaction mechanism was proposed as depicted in Scheme 2. First, the CF_3 radical may be generated under the reaction conditions from Togni's reagent in the presence of Cu(II) (step 1).[8g] The CF_3 radical may add to the vinyl azide **2a** to form the putative radical intermediate **A**, which then could be trapped by Cu(II) to give **B** (step 2).[12a,b] Intermediate **B** would react with Rh(III) via an iminyl rhodium intermediate **C** to generate rhodacyclic intermediate **D**.[12c] Insertion of alkyne **1a** would afford intermediate **E**, which undergoes reductive elimination to produce **4a**, along with the Rh(I) species.[12c] A redox reaction between Rh(I) and Cu(III) regenerates the Rh(III) species (step 3).[12c]

In summary, we have developed a multicomponent cascade protocol that provides direct, concise access to trifluoroethylisoquinolines in moderate to good yield with good chemoselectivity. This protocol combines, for the first time, traditional Rh-catalyzed C−H activation and Togni's reagent. In this way, it provides a novel approach to constructing complex trifluoromethylated compounds in a single operation. The convenience of this method suggests that it is likely to find broad application in drug synthesis, given the frequent use of fluorine-containing compounds as bioactive agents.

EXPERIMENTAL SECTION

All manipulations were carried out under a nitrogen atmosphere using standard Schlenk techniques. The solvents were distilled under nitrogen from sodium-benzophenone (THF, toluene, dioxane) or calcium hydride (DMF, MeCN, 1,2-DCE) before being used. (1-Azidovinyl)benzene and its derivatives[13] as well as $[Cp^*RhCl_2]_2$[14] were prepared according to the literature methods. Chemical shifts (δ, ppm) in the ^{1}H NMR spectra were recorded using TMS as the

DOI: 10.1021/acs.joc.5b01995
J. Org. Chem. 2016, 81, 265−270

internal standard. Chemical shifts in ^{13}C {^{1}H} NMR spectra were internally referenced to $CHCl_3$ (δ = 77.16 ppm).

Typical Procedure for the Synthesis of Trifluoroethyl Isoquinolines (4). To a mixture of $[Cp^*RhCl_2]_2$ (11.8 mg, 0.019 mmol), $Cu(OAc)_2$ (36.3 mg, 0.2 mmol), 1,2-diphenylacetylene (35.6 mg, 0.2 mmol), and Togni's reagent (113.7 mg, 0.36 mmol) in acetonitrile (1 mL) was added vinyl azide (58.0 mg, 0.4 mmol) under a N_2 atmosphere. The reaction mixture was stirred at 90 °C for 3 h, and the progress was monitored using TLC detection. After completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (PE/EA = 100:1) on silica gel to afford the desired products **4**.

*3,4-Diphenyl-1-(2,2,2-trifluoroethyl)isoquinoline (**4a**).* The product **4a** was obtained in 78% yield (56.7 mg) as a white solid after column chromatography (PE/EA = 100:1). Mp: 123.4−124.8 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.25 (2H, q, J = 10.4 Hz), 7.18−7.25 (5H, m), 7.34−7.39 (5H, m), 7.58−7.72 (3H, m), 8.18 (1H, d, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.2 (q, J = 28.8 Hz), 125.1, 125.9 (q, J = 276.6 Hz), 126.6, 126.7, 127.4, 127.6, 127.8, 128.5, 130.3, 130.4, 131.2, 131.3, 136.8, 137.2, 140.5, 149.8, 149.9 (q, J = 3.4 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −62.8 (t, J = 10.2 Hz); HRMS (EI, TOF) calcd for $C_{23}H_{16}F_3N^+$ $[M]^+$: 363.1235, found: 363.1233.

*6-Methoxy-3,4-diphenyl-1-(2,2,2-trifluoroethyl)isoquinoline (**4b**).* The product **4b** was obtained in 66% yield (51.9 mg) as a white solid after column chromatography (PE/EA = 100:1). Mp: 125.1−127.0 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.72 (3H, s), 4.18 (2H, q, J = 10.4 Hz), 6.93 (1H, d, J = 2.4 Hz), 7.18−7.28 (6H, m), 7.33−7.37 (5H, m), 8.08 (1H, d, J = 9.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.1 (q, J = 28.6 Hz), 55.4, 104.6, 119.9, 122.4, 125.9 (q, J = 277.5 Hz), 127.1, 127.3, 127.6, 127.8, 128.6, 130.3, 130.4, 131.2, 137.5, 139.0, 140.7, 149.2 (q, J = 3.3 Hz), 150.4, 160.8; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −62.9 (t, J = 10.6 Hz); HRMS (EI, TOF) calcd for $C_{24}H_{18}F_3NO^+$ $[M]^+$: 393.1340, found: 393.1342.

