HETEROCYCLES, Vol. 100, No. 3, 2020, pp. 371 - 382. © 2020 The Japan Institute of Heterocyclic Chemistry
Received, 10th January, 2020, Accepted, 19th February, 2020, Published online, 28th February, 2020
DOI: 10.3987/COM-20-14204

EFFICIENT SYNTHESIS OF FLUORINATED BENZIMIDAZOLINES, BENZOXAZOLINES AND BENZOTHIAZOLINES CATALYZED BY $Hf(OTf)_4$

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Abstract – Hafnium triflate was identified as a highly efficient catalyst for the synthesis of a diversity of fluorinated benzimidazolines, benzoxazolines, and benzothiazolines. For the first time, more complicated *N*-substituted benzimidazolines were synthesized via the $Hf(OTf)_4$-catalyzed method. With the assistance of ^{19}F NMR, the catalytic roles of Hf(IV) on the activation of fluorinated ketone and fluorinated imine intermediate were revealed.

INTRODUCTION

As the key intermediate heterocycles in benzimidazole synthesis from *o*-phenylenediamines and aldehydes, benzimidazolines could dehydrogenize to form benzimidazoles.[1] Therefore, benzimidazolines have long been applied as selective reducing agents[2-4] and organic "hydrides".[5] However, alkyl ketone-derived benzimidazolines are typically unstable and susceptible to hydrolysis upon column chromatography. It is well known that introducing fluorine atom(s) to organic compounds may significantly affect their properties, such as stability, lipophilicity, bioavailability, etc.[6,7] Fluorinated compounds have been widely applied in pharmaceutical,[8-10] agricultural,[11] and materials chemistry[12] due to their unique properties. Recently, the report by Akiyama et al. confirmed that 2-aryl-2-trifluoromethyl-benzimidazolines are stable compounds. Their research indicated that these fluorinated benzimidazolines could be employed as a new type of trifluoromethylation reagent.[13]

Due to the strong electron-withdrawing effect of fluorine atoms, the reactivity of fluorinated ketones with *o*-phenylenediamines was much lower than that of regular ketones. Previously, solid acids, such as Nafion®-H[14] and K-10 montmorillonite[15] have been employed under thermal or microwave heating conditions for the condensation-cyclization of fluorinated ketones with *o*-phenylenediamines. However,

large catalyst loading and critical reaction conditions limit their applications. More recently, phosphotungstic acid (PWA),[16] a solid heteropoly acid, has also been utilized for the synthesis of fluorinated benzimidazolines in toluene. Although 1 mol% catalyst loading seems low, however, considering its huge molecular weight, the catalytic efficacy of PWA is still far from satisfactory. Up to date, only a limited number of metal Lewis acids, including $Ga(OTf)_3$/$Ga(HCF_2CF_2SO_3)_3$,[17,18] $Cu(OTf)_2$,[17] and $Sc(OTf)_3$,[19] have been reported as effective catalysts for this reaction with moderate to good yields.

In the past few years, our research on the catalytic activity of Group IVB transition metal Lewis acids has showed that hafnium(IV) salts, such as $HfCl_4$ and $Hf(OTf)_4$ exhibited superior reactivity to other metal Lewis acids in many reactions,[20] especially those involving carbonyl-transformations, due to their strong activation capability on carbonyl group.[21-25] However, in the reactions of fluorinated ketones, which are much more difficult to coordinate with Lewis acids due to the strong electron-withdrawing effect of fluorine atoms,[26] the application of $Hf(OTf)_4$ as a catalyst has never been explored before.[27] We report herein the identification of $Hf(OTf)_4$ as a highly potent catalyst for efficient preparation of fluorinated benzimidazolines, benzoxazolines, benzothiazolines, and even more complicated *N*-substituted fluorinated benzimidazolines. In addition, ^{19}F NMR tracing experiments clearly illustrated the catalytic roles of $Hf(OTf)_4$.

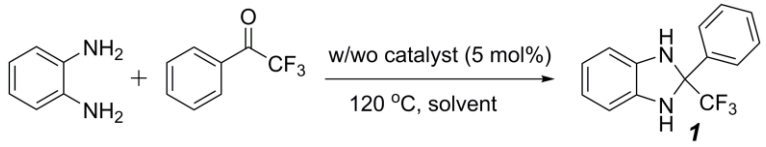
RESULTS AND DISCUSSION

In the preliminary experiment, we compared the catalytic activity of $Hf(OTf)_4$ with $Ga(OTf)_3$ and $Cu(OTf)_2$ at 5 mol% level in a model reaction, which contained *o*-phenylenediamine and trifluoroacetophenone in 1:1.5 molar ratio and was heated in CH_2Cl_2 at 120 ºC in a sealed tube. The results in Table 1 showed that the condensation-cyclization of trifluoroacetophenone with *o*-phenylenediamine was sluggish and very low-yielding (12%, 24 h) without catalyst. $Cu(OTf)_2$ accelerated the reaction (8 h) and afforded **1** in 70% yield, but it also resulted in the formation of orange-colored byproducts. The reaction catalyzed by $Ga(OTf)_3$ was more efficient and required 4 h to afford **1** in 88% yield, which was in good agreement with the previous report.[17] Interestingly, $Hf(OTf)_4$ appeared as a much more potent catalyst than the above two metal Lewis acids and afforded **1** in 97% yield within only 1 h under the same conditions.

