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电化学氧化下喹喔啉-2(1*H*)-酮的三氟甲基化及电描述符对反应性能的评价

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摘要 通过使用廉价易得且易于处理的 CF_3SO_2Na 作为 CF_3 源，实现了操作简单的电化学氧化喹喔啉-2(1*H*)-酮的 C—H 三氟甲基化. 由于没有使用任何催化剂或氧化剂，该方法符合绿色和可持续发展的要求. 最重要的是，使用“电描述符图”来评估底物的反应活性，可以清楚地看到反应/非反应边界和产量变化趋势.

关键词 喹喔啉-2(1*H*)-酮；电化学合成；三氟甲基化；三氟甲基亚磺酸钠；电化学描述符

Electrochemical Oxidative C—H Trifluoromethylation of Quinoxalin-2(1*H*)-ones and the Performance Evaluation via Electro-descriptors

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Abstract An operationally simple electrochemical oxidative C—H trifluoromethylation of quinoxalin-2(1*H*)-ones was achieved by employing the inexpensive, readily available and easy processing CF_3SO_2Na as CF_3 source. In the absence of any catalysts or oxidant reagents, this method is more in line with the requirements of green and sustainable development. Most importantly, “electric-descriptor-diagram” was used to evaluate the reaction substrates. The reactive/non-reactive boundary and the trend of yield change can been clearly seen.

Keywords qinoxalin-2(1*H*)-ones; electrochemical synthesis; trifluoromethylation; sodium trifluoromethanesulfinate; electro-descriptors

1 Introduction

Quinoxalin-2(1*H*)-one derivative, especially 3-substituted quinoxalin-2(1*H*)-ones are highly significant *N*-heterocyclic compounds that are not only versatile synthetic intermediates but also the most ubiquitous scaffolds in natural products, pharmaceuticals and functional materials.[1] Consequently, the development of efficient methodologies for preparation of diverse 3-substituted quinoxalin-2(1*H*)-one derivative is highly desirable. Especially over the past few decades, a number of approaches have been developed in this area with the tireless efforts of researchers. Alkylation,[2] alkoxylation,[3] (hetero)arylation,[4] acylation,[5] perfluoroalkylation,[6] cyanation,[7] difluorination,[8] amination,[9] thioetherification[10] and phosphonatation[11] of quinoxalin-2(1*H*)-one at C(3) position via direct C—H functionalization have been reported.

At the same time, the fluorine-containing compounds, particularly trifluoromethyl compounds, have attracted considerable attention in the fields of pharmaceutical, agrochemical and functional material.[12] The trifluoromethyl group is highly electron withdrawing, and incorporation of trifluoromethyl group into functionalized molecules can

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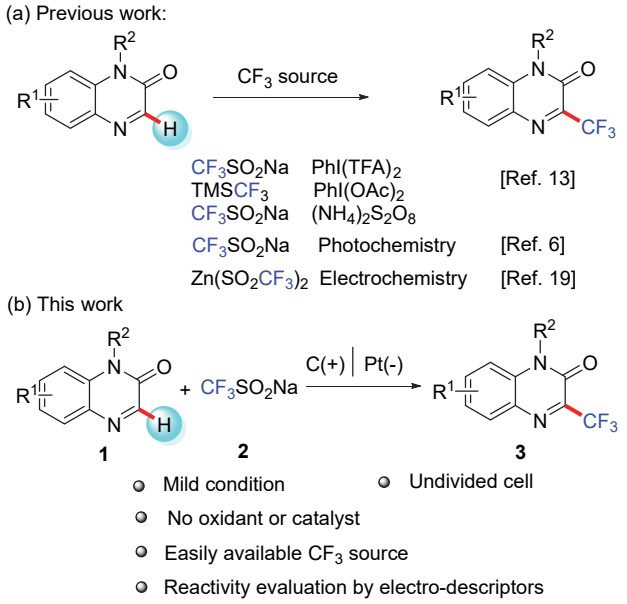
remarkably improve desirable properties, such as lipophilicity, metabolic stability and bioavailability.[12a,13] Therefore, a series of significant synthetic strategies for trifluoromethylation have been developed with the extensive efforts of researchers.[14] Among of them, direct C—H trifluoromethylation through radical pathway which initiated by redox chemical reagents or photocatalysts has been proved to be one of the most effective methods. In particular, considering the potential application of quinoxalin-2(1*H*)-one trifluoromethylation, several cases have achieved at the C(3) position by this method in recent years. Some groups have successively reported the radical C—H trifluoromethylation of quinoxalin-2(1*H*)-one initiated by $PhI(TFA)_2$, $PhI(OAc)_2$ or $(NH_4)_2S_2O_8$.[15] Nevertheless, these protocols suffer from the use of inert gases, excess amounts of oxidizing reagents, as well as additives. To overcome these shortcomings, in 2019, Jin's and Duan's group almost at the same time developed the practical approach for C—H perfluoroalkylation of quinoxalinones under aerobic oxidation condition with the irradiation of blue LEDs. However, these methods suffer from the disadvantages of photocatalyst or long reaction time (Scheme 1a).[6]