*6-Methyl-3,4-diphenyl-1-(2,2,2-trifluoroethyl)isoquinoline (**4c**).* The product **4c** was obtained in 72% yield (54.3 mg) as a pale yellow solid after column chromatography (PE/EA = 100:1). Mp: 101.0−102.3 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.43 (3H, s), 4.20 (2H, q, J = 10.4 Hz), 7.18−7.24 (5H, m), 7.33−7.38 (5H, m), 7.45−7.48 (2H, m), 8.07 (1H, d, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.3, 40.2 (q, J = 27.9 Hz), 125.0, 125.1, 125.5, 125.9 (q, J = 276.7 Hz), 127.3, 127.5, 127.8, 128.5, 129.6, 130.4, 130.7, 131.4, 137.1, 137.4, 140.6, 140.8, 149.6 (q, J = 3.4 Hz), 149.9; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −62.8 (t, J = 10.1 Hz); HRMS (EI, TOF) calcd for $C_{24}H_{18}F_3N^+$ $[M]^+$: 377.1391, found: 377.1388.

*6-(tert-Butyl)-3,4-diphenyl-1-(2,2,2-trifluoroethyl)isoquinoline (**4d**).* The product **4d** was obtained in 67% yield (56.1 mg) as a white solid after column chromatography (PE/EA = 100:1). Mp: 141.0−142.6 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.28 (9H, s), 4.21 (2H, q, J = 10.4 Hz), 7.16−7.25 (5H, m), 7.34−7.37 (5H, m), 7.65 (1H, d, J = 1.7 Hz), 7.72 (1H, dd, J = 1.9, 8.9 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 30.9, 35.4, 40.1 (q, J = 28.9 Hz), 121.6, 124.9, 125.0, 125.9 (q, J = 276.5 Hz), 126.3, 127.2, 127.5, 127.8, 128.4, 130.4, 131.3, 136.9, 137.3, 140.7, 149.4 (q, J = 3.1 Hz), 149.9, 153.4; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −62.8 (t, J = 10.1 Hz); HRMS (EI, TOF) calcd for $C_{27}H_{24}F_3N^+$ $[M]^+$: 419.1861, found: 419.1863.

*6-(Methylthio)-3,4-diphenyl-1-(2,2,2-trifluoroethyl)isoquinoline (**4e**).* The product **4e** was obtained in 74% yield (60.5 mg) as a white solid after column chromatography (PE/EA = 100:1). Mp: 121.5−123.0 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.36 (3H, s), 4.19 (2H, q, J = 10.4 Hz), 7.18−7.24 (5H, m), 7.34−7.37 (6H, m), 7.48 (1H, dd, J = 1.9 Hz), 8.04 (1H, d, J = 8.9 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.9, 40.1 (q, J = 29.0 Hz), 120.4, 124.3, 125.3, 125.8 (q, J = 125.8 Hz), 126.2, 127.4, 127.7, 128.8, 128.5, 130.0, 130.4, 131.2, 137.1, 137.3, 140.4, 142.8, 149.6 (q, J = 3.1 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −62.9 (t, J = 10.1 Hz); HRMS (EI, TOF) calcd for $C_{24}H_{18}F_3NS^+$ $[M]^+$: 409.1112, found: 409.1116.

*3,4,6-Triphenyl-1-(2,2,2-trifluoroethyl)isoquinoline (**4f**).* The product **4f** was obtained in 68% yield (59.7 mg) as a pale yellow solid after column chromatography (PE/EA = 100:1). Mp: 149.0−151.0 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.27 (2H, q, J = 10.4 Hz), 7.20−7.24 (3H, m), 7.27−7.29 (2H, m), 7.37−7.46 (8H, m), 7.55−7.57 (2H, m), 7.88−7.91 (2H, m), 8.26 (1H, d, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.2 (q, J = 28.8 Hz), 124.3, 125.7, 125.8, 125.9 (q, J = 276.6 Hz), 127.1, 127.4, 127.7, 127.8, 128.3, 128.6, 129.1, 130.4, 131.3, 131.4, 137.1, 137.2, 140.2, 140.5, 142.9, 149.8 (q, J = 3.0 Hz), 150.4 Hz; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −62.8 (t, J = 10.1 Hz); HRMS (EI, TOF) calcd for $C_{29}H_{20}F_3N^+$ $[M]^+$: 439.1548, found: 439.1542.