The $Hf(OTf)_4$-catalyzed synthesis of fluorinated benzimidazoline **1** exhibited notable solvent effect (Table 1, entries 5–8). The reaction performed in acetonitrile was much slower (12 h) and afforded a significant amount of a polar byproduct (56% yield). The reactions in toluene, THF, and EtOH were all good-yielding (82–90% yield). While the reactions in toluene and THF needed 7 h and 5 h, respectively,

the one in EtOH only took 1.5 h. These results confirmed that CH_2Cl_2 is the most suitable solvent for the condensation-cyclization of trifluoroacetophenone with *o*-phenylenediamine.

Table 1. The effects of catalyst and solvent on the synthesis of benzimidazoline **1**

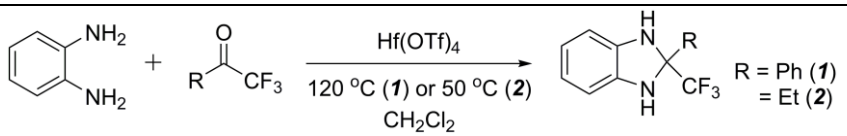


Entry	Catalyst	Solvent	Reaction time (h)	Isolated yield of **1** (%)
1	--	CH_2Cl_2	24	12[a]
2	$Cu(OTf)_2$	CH_2Cl_2	8	70
3	$Ga(OTf)_3$	CH_2Cl_2	4	88
4	$Hf(OTf)_4$	CH_2Cl_2	1	97
5	$Hf(OTf)_4$	MeCN	12	56
6	$Hf(OTf)_4$	toluene	7	82
7	$Hf(OTf)_4$	THF	5	89
8	$Hf(OTf)_4$	EtOH	1.5	90

[a]The imine intermediate was isolated in 8% yield.

In the following research, we gradually reduced the amount of $Hf(OTf)_4$ catalyst from 5 mol% to 1 mol%. As shown in Table 2, the reaction time of trifluoroacetophenone was prolonged to 3 h without any effect on the yield of **1**, when as low as 2 mol% $Hf(OTf)_4$ was used. Further lowering to 1 mol% catalyst caused even longer reaction time (8 h) and lowered yield due to the incomplete consumption of starting materials. Similar trend was observed on the reaction of trifluorobutan-2-one when the reaction was performed at a much lower temperature (50 °C). Only 2 mol% of $Hf(OTf)_4$ was needed for efficient formation of benzimidazoline **2**.

Table 2. The effect of $Hf(OTf)_4$ amount on the synthesis of **1**

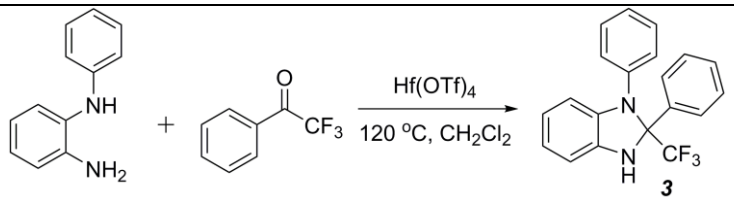


Entry	$Hf(OTf)_4$ (mol%)	Reaction time (h)		Isolated yield of **1** or **2** (%)	
		R= Ph	R=Et	R=Ph	R=Et
1	5	1	1	97	96

2	3	2	2	97	97
3	2	3	4	96	96
4	1	8	10	91	89

To extend the scope of $Hf(OTf)_4$ catalyst on the synthesis of fluorinated benzimidazolines, we attempted to promote the reaction of fluorinated ketones with *N*-substituted *o*-phenylenediamines, which has never been reported before. As shown in Table 3, when 5 mol% of $Hf(OTf)_4$ was used, the reaction of *N*-phenyl-*o*-phenylenediamine was significantly slower (6 h) than that of the unsubstituted *o*-phenylenediamine, which is possibly due to the steric effect resulted from *N*-substitution. But the $Hf(OTf)_4$-catalyzed reaction was still high-yielding (93%). However, less $Hf(OTf)_4$ (3 mol%) lead to remarkably prolonged reaction time (24 h) and incomplete consumption of starting materials.

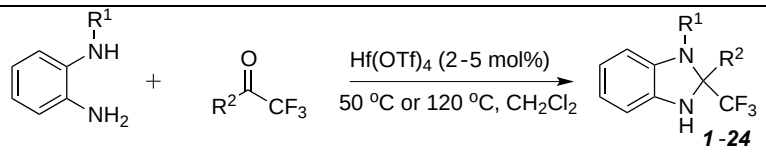
Table 3. Synthesis of *N*-substituted benzimidazoline **3**

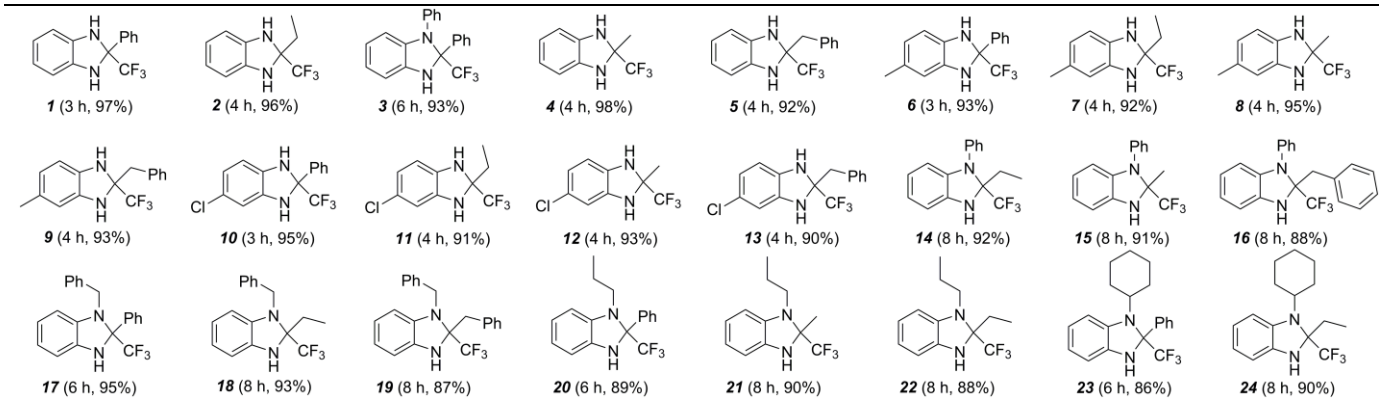


Entry	mol%	Reaction time (h)	Isolated yield of **3** (%)
1	5	6	93
2	3	24	84

With the optimized reaction conditions, a diversity of fluorinated benzimidazolines were synthesized (Table 4). The reactions of both aryl trifluoromethyl ketones and alkyl trifluoromethyl ketones with *o*-phenylenediamines only required 2 mol% $Hf(OTf)_4$ and afforded the corresponding fluorinated benzimidazolines (**1**,**2**,**4**–**13**) in excellent yields (91–98%) within 3–4 h. In comparison, when various *N*-substituted *o*-phenylenediamines were employed as substrates, 5 mol% $Hf(OTf)_4$ and longer reaction time (6–8 h) were required to afford the corresponding *N*-substituted benzimidazolines (**3**,**14**–**24**) in 86–95% yields.

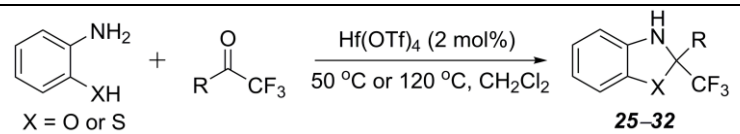
Table 4. $Hf(OTf)_4$-Catalyzed synthesis of fluorinated benzimidazolines (**1**–**24**)

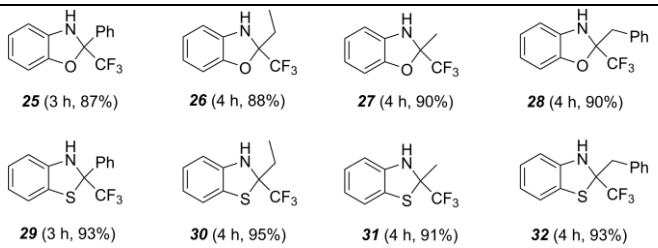




The application of $Hf(OTf)_4$ to the synthesis of closely related fluorinated benzoxazolines and benzothiazolines was also explored. It was determined that 2 mol% $Hf(OTf)_4$ was sufficient to catalyze the condensation-cyclization of aryl trifluoromethyl ketones (120 °C)/alkyl trifluoromethyl ketones (50 °C) with *o*-aminophenol or *o*-aminothiophenol. The corresponding products (**25**–**32**) were obtained in 87–94% yields in 3–4 h (Table 5).

Table 5. Synthesis of fluorinated benzoxazolines and benzothiazolines (**25**–**32**)





To clarify the roles of $Hf(OTf)_4$ on the formation of fluorinated benzimidazolines, we investigated its catalytic effects on the condensation step and cyclization step separately. First, we compared the condensation of aniline, instead of *o*-phenylenediamine, with trifluoroacetophenone in the absence or presence of 5 mol% $Hf(OTf)_4$ by ^{19}F NMR. It was determined that no imine product **33** formed after 12 h without catalyst. In contrast, 5 mol% $Hf(OTf)_4$ resulted in the formation of corresponding imine in ~7% yield after heating at 120 ºC for 2 h (Figure 1A). These results revealed that trifluoromethyl imine (**33**) is extremely difficult to form both kinetically and dynamically, especially without the following cyclization step. But the coordination of Hf(IV) cation with trifluoroacetophenone notably promoted its condensation

with aniline. However, it should be also noted that the strong electron-withdrawing CF_3 group also limited the catalytic effect of the Lewis acid.