*6-Chloro-3,4-diphenyl-1-(2,2,2-trifluoroethyl)isoquinoline (**4g**).* The product **4g** was obtained in 66% yield (52.5 mg) as a pale yellow solid after column chromatography (PE/EA = 100:1). Mp: 148.5−150.5 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.21 (2H, q, J = 10.4 Hz), 7.19−7.23 (5H, m), 7.34−7.40 (5H, m), 7.57 (1H, dd, J = 1.0, 9.0 Hz), 7.67 (1H, d, J = 2.0 Hz), 8.11 (1H, d, J = 9.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.3 (q, J = 28.9 Hz), 124.9, 125.5, 125.8 (q, J = 276.6 Hz), 127.0, 127.6, 127.9, 128.0, 128.4, 128.7, 130.4, 130.5, 131.2, 136.5, 136.9, 137.9, 140.0, 149.9 (q, J = 3.4 Hz), 151.0; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −62.9 (t, J = 10.5 Hz); HRMS (EI, TOF) calcd for $C_{23}H_{15}ClF_3N^+$ $[M]^+$: 397.0845, found: 397.0843.

*6-Bromo-3,4-diphenyl-1-(2,2,2-trifluoroethyl)isoquinoline (**4h**).* The product **4h** was obtained in 62% yield (54.8 mg) as a pale yellow solid after column chromatography (PE/EA = 100:1). Mp: 170.0−171.9 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.21 (2H, q, J = 10.4 Hz), 7.20−7.23 (5H, m), 7.33−7.36 (2H, m), 7.38−7.41 (3H, m), 7.72 (1H, dd, J = 1.8, 9.0 Hz), 7.86 (1H, d, J = 1.8 Hz), 8.04 (1H, d, J = 9.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.2 (q, J = 29.1), 125.1, 125.6, 125.8 (q, J = 276.6 Hz), 126.9, 127.6, 127.6, 127.9, 128.0, 128.7, 128.9, 130.3, 130.4, 130.9, 131.2, 136.4, 138.2, 140.1, 150.0 (q, J = 3.2 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −62.9 (t, J = 10.6 Hz); HRMS (EI, TOF) calcd for $C_{23}H_{15}BrF_3N^+$ $[M]^+$: 441.0340, found: 441.0339.

*7-Bromo-3,4-diphenyl-1-(2,2,2-trifluoroethyl)isoquinoline (**4i**).* The product **4i** was obtained in 48% yield (42.5 mg) as a pale yellow solid after column chromatography (PE/EA = 100:1). Mp: 150.0−152.0 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.19 (2H, q, J = 10.4 Hz), 7.19−7.22 (5H, m), 7.34−7.39 (5H, m), 7.58 (1H, d, J = 9.0 Hz), 7.67 (1H, q, J = 1.9, 9.1 Hz), 8.3 (1H, d, J = 1.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.1 (q, J = 29.1), 121.6, 125.7 (q, J = 276.5), 127.4, 127.6, 127.7, 127.8, 127.9, 128.6, 128.7, 130.4, 131.1, 131.2, 133.8, 135.5, 136.6, 140.0, 149.8 (q, J = 3.3 Hz), 150.2; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −62.8 (t, J = 10.6 Hz); HRMS (EI, TOF) calcd for $C_{23}H_{15}BrF_3N^+$ $[M]^+$: 441.0340, found: 441.0330.

*8-Methoxy-3,4-diphenyl-1-(2,2,2-trifluoroethyl)isoquinoline (**4j**).* The product **4j** was obtained in 64% yield (50.4 mg) as a white solid after column chromatography (PE/EA = 100:1). Mp: 124.1−126.0 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.05 (3H, s), 4.60 (2H, q, J = 10.6 Hz), 6.95 (1H, d, J = 7.6 Hz), 7.17−7.24 (6H, m), 7.33−7.39 (5H, m), 7.47 (1H, t, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.2 (q, J = 27.9 Hz), 55.8, 106.8, 119.1, 119.3, 126.5 (q, J = 276.6 Hz), 127.3, 127.5, 127.7, 128.5, 130.3, 130.4, 131.4, 137.8, 139.4, 140.4, 149.0 (q, J = 3.7 Hz), 157.0; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −63.0 (t, J = 10.5 Hz); HRMS (EI, TOF) calcd for $C_{24}H_{18}F_3NO^+$ $[M]^+$: 393.1340, found: 393.1335.