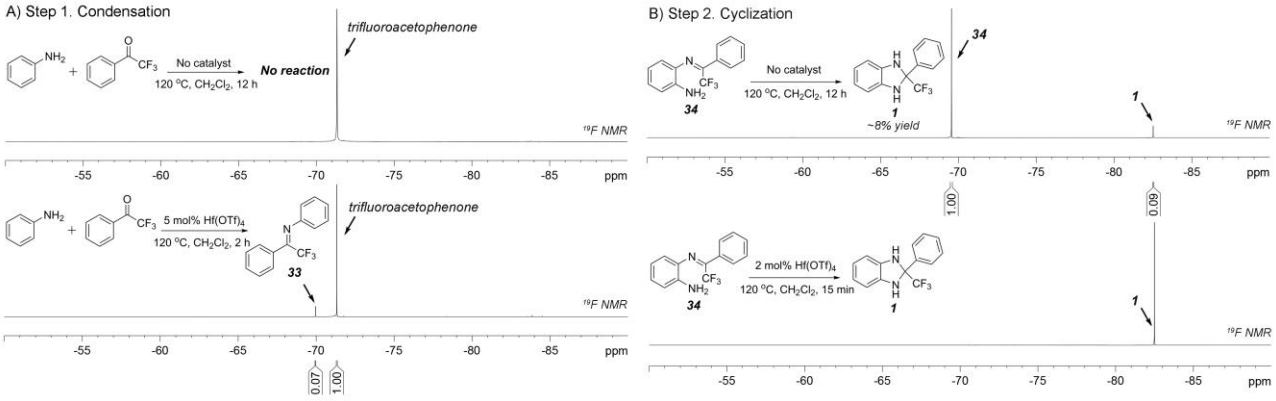


Figure 1. The catalytic roles of $Hf(OTf)_4$ on the condensation step (A) and cyclization step (B) revealed by ^{19}F NMR.

Secondly, we isolated the putative condensation intermediate (**34**) of trifluoroacetophenone and *o*-phenylenediamine and confirmed its structure by both NMR and MS.^{19}F NMR tracing showed that heating **34** at 120 ºC alone resulted in the cyclization of a very small portion of **34** (~8%) to **1** over 12 h. However, in the presence of 2 mol% $Hf(OTf)_4$, **34** was quantitatively converted to **1** within 15 min (Figure 1B). These results clearly showed that $Hf(OTf)_4$ also drastically promoted the intramolecular cyclization step.

Finally, ^{19}F NMR tracing of the reaction of trifluoroacetophenone and *o*-phenylenediamine well agreed with our observations on individual steps. As shown in the Figure 2A, the reaction proceeded smoothly via the imine intermediate **34**. However, it is noteworthy that the amount of **34** was surprisingly low (<1%) throughout the entire reaction process. In contrast, the result in Table 1 (entry 1) showed that the amount of imine **34** could accumulate up to 8% in the reaction without $Hf(OTf)_4$.

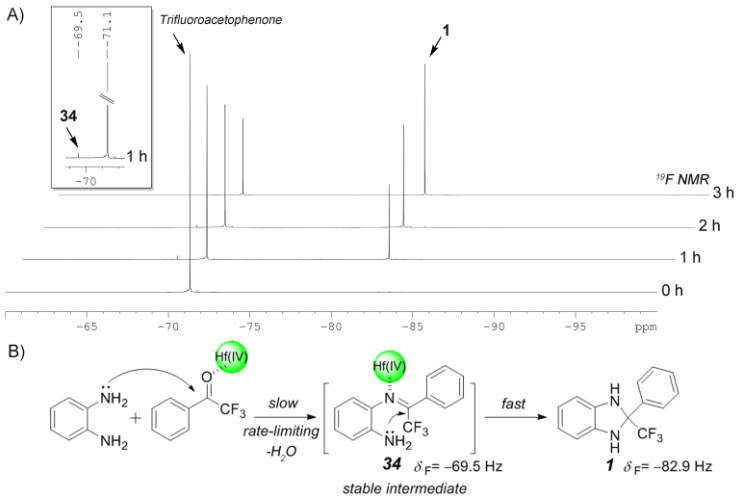


Figure 2. ^{19}F NMR tracing of the $Hf(OTf)_4$-catalyzed synthesis of **1** (A) and the proposed catalytic mechanism (B).

As proposed in the plausible mechanism, the above observations indicated that 1) the condensation reaction is the rate-limiting step, 2) the cyclization is relatively much faster and is the driving force of the overall reaction, and 3) the intermediate imine **34** was quickly consumed due to the highly promoted intramolecular cyclization of **34** by $Hf(OTf)_4$.