*6,7-Dimethoxy-3,4-diphenyl-1-(2,2,2-trifluoroethyl)isoquinoline (**4k**) and 5,6-Dimethoxy-3,4-diphenyl-1-(2,2,2-trifluoroethyl)-isoquinoline (**4k′**).* The two isomers were prepared from 4-(1-azidovinyl)-1,2-dimethoxybenzene **2k** (82.0 mg, 0.4 mmol) following the typical procedure. The major product **4k** was obtained in 54% yield (45.7 mg) as a pale yellow solid and the isomer **4k′** was obtained in 21% yield (17.8 mg) as a pale yellow solid after column chromatography (PE/EA = 200:1). Mp, ^{1}H and ^{13}C NMR were described for the major isomer **4k**. Mp: 149.0−151.1 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.76 (3H, s), 4.07 (3H, s), 4.19 (2H, q, J = 10.4 Hz), 6.94 (1H, s), 7.16−7.19 (3H, m), 7.22−7.25 (2H, m), 7.32−7.37 (6H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.4 (q, J = 29.0 Hz), 55.9, 56.2, 103.3, 104.8, 122.9, 126.1 (q, J = 275.9 Hz), 127.1, 127.6, 127.7, 128.5, 130.3, 131.1, 133.7, 137.6, 140.6, 147.2 (q, J = 3.2 Hz), 149.1, 150.2, 152.8; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −62.6 (t, J = 10.5 Hz); HRMS (EI, TOF) calcd for $C_{25}H_{20}F_3NO_2^+$ $[M]^+$: 423.1446, found: 423.1447.

*6,7-Dimethyl-3,4-diphenyl-1-(2,2,2-trifluoroethyl)isoquinoline (**4l**).* The product **4l** was obtained in 82% yield (66.5 mg) as a white

DOI: 10.1021/acs.joc.5b01995
J. Org. Chem. 2016, 81, 265−270

solid after column chromatography (PE/EA = 100:1). Mp: 105.0−107.2 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.34 (3H, s), 2.49 (3H, m), 4.20 (2H, q, J = 10.5 Hz), 7.13−7.23 (5H, m), 7.32−7.38 (5H, m), 7.42 (1H, s), 7.90 (1H, s); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.7, 20.8, 40.0 (q, J = 28.5 Hz), 124.5, 125.7, 125.9, 126.0 (q, J = 276.2 Hz), 127.1, 127.4, 127.7, 128.4, 128.4, 130.4, 130.5, 131.3, 135.7, 137.4, 137.5, 140.7, 140.9, 148.8 (q, J = 3.2 Hz), 149.1; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −62.8 (t, J = 10.1 Hz); HRMS (EI, TOF) calcd for $C_{25}H_{20}F_3N^+$ $[M]^+$: 391.1548, found: 391.1549.

*7-Methoxy-3,4-diphenyl-1-(2,2,2-trifluoroethyl)benzo[g]-isoquinoline (**4m**).* The product **4m** was obtained in 63% yield (55.8 mg) as yellow solid after column chromatography (PE/EA = 100:1). Mp: 165.1−168.0 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.89 (3H, s), 4.35 (2H, q, J = 10.4 Hz), 7.02 (1H, d, J = 2.2 Hz), 7.18−7.24 (4H, m), 7.31−7.34 (2H, m), 7.70−7.44 (5H, m), 7.98 (1H, d, J = 9.2 Hz), 8.04 (1H, s), 8.67 (1H, s); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.5 (q, J = 28.8 Hz), 55.5, 103.8, 122.1, 123.4, 123.6, 125.0, 126.0 (q, J = 276.6 Hz), 127.2, 127.6, 127.8, 128.5, 128.6, 129.7, 130.5, 130.7, 131.5, 134.1, 135.6, 137.8, 140.6, 147.4,151.4 (q, J = 3.3 Hz), 159.0; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −62.4 (t, J = 10.6 Hz); HRMS (EI, TOF) calcd for $C_{28}H_{20}F_3NO^+$ $[M]^+$: 443.1497, found: 443.1499.

*4,5-Diphenyl-7-(2,2,2-trifluoroethyl)thieno[2,3-c]pyridine (**4n**).* The product **4n** was obtained in 45% yield (33.2 mg) as an off-white solid after column chromatography (PE/EA = 100:1). Mp: 114.1−115.4 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.98 (2H, q, J = 10.4 Hz), 7.20−7.25 (6H, m), 7.31−7.37 (5H, m), 7.66 (1H, d, J = 5.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 42.4 (q, J = 29.4 Hz), 124.3, 125.8 (q, J = 275.9 Hz), 127.5, 127.7, 127.9, 128.5, 130.2, 130.4, 130.5, 131.6, 135.7, 137.8, 139.9, 143.9 (q, J = 3.3 Hz), 146.9, 151.4; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −62.9 (t, J = 10.0 Hz); HRMS (EI, TOF) calcd for $C_{21}H_{14}F_3NS^+$ $[M]^+$: 369.0799, found: 369.0789.

*3,4-Bis(4-methoxyphenyl)-1-(2,2,2-trifluoroethyl)isoquinoline (**4o**).* The product **4o** was obtained in 72% yield (60.9 mg) as a white solid after column chromatography (PE/EA = 100:1). Mp: 146.1−147.9 °C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.77 (3H, s), 3.85 (3H, s), 4..22 (2H, q, J = 10.4 Hz), 6.74−6.78 (2H, m), 6.91−6.95 (2H, m), 7.13−7.17 (2H, m), 7.32−7.36 (2H, m), 7.56−7.62 (2H, m), 7.69−7.73 (1H, m), 8.13−8.16 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.1 (q, J = 28.9 Hz), 55.3, 55.4, 113.3, 114.1, 125.1, 125.9 (q, J = 276.8 Hz), 126.4, 126.6, 127.0, 129.5, 130.1, 130.2, 131.7, 132.4, 133.1, 137.3, 149.5, 149.6 (q, J = 3.4 Hz), 158.9, 159.0; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −62.8 (t, J = 10.1 Hz); HRMS (EI, TOF) calcd for $C_{25}H_{20}F_3NO_2^+$ $[M]^+$: 423.1444, found: 423.1446.

*3,4-Di-p-tolyl-1-(2,2,2-trifluoroethyl)isoquinoline (**4p**).* The product **4p** was obtained in 76% yield (59.4 mg) as a white solid after column chromatography (PE/EA = 100:1). Mp: 119.3−120.5 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.3 (3H, s), 2.4 (3H, s), 4..22 (2H, q, J = 10.4 Hz), 7.02 (2H, d, J = 8.0 Hz), 7.12 (2H, d, J = 8.0 Hz), 7,19 (2H, d, J = 7.8 Hz), 7.29 (2H, d, J = 8.0 Hz), 7.57−7.62 (2H, m), 7.68−7.71 (1H, m), 8.15 (1H, d, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.3, 21.5, 40.1 (q, J = 28.8 Hz), 125.1, 126.0 (q, J = 276.5 Hz), 126.5, 126.7, 127.1, 128.6, 129.3130.1, 130.3, 130.9, 131.1, 134.3, 137.0, 137.1, 137.2, 137.7, 149.6 (q, J = 3.4 Hz), 149.7; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −62.8 (t, J = 10.0 Hz); HRMS (EI, TOF) calcd for $C_{25}H_{20}F_3N^+$ $[M]^+$: 391.1548, found: 391.1549.

*3,4-Bis(4-chlorophenyl)-1-(2,2,2-trifluoroethyl)isoquinoline (**4q**).* The product **4q** was obtained in 68% yield (58.7 mg) as a pale yellow solid after column chromatography (PE/EA = 100:1). Mp: 126.6−128.4 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.23 (2H, d, J = 10.4 Hz), 7.16−7.23 (4H, m), 7.28−7.31 (2H, m), 7.37−7.41 (2H, m), 7.64−7.70 (3H, m), 8.18−8.20 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.1 (q, J = 29.0 Hz), 125.3, 125.8 (q, J = 276.8 Hz), 126.3, 126.7, 127.8, 128.2, 129.1, 130.0, 130.8, 131.7, 132.6, 133.7, 140.0, 135.4, 136.6, 138.6, 148.6, 150.5 (q, J = 3.4 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −62.8 (t, J = 10.3 Hz); HRMS (EI, TOF) calcd for $C_{23}H_{14}Cl_2F_3N^+$ $[M]^+$: 431.0455, found: 431.0454.

*3,4-Di(thiophen-2-yl)-1-(2,2,2-trifluoroethyl)isoquinoline (**4r**).* The product **4r** was obtained in 82% yield (61.5 mg) as a pale yellow solid after column chromatography (PE/EA = 100:1). Mp: 115.1−117.5 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.18 (2H, q, J = 10.4 Hz), 6.80 (1H, dd, J = 1.0, 3.8 Hz), 6.91 (1H, dd, J = 3.8, 5.0 Hz), 7.11 (1H, dd, J = 1.0, 3.4 Hz), 7.29 (1H, dd, J = 3.4, 5.0 Hz), 7.31 (1H, dd, J = 1.0, 5.0 Hz), 7,56−7.67 (4H, m), 8.08 (1H, d, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 39,8 (q, J = 29.0 Hz), 120.7, 124.9, 125.7 (q, J = 275.6 Hz), 126.0, 126.4, 127.3, 127.8, 127.9, 128.0, 128.1, 128.5, 129.5, 130.8, 137.3, 138.6, 144.4, 144.8, 150.8 (q, J = 3.1 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −62.7 (t, J = 10.6 Hz); HRMS (EI, TOF) calcd for $C_{19}H_{12}F_3NS_2^+$ $[M]^+$: 375.0363, found: 375.0367.