EXPERIMENTAL

General chemical reagents and solvents were obtained from commercial suppliers. All reactions were monitored by thin layer chromatography on plates coated with 0.25 mm silica gel 60 F_{254}. TLC plates were visualized by UV irradiation (254 nm). Flash column chromatography employed silica gel (particle size 32–63 μm). Melting points were determined with a Thomas-Hoover melting point apparatus and uncorrected. NMR spectra were obtained with a Bruker AV-400 instrument with chemical shifts reported in parts per million (ppm, δ) and referenced to $CDCl_3$. IR spectra were recorded on a Bruker Vertex-70 spectrometer. Low-resolution and high-resolution mass spectra were reported as *m/z* and obtained with an ion trap and a TOFQ mass spectrometer, respectively.

General procedure for the $Hf(OTf)_4$-catalyzed synthesis of fluorinated benzimidazolines (1–24), benzoxazolines (25–28), and benzothiazolines (29–32). To a solution of 1,2-phenylenediamine or *N*-substituted *o*-phenylenediamine/2-aminophenol/2-aminothiophenol (1.0 mmol) and $Hf(OTf)_4$ (0.02 mmol or 0.05 mmol (*N*-substituted *o*-phenylenediamine) in CH_2Cl_2 (5 mL) in a sealed pressure tube was added trifluorinated ketone (1.5 mmol). The reaction was stirred at 50 °C (alkyl trifluoromethyl ketone) or 120 °C (aryl trifluoromethyl ketone) for 3–8 h. The reaction was cooled to room temperature and concentrated *in vacuo*. Flash column chromatography on silica gel (hexane/CH_2Cl_2 = 4:1) afforded

products **1**–**32** in pure form. The characterization data of benzimidazolines (**1**,**2**,**4**–**13**), benzoxazolines (**26**–**27**), and benzothiazolines (**29**–**31**) were identical to those reported in literatures. [13,16–18,28]

2,3-Diphenyl-2-trifluoromethyl-1*H*-benzimidazoline (3): a white solid, mp 141–142 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53–7.34 (m, 5H), 7.17 (t, J = 8.0 Hz, 1H), 6.93 (t, J = 7.5 Hz, 1H), 6.87–6.76 (m, 5H), 6.65 (t, J = 7.6 Hz, 1H), 6.14 (s, 1H), 4.18 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.8, 141.8, 135.6, 134.1, 133.6, 129.2, 128.7 (×2), 128.5 (×3), 126.3 (q, $^{1}J_{C\text{-}F}$ = 289.4 Hz), 123.2, 122.2, 121.8, 121.6, 119.2, 118.4, 117.9, 71.7 (q, $^{2}J_{C\text{-}F}$ = 24.3 Hz) ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -65.4 ppm; IR (KBr): ν_{max} 3052, 2951, 2828, 1593, 1526, 1491, 1475, 1458, 1012, 994, 841, 783, 765, 753 cm^{-1}; HRMS (ESI+): *m/z* calcd for $C_{20}H_{16}F_3N_2$ $[M+H]^+$ 341.1260; found 341.1264.

2-Ethyl-3-phenyl-2-trifluoromethyl-1*H*-benzimidazoline (14): a white solid, mp 87–88 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.38 (m, 4H), 7.33–7.27 (m, 1H), 6.70–6.66 (m, 3H), 6.46–6.39 (m, 1H), 4.13 (s, 1H), 2.09 (q, J = 7.5 Hz, 1H), 1.88 (q, J = 7.5 Hz, 1H), 1.07 (t, J = 7.3 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.5, 139.8, 138.0, 129.6 (×2), 127.6 (×2), 126.6, 124.8 (q, $^{1}J_{C\text{-}F}$ = 290.5 Hz), 120.3, 119.6, 108.6, 107.7, 86.2 (q, $^{2}J_{C\text{-}F}$ = 28.0 Hz), 24.6, 6.5 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -81.5 ppm; IR (KBr): ν_{max} 3058, 2941, 2829, 1586, 1531, 1495, 1482, 1459, 1017, 995, 783, 765, 752 cm^{-1}; HRMS (ESI+): *m/z* calcd for $C_{16}H_{16}F_3N_2$ $[M+H]^+$ 293.1260; found 293.1257.

2-Methyl-3-phenyl-2-trifluoromethyl-1*H*-benzimidazoline (15): a white solid, mp 94–95 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.28 (m, 5H), 6.75–6.66 (m, 3H), 6.39–6.34 (m, 1H), 4.08 (s, 1H), 1.56 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.9 (×2), 137.9, 129.6 (×2), 128.8 (×2), 127.1, 124.6 (q, $^{1}J_{C\text{-}F}$ = 287.2 Hz), 121.0, 120.1, 109.6, 109.2, 83.3 (q, $^{2}J_{C\text{-}F}$ = 29.8 Hz), 20.3 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -83.9 ppm; IR (KBr): ν_{max} 3055, 2949, 2835, 1597, 1526, 1499, 1474, 1456, 1018, 993, 784, 765, 758 cm^{-1}; HRMS (ESI+): *m/z* calcd for $C_{15}H_{14}F_3N_2$ $[M+H]^+$ 279.1104; found 279.1108.