*4-Methyl-3-phenyl-1-(2,2,2-trifluoroethyl)isoquinoline (**4s**).* The product **4v** was obtained in 70% yield (42.1 mg) as a white solid after column chromatography (PE/EA = 100:1). The structure of **4e** was confirmed by NOESY correlation. Mp: 109.2−111.0 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.66 (3H, s), 4.16 (2H, d, J = 10.4 Hz), 7.38−7.43 (1H, m), 7.46−7.50 (2H, m), 7.57−7.60 (2H, m), 7.64−7.68 (1H, m), 7.75−7.80 (1H, m), 8.10 (1H, d, J = 8.5 Hz), 8.15 (1H, d, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.8, 40.0 (q, J = 28.8 Hz), 124.5, 124.9, 125.7, 125.9 (q, J = 275.3 Hz), 126.5, 127.1, 127.9, 128.3, 130.1, 130.3, 137.0, 141.1, 148.2 (q, J = 3.2 Hz), 151.2; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −63.0 (t, J = 10.2 Hz); HRMS (EI, TOF) calcd for $C_{18}H_{14}F_3N^+$ $[M]^+$: 301.1078, found: 301.1079.

*4-Hexyl-3-phenyl-1-(2,2,2-trifluoroethyl)isoquinoline (**4t**).* The product **4t** was obtained in 74% yield (54.9 mg) as a pale yellow solid after column chromatography (PE/EA = 100:1). Mp: 58.1−59.8 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.85 (3H, t, J = 7.0 Hz), 1.19−1.25 (4H, m), 1.30−1.37 (2H, m), 1.60−1.70 (2H, m), 2.97−3.02 (2H, m), 4.15 (2H, q, J = 10.4 Hz), 7.39−7.43 (1H, m), 7.45−7.52 (4H, m), 7.62−7.67 (1H, m), 7.74−7.79 (1H, m), 8.10 (1H, d, J = 8.5 Hz), 8.16 (1H, d, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.2, 22.7, 28.8, 29.7, 31.3, 31.5, 40.1 (q, J = 29.0 Hz), 124.6, 125.9 (q, J = 276.5 Hz), 126.0, 127.0, 127.8, 128.4, 129.4, 130.0, 130.2, 136.2, 141.4, 148.1 (q, J = 3.4 Hz), 151.5; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −63.0 (t, J = 10.6 Hz); HRMS (EI, TOF) calcd for $C_{23}H_{24}F_3N^+$ $[M]^+$: 371.1861, found: 371.1856.

*Ethyl 3-Phenyl-1-(2,2,2-trifluoroethyl)isoquinoline-4-carboxylate (**4u**).* The product **4u** was obtained in 40% yield (28.7 mg) as a pale yellow solid after column chromatography (PE/EA = 200:1). The structure of **4v** was confirmed by NOESY correlation. Mp: 108.5−110.0 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.06 (3H, t, J = 7.2 Hz), 4.21 (2H, q, J = 10.3 Hz), 4.26 (2H, q, J = 7.2 Hz), 7.42−7.50 (3H, m), 7.66−7.81 (4H, m), 8.07 (1H, d, J = 8.4 Hz), 8.17 (1H, d, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.8, 40.2 (q, J = 29.2 Hz), 62.0, 123.9, 125.0, 125.5, 125.6 (q, J = 276.7 Hz), 126.1, 128.1, 128.6, 128.8, 129.0, 131.6, 134.2, 139.8, 149.8, 152.0 (q, J = 3.1 Hz), 168.7; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −62.8 (t, J = 10.1 Hz); HRMS (EI, TOF) calcd for $C_{20}H_{16}F_3NO_2^+$ $[M]^+$: 359.1133, found: 359.1129.

*3,4-Diethyl-1-(2,2,2-trifluoroethyl)isoquinoline (**4v**).* The product **4v** was obtained in 63% yield (33.6 mg) as a pale yellow solid after column chromatography (PE/EA = 100:1). Mp: 42.6−44.1 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.29−1.37 (6H, m), 3.00 (2H, q, J = 7.56 Hz), 3.08 (2H, q, J = 7.56 Hz), 4.08 (2H, q, J = 10.5 Hz), 7.56 (1H, q, J = 7.24 Hz), 7.67−7.72 (1H, m), 8.04 (1H, d, J = 8.6 Hz), 8.07 (1H, d, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.8, 15.2, 20.9, 28.4, 39.9 (q, J = 28.7 Hz), 123.7, 125.9 (q, J = 125.9 Hz), 126.1, 126.5, 129.7, 129.9, 135.8, 148.0 (q, J = 3.8 Hz), 153.4; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −63.2 (t, J = 10.3 Hz); HRMS (EI, TOF) calcd for $C_{15}H_{16}F_3N^+$ $[M]^+$: 267.1235, found: 267.1232.