2-Benzyl-3-phenyl-2-trifluoromethyl-1*H*-benzimidazoline (16): a white solid, mp 108–109 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.43 (m, 4H), 7.39–7.27 (m, 4H), 7.24–7.19 (m, 2H), 6.73–6.67 (m, 3H), 6.45–6.38 (m, 1H), 4.22 (s, 1H), 3.38 (d, J = 14.7 Hz, 1H), 3.25 (d, J = 14.7 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.2, 139.9, 137.6, 133.5, 130.6 (×2), 129.7 (×2), 129.0 (×2), 128.7 (×2), 127.5, 127.0, 124.7 (q, $^{1}J_{C\text{-}F}$ = 290.2 Hz), 120.5, 119.9, 109.1, 108.1, 85.4 (q, $^{2}J_{C\text{-}F}$ = 27.9 Hz), 38.8 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -60.5 ppm; IR (KBr): ν_{max} 3064, 2948, 2835, 1595, 1526, 1495, 1476, 1454, 1021, 995, 845, 784, 767, 752 cm^{-1}; HRMS (ESI+): *m/z* calcd for $C_{21}H_{18}F_3N_2$ $[M+H]^+$ 355.1417; found 355.1411.

3-Benzyl-2-phenyl-2-trifluoromethyl-1*H*-benzimidazoline (17): a white solid, mp 157–158 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64–7.59 (m, 2H), 7.47–7.27 (m, 3H), 7.25–7.20 (m, 5H), 6.74–6.62 (m, 3H), 6.15–6.09 (m, 1H), 4.43 (s, 1H), 4.18 (d, J = 16.6 Hz, 1H), 4.07 (d, J = 16.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.7, 138.1, 137.5, 136.7, 130.0, 129.2 (×2), 128.9, 128.7, 127.1, 126.7 (×2),

126.6 (×2), 124.7 (q, $^{1}J_{C\text{-}F}$ = 286.8 Hz), 121.0, 119.3, 108.2, 106.7, 87.5 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz), 51.2 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -76.5 ppm; IR (KBr): ν_{max} 3062, 2945, 2827, 1594, 1526, 1497, 1473, 1458, 1015, 997, 843, 785, 769, 752 cm^{-1}; HRMS (ESI+): *m/z* calcd for $C_{21}H_{18}F_3N_2$ $[M+H]^+$ 355.1417; found 355.1415.

3-Benzyl-2-ethyl-2-trifluoromethyl-1*H*-benzimidazoline (18): a white solid, mp 103–104 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44–7.27 (m, 5H), 6.65–6.57 (m, 3H), 6.09–6.03 (m, 1H), 4.58 (d, *J* = 16.5 Hz, 1H), 4.44 (d, *J* = 16.5 Hz, 1H), 4.04 (s, 1H), 2.23 (q, *J* = 7.6 Hz, 1H), 1.90 (q, *J* = 7.6 Hz, 1H), 1.04 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.2, 138.0, 137.4, 128.8 (×2), 127.2, 126.7 (×2), 125.0 (q, $^{1}J_{C\text{-}F}$ = 289.4 Hz), 120.5, 118.7, 107.6, 105.8, 86.0 (q, $^{2}J_{C\text{-}F}$ = 28.2 Hz), 48.5, 24.5, 6.6 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -81.9 ppm; IR (KBr): ν_{max} 3057, 2957, 2828, 1592, 1526, 1499, 1473, 1458, 1020, 993, 788, 765, 756 cm^{-1}; HRMS (ESI+): *m/z* calcd for $C_{17}H_{18}F_3N_2$ $[M+H]^+$ 307.1417; found 307.1421.

2,3-Dibenzyl-2-trifluoromethyl-1*H*-benzimidazoline (19): a white solid, mp 102–103 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.27 (m, 10H), 6.60–6.50 (m, 3H), 6.00 (d, *J* = 6.5 Hz, 1H), 4.68 (d, *J* = 16.4 Hz, 1H), 4.53 (d, *J* = 16.4 Hz, 1H), 4.22 (s, 1H), 3.40 (d, *J* = 14.7 Hz, 1H), 3.35 (d, *J* = 14.7 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.6, 137.7, 136.9, 133.2, 130.8 (×2), 128.8 (×4), 127.6, 127.3, 126.9 (×2), 125.0 (q, $^{1}J_{C\text{-}F}$ = 277.7 Hz), 120.6, 118.9, 108.1, 106.3, 85.6 (q, $^{2}J_{C\text{-}F}$ = 27.6 Hz), 48.7, 37.9 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -61.6 ppm; IR (KBr): ν_{max} 3057, 2943, 2824, 1598, 1534, 1496, 1476, 1454, 1019, 993, 853, 785, 767, 754 cm^{-1}; HRMS (ESI+): *m/z* calcd for $C_{22}H_{20}F_3N_2$ $[M+H]^+$ 369.1573; found 369.1580.