*3,4-Diphenyl-1-(((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)-isoquinoline **6**.* To a mixture of $[Cp^*RhCl_2]_2$ (10.5 mg, 0.017 mmol), $Cu(OAc)_2$ (36.3 mg, 0.2 mmol), 1,2-diphenylacetylene (35.6 mg, 0.2 mmol), and TEMPO (62.4 mg, 0.4 mmol) in acetonitrile (1 mL) was added vinyl azide (52.4 mg, 0.4 mmol) under a N_2 atmosphere. After completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (PE/EA = 50:2) on silica gel to afford the desired products **6** in 35% isolated yield. Mp: 137.4−138.9 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.14 (6H, s), 1.4 (6H, s), 1.51−1.59 (6H, m), 5.51 (2H, s), 7.16−7.26 (6H, m), 7.33−7.39 (5H, m), 7.56−7.68 (3H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.3, 20.4, 33.6, 39.9, 60.2, 80.8, 126.1, 126.4, 126.5, 126.6, 127.0, 127.3, 127.6, 128.4, 130.0, 130.5, 131.4, 136.7, 137.7,

DOI: 10.1021/acs.joc.5b01995
J. Org. Chem. 2016, 81, 265−270

140.9, 149.2, 156.7; HRMS (EI, TOF) calcd for $C_{31}H_{34}N_2O^+$ $[M]^+$: 450.2671, found: 450.2676.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01995.

Copies of ^1H, ^{13}C, and ^{19}F NMR spectra for products **4a**−**4v** and **6** (PDF)

X-ray crystallographic data for **4b** (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: liupn@ecust.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the National Natural Science Foundation of China (Project Nos. 21421004, 21172069, 21372072 and 21190033), NCET (NCET-13-0798), the Basic Research Program of the Shanghai Committee of Sci. & Tech. (Project No. 13M1400802), and the Fundamental Research Funds for the Central Universities.

■ REFERENCES

(1) (a) Müller, K.; Faeh, C.; Diederich, F. *Science* **2007**, *317*, 1881. (b) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2008**, *37*, 320. (c) Furuya, T.; Kamlet, A. S.; Ritter, T. *Nature* **2011**, *473*, 470. (d) Pacheco, M. C.; Purser, S.; Gouverneur, V. *Chem. Rev.* **2008**, *108*, 1943. (e) Chen, P.; Liu, G. *Synthesis* **2013**, *45*, 2919.

(2) Liu, H.; Gu, Z.; Jiang, X. *Adv. Synth. Catal.* **2013**, *355*, 617.

(3) (a) Prakash, G. K. S.; Mandal, M. *J. Fluorine Chem.* **2001**, *112*, 123. (b) Singh, R. P.; Shreeve, J. M. *Tetrahedron* **2000**, *56*, 7613. (c) Liu, X.; Xu, C.; Wang, M.; Liu, Q. *Chem. Rev.* **2015**, *115*, 683.

(4) Yagupolskii, L. M.; Maletina, I. I.; Kondratenko, N. V.; Orda, V. V. *Synthesis* **1978**, *1978*, 835.

(5) (a) Umemoto, T. *Chem. Rev.* **1996**, *96*, 1757. (b) Umemoto, T.; Adachi, K.; Ishihara, S. *J. Org. Chem.* **2007**, *72*, 6905.

(6) (a) Eisenberger, P.; Gischig, S.; Togni, A. *Chem. - Eur. J.* **2006**, *12*, 2579. (b) Kieltsch, I.; Eisenberger, P.; Togni, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 754.

(7) (a) Noritake, S.; Shibata, N.; Nakamura, S.; Toru, T.; Shiro, M. *Eur. J. Org. Chem.* **2008**, *2008*, 3465. (b) Urban, C.; Cadoret, F.; Blazejewski, J. C.; Magnier, E. *Eur. J. Org. Chem.* **2011**, 4862. (c) Nomura, Y.; Tokunaga, E.; Shibata, N. *Angew. Chem., Int. Ed.* **2011**, *50*, 1885.

(8) (a) Mejia, E.; Togni, A. *ACS Catal.* **2012**, *2*, 521. (b) Shimizu, R.; Egami, H.; Nagi, T.; Chae, J.; Hamashima, Y.; Sodeoka, M. *Tetrahedron Lett.* **2010**, *51*, 5947. (c) Zhu, R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2012**, *134*, 12462. (d) Kong, W.; Casimiro, M.; Merino, E.; Nevado, C. *J. Am. Chem. Soc.* **2013**, *135*, 14480. (e) Yu, Q.; Ma, S. *Chem. - Eur. J.* **2013**, *19*, 13304. (f) Gao, P.; Shen, Y. W.; Fang, R.; Hao, X. H.; Qiu, Z. H.; Yang, F.; Yan, X. B.; Wang, Q.; Gong, X. J.; Liu, X. Y.; Liang, Y. M. *Angew. Chem., Int. Ed.* **2014**, *53*, 7629. (g) Li, Y.; Lu, Y.; Qiu, G.; Ding, Q. *Org. Lett.* **2014**, *16*, 4240. (h) Koller, R.; Stanek, K.; Stolz, D.; Aardoom, R.; Niedermann, K.; Togni, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 4332−4336. (i) Kieltsch, I.; Eisenberger, P.; Togni, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 754. (j) Eisenberger, P.; Kieltsch, I.; Armanino, N.; Togni, A. *Chem. Commun.* **2008**, 1575.