2-Phenyl-3-propyl-2-trifluoromethyl-1*H*-benzimidazoline (20): a white solid, mp 71–72 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58–7.53 (m, 2H), 7.44–7.39 (m, 3H), 6.79 (t, *J* = 7.5 Hz, 1H), 6.68–6.55 (m, 2H), 6.42 (d, *J* = 7.5 Hz, 1H), 4.26 (s, 1H), 3.06–2.85 (m, 2H), 1.72–1.58 (m, 2H), 0.85 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.8, 137.2, 137.0, 129.7, 128.9 (×2), 126.8 (×2), 124.7 (q, $^{1}J_{C\text{-}F}$ = 287.4 Hz), 121.0, 118.2, 108.1, 104.4, 87.1 (q, $^{2}J_{C\text{-}F}$ = 29.7 Hz), 47.9, 21.5, 11.5 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -76.5 ppm; IR (KBr): ν_{max} 3065, 2945, 2826, 1593, 1529, 1497, 1479, 1453, 1017, 994, 787, 769, 752 cm^{-1}; HRMS (ESI+): *m/z* calcd for $C_{17}H_{18}F_3N_2$ $[M+H]^+$ 307.1417; found 307.1423.

2-Methyl-3-propyl-2-trifluoromethyl-1*H*-benzimidazoline (21): a white solid, mp 69–70 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.77 (t, *J* = 7.5 Hz, 1H), 6.66–6.53 (m, 2H), 6.38 (d, *J* = 7.5 Hz, 1H), 3.94 (s, 1H), 3.35–3.10 (m, 2H), 1.79–1.68 (m, 2H), 1.66 (s, 3H), 1.01 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.7, 136.8, 124.8 (q, $^{1}J_{C\text{-}F}$ = 288.1 Hz), 120.8, 118.0, 108.4, 104.8, 82.7 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz), 46.1, 21.9, 19.4, 11.5 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -83.7 ppm; IR (KBr): ν_{max} 3058, 2944, 2828, 1587, 1532, 1487, 1476, 1453, 1017, 998, 784, 765, 754 cm^{-1}; HRMS (ESI+): *m/z* calcd for $C_{12}H_{16}F_3N_2$ $[M+H]^+$ 245.1260; found 245.1254.

2-Ethyl-3-propyl-2-trifluoromethyl-1*H*-benzimidazoline (22): a white solid, mp 65–66 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.71 (t, J = 7.4 Hz, 1H), 6.61–6.50 (m, 2H), 6.32 (d, J = 7.5 Hz, 1H), 3.91 (s, 1H), 3.18 (t, J = 7.9 Hz, 2H), 2.25–2.10 (m, 1H), 1.84–1.70 (m, 3H), 1.04–0.91 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.3, 137.2, 124.9 (q, $^{1}J_{C\text{-}F}$ = 289.3 Hz), 120.4, 117.7, 107.4, 103.7, 85.5 (q, $^{2}J_{C\text{-}F}$ = 28.4 Hz), 45.9, 24.2, 21.7, 11.5, 6.3 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -82.5 ppm; IR (KBr): ν_{max} 3063, 2948, 2827, 1593, 1528, 1491, 1476, 1458, 1013, 995, 788, 763, 754 cm^{-1}; HRMS (ESI+): *m/z* calcd for $C_{13}H_{18}F_3N_2$ $[M+H]^+$ 259.1417; found 259.1421.

3-Cyclohexyl-2-phenyl-2-trifluoromethyl-1*H*-benzimidazoline (23): a white solid, mp 141–142 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69–7.64 (m, 2H), 7.44–7.38 (m, 3H), 6.77–6.69 (m, 1H), 6.67–6.56 (m, 3H), 4.28 (s, 1H), 2.92–2.81 (m, 1H), 2.06–1.90 (m, 3H), 1.85–1.78 (m, 1H), 1.63–1.54 (m, 2H), 1.26–1.06 (m, 3H), 0.94–0.78 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.8, 137.7, 137.5, 129.6, 128.6 (×2), 127.5 (×2), 124.9 (q, $^{1}J_{C\text{-}F}$ = 289.8 Hz), 120.5, 117.3, 108.1, 106.9, 86.1 (q, $^{2}J_{C\text{-}F}$ = 29.2 Hz), 55.2, 30.0, 28.2, 26.6, 26.3, 25.8 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -77.3 ppm; IR (KBr): ν_{max} 3058, 2943, 2829, 1591, 1526, 1497, 1476, 1454, 1014, 997, 789, 763, 752 cm^{-1}; HRMS (ESI+): *m/z* calcd for $C_{20}H_{22}F_3N_2$ $[M+H]^+$ 347.1730; found 347.1726.

3-Cyclohexyl-2-ethyl-2-trifluoromethyl-1*H*-benzimidazoline (24): a white solid, mp 101–102 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.69–6.59 (m, 1H), 6.57–6.46 (m, 3H), 3.92 (s, 1H), 3.21–3.10 (m, 1H), 2.27–2.02 (m, 3H), 1.93–1.68 (m, 6H), 1.39–1.18 (m, 3H), 1.04 (t, J = 7.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.6, 137.6, 125.2 (q, $^{1}J_{C\text{-}F}$ = 291.9 Hz), 119.9, 116.7, 107.7, 106.4, 85.1 (q, $^{2}J_{C\text{-}F}$ = 27.7 Hz), 53.9, 30.0, 28.8, 26.7, 26.6, 25.8, 23.9, 6.8 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -82.2 ppm; IR (KBr): ν_{max} 3053, 2942, 2824, 1591, 1525, 1494, 1476, 1456, 1015, 996, 782, 764, 755 cm^{-1}; LRMS (ESI+): *m/z* calcd for $C_{16}H_{22}F_3N_2$ $[M+H]^+$ 299.1730; found 299.1734.