(9) (a) Li, Y.; Studer, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 8221. (b) Ilchenko, N. O.; Janson, P. G.; Szabó, K. J. *J. Org. Chem.* **2013**, *78*, 11087. (c) Liang, Z.; Wang, F.; Chen, P.; Liu, G. *J. Fluorine Chem.* **2014**, *167*, 55. (d) He, Y. T.; Li, L. H.; Yang, Y. F.; Zhou, Z. Z.; Hua, H. L.; Liu, X. Y.; Liang, Y. M. *Org. Lett.* **2014**, *16*, 270. (e) He, Y. T.; Li, L. H.; Yang, Y. F.; Zhou, Z. Z.; Hua, H. L.; Liu, X. Y.; Liang, Y. M. *Org. Lett.* **2014**, *16*, 3896. (f) Wang, F.; Wang, D.; Mu, X.; Chen, P.; Liu, G. *J. Am. Chem. Soc.* **2014**, *136*, 10202. (g) Wang, F.; Qi, X.; Liang, Z.; Chen, P.; Liu, G. *Angew. Chem., Int. Ed.* **2014**, *53*, 1881. (h) Liang, Z.; Wang, F.; Chen, P.; Liu, G. *Org. Lett.* **2015**, *17*, 2438.

(10) (a) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624. (b) Wencel-Delord, J.; Dröge, T.; Liu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40*, 4740. (c) Song, G.; Wang, F.; Li, X. *Chem. Soc. Rev.* **2012**, *41*, 3651. (d) Li, D. Y.; Chen, H. J.; Liu, P. N. *Org. Lett.* **2014**, *16*, 6176. (e) Li, D. Y.; Mao, X. F.; Chen, H. J.; Chen, G. R.; Liu, P. N. *Org. Lett.* **2014**, *16*, 3476. (f) Li, X. G.; Liu, K.; Zou, G.; Liu, P. N. *Adv. Synth. Catal.* **2014**, *356*, 1496. (g) Li, X. G.; Sun, M.; Liu, K.; Jin, Q.; Liu, P. N. *Chem. Commun.* **2015**, *51*, 2380.

(11) (a) Li, D. Y.; Shang, X. S.; Chen, G. R.; Liu, P. N. *Org. Lett.* **2013**, *15*, 3848. (b) Li, D. Y.; Shi, K. J.; Mao, X. F.; Chen, G. R.; Liu, P. N. *J. Org. Chem.* **2014**, *79*, 4602. (c) Siyang, H. X.; Wu, X. R.; Liu, H. L.; Wu, X. Y.; Liu, P. N. *J. Org. Chem.* **2014**, *79*, 1505. (d) Li, X. G.; Sun, M.; Liu, K.; Liu, P. N. *Adv. Synth. Catal.* **2015**, *357*, 395. (e) Li, D. Y.; Chen, H. J.; Liu, P. N. *Adv. Synth. Catal.* **2015**, *357*, 1193.

(12) (a) Wang, Y. F.; Lonca, G. H.; Le Runigo, M. L.; Chiba, S. *Org. Lett.* **2014**, *16*, 4272. (b) Wang, Y. F.; Lonca, G. H.; Chiba, S. *Angew. Chem., Int. Ed.* **2014**, *53*, 1067. (c) Wang, Y. F.; Toh, K. K.; Lee, J. Y.; Chiba, S. *Angew. Chem., Int. Ed.* **2011**, *50*, 5927. (d) Wang, Y. F.; Chiba, S. *J. Am. Chem. Soc.* **2009**, *131*, 12570. (e) Chiba, S.; Wang, Y. F.; Lapointe, G.; Narasaka, K. *Org. Lett.* **2008**, *10*, 313. (f) Wang, Y. F.; Toh, K. K.; Chiba, S.; Narasaka, K. *Org. Lett.* **2008**, *10*, 5019.

(13) (a) Hassner, A.; Fowler, F. W. *Tetrahedron Lett.* **1967**, *8*, 1545. (b) Fowler, F. W.; Hassner, A.; Levy, L. A. *J. Am. Chem. Soc.* **1967**, *89*, 2077.

(14) White, C.; Yates, A.; Maitlis, P. M. *Inorg. Synth.* **1992**, *29*, 228.

DOI: 10.1021/acs.joc.5b01995
J. Org. Chem. 2016, 81, 265−270