2-Phenyl-2-(trifluoromethyl)benzoxazoline (25) a white solid, mp 81–82 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73–7.67 (m, 2H), 7.49–7.45 (m, 3H), 6.99–6.85 (m, 4H), 4.39 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.5, 135.8, 135.5, 130.2, 129.0 (×2), 126.0 (×2), 123.2 (q, $^{1}J_{C\text{-}F}$ = 286.1 Hz), 123.0, 122.2, 112.8, 108.8, 97.9 (q, $^{2}J_{C\text{-}F}$ = 32.2 Hz) ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -83.8 ppm; IR (KBr): ν_{max} 3058, 2945, 2828, 1599, 1524, 1495, 1477, 1454, 1010, 986, 772, 764, 759 cm^{-1}; HRMS (ESI+): *m/z* calcd for $C_{14}H_{11}F_3NO$ $[M+H]^+$ 266.0787; found 266.0782.

2-Benzyl-2-(trifluoromethyl)benzoxazoline (28): a white solid, mp 78–79 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.24 (m, 5H), 6.79–6.68 (m, 3H), 6.67–6.59 (m, 1H), 3.89 (s, 1H), 3.56 (d, J = 14.8 Hz, 1H), 3.20 (d, J = 14.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.8, 136.3, 132.0, 130.8 (×2), 129.0 (×2), 128.0, 123.3 (q, $^{1}J_{C\text{-}F}$ = 286.5 Hz), 122.5, 121.8, 112.2, 108.3, 98.0 (q, $^{2}J_{C\text{-}F}$ = 30.8 Hz), 38.1 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -85.3 ppm; IR (KBr): ν_{max} 3046, 2945, 2832, 1596, 1525, 1495,

1487, 1457, 1010, 998, 782, 769, 760 cm^{-1}; HRMS (ESI+): *m/z* c alcd for $C_{15}H_{13}F_3NO$ $[M+H]^+$ 280.0944; found 280.0939.

2-Benzyl-2-(trifluoromethyl)benzothiazoline (32): a yellow solid, mp 73–74 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.38–7.28 (m, 5H), 7.00 (d, J = 7.6 Hz, 1H), 6.92 (t, J = 7.5 Hz, 1H), 6.75 (t, J = 7.5 Hz, 1H), 6.62 (d, J = 7.8 Hz, 1H), 4.26 (s, 1H), 3.42 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.3, 133.5, 131.2 (×2), 128.6 (×2), 127.8, 126.0 (q, $^1J_{C\text{-}F}$ = 283.1 Hz), 125.8 (×2), 121.4 (×2), 110.7, 79.3 (q, $^2J_{C\text{-}F}$ = 28.9 Hz), 40.7 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -80.6 ppm; IR (KBr): ν_{max} 3056, 2947, 2825, 1596, 1534, 1496, 1477, 1458, 1014, 996, 787, 764, 754 cm^{-1}; HRMS (ESI+): *m/z* calcd for $C_{15}H_{13}F_3NS$ $[M+H]^+$ 296.0715; found 296.0721.

***N*-(2,2,2-Trifluoro-1-phenylethylidene)-1,2-phenylenediamine (34):** To a solution of 1,2-phenylene-diamine (216 mg, 2.0 mmol) in CH_2Cl_2 (10 mL) in a sealed pressure tube was added 2,2,2-trifluoro-1-phenylethanone (522 mg, 3.0 mmol). The reaction was stirred at 120 °C for 12 h. The reaction was cooled to room temperature and concentrated in vacuo. Flash column chromatography on silica gel afforded **34** (42 mg, 8%) as yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.44–7.33 (m, 3H), 7.32–7.28 (m, 2H), 6.93 (t, J = 7.8 Hz, 1H), 6.74 (d, J = 7.9 Hz, 1H), 6.38 (t, J = 7.8 Hz, 1H), 6.22 (d, J = 7.9 Hz, 1H), 4.09 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.4 (q, $^2J_{C\text{-}F}$ = 33.6 Hz), 142.1, 132.3, 130.9, 130.6, 129.0 (×2), 128.5 (×2), 128.2, 120.4, 120.3 (q, $^1J_{C\text{-}F}$ = 277.1 Hz), 117.9, 115.8 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -69.5 ppm; IR (KBr): ν_{max} 3457, 3421, 2959, 2923, 2853, 1611, 1491, 1377, 1327, 1261, 1192, 1096, 1021, 799, 743 cm^{-1}; HRMS (ESI+): *m/z* calcd for $C_{14}H_{12}F_3N$ $[M+H]^+$ 265.0947; found 265.0945.

ACKNOWLEDGEMENTS

We thank the National Natural Science Foundation of China (21961013) for financial support.

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