Scheme 1 Methods for trifluoromethylation of quinoxalin-2(1*H*)-ones

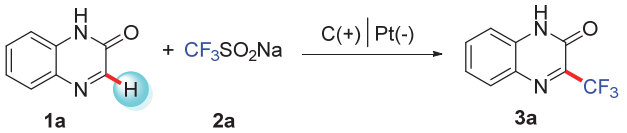
With the continuous requirements for green and sustainable development, it is precisely because of the use of electrical current to replace hazardous chemical redox reagents and proton acceptors, reducing the footprint of undesirable byproducts, that electrochemical organic synthesis has received continuous attention as a synthetic strategy.[16] By utilizing electrochemical analysis which has powerful functions such as quantitative analysis and mechanism research, electrochemical organic synthesis will make great progress. Among them, it has been reported that the redox potentials of different substrates and different functional groups in the same substrate measured by cyclic voltammetry (CV) can be used to speculate or prove the reaction mechanism.[17] In 2014, radical C—H trifluoromethylation of heteroarenes under electrochemical condition which employed divided cells and Et_4NClO_4/DMSO (dimethyl sulfoxide) supporting electrolyte was reported by Baran, Blackmond, and co-workers.[18] Recently, Zeng's group described an alternative electrochemical trifluoromethylation methodology of quinoxalin-2(1*H*)-one by virtue of the *in situ* generated sulfonyl hypobromite intermediate in a beaker-type undivided cell.[19] Obviously, both reactions used expensive and poor stable $(SO_2CF_3)_2Zn$ as CF_3 source which limited the application. Meanwhile, in the above cases and most reports on electrochemical organic synthesis, researchers only use the onset potential to evaluate the reaction mechanism or experimental results. It is difficult to show clearly the change of yield and the boundary between reactive and non-reactive conditions/substrates. Recently, Ding's group[20] took the lead in developing an experimentally-derived descriptors system for predicting the reactivity of organic reactions. Through the so-called "electric-descriptor-diagram", which combines electrochemical parameters such as onset potential, Tafel slope and effective voltage to evaluate reaction conditions and predict reaction activity, satisfactory results have been obtained. This provides a promising tool for predicting and screening substrates, optimizing reaction conditions and studying mechanism in electrochemical organic synthesis. Inspired by the recent development of electrochemical aryl(alkyl)trifluorome-thylation of allyl alcohols pioneered by the Lei group,[21] we conducted electrochemical oxidative trifluoromethylation of quinoxalin-2(1*H*)-one projects which employed the inexpensive, readily available and easy processing CF_3SO_2Na as CF_3 source and obtained a relatively accurate performance evaluation by "electric-descriptor-diagram".

2 Results and discussion

Our investigation was started by choosing quinoxalin-2(1*H*)-one (**1a**) and CF_3SO_2Na (**2a**) as reaction partners for optimization studies (Table 1). After considerable efforts, 3-(trifluoromethyl)quinoxalin-2(1*H*)-one **3a** could be obtained in 81% isolated yield with a graphite rod anode and platinum cathode under constant current (20 mA) for 4 h in the presence of ^{n}Bu$_4$NBF$_4$ as the electrolyte and CH_3CN/HOAc/H_2O (V∶V∶V=9.0∶0.5∶0.5) as the cosolvent (Entry 1). Removal of H_2O or HOAc caused a significant reduction in 30%～53% yield, revealing that the mixed solvent was crucial for producing a C—H trifluoromethylation product (Entries 2～4). Other solvent, such as *N*,*N*'-dimethylformamide (DMF) gave disappointing yield (Entry 5). Electrolytes such as ^{n}Bu$_4$NPF$_6$, tetrabutylammonium iodide (TBAI) and tetrabutylammonium bromide (TBAB) were subsequently investigated. However, all led to the product **3a** in lower yield, especially the use of TBAI resulted in no product (Entry 6). Further experiments have

shown that a change of the anode with platinum plate or reticulated vitreous carbon (RVC) leads to a decrease of yield significantly (Entry 7). Subsequently, it was proved to be less efficient when the operating current was changed (10 or 30 mA) (Entries 8, 9). It is also noteworthy that there was no conversion of substrates under no electric current conditions (Entry 10).

Table 1 Optimization of the reaction conditions[a]



Entry	Variation from the standard reaction conditions	Yield[b]/%
1	None	81
2	No H_2O and HOAc	30
3	No HOAc	53
4	No H_2O	46
5	DMF instead of CH_3CN	Trace
6	$^nBu_4NPF_6$, TBAI and TBAB instead of $^nBu_4NBF_4$	61, 0, 19
7	Pt, RVC instead of C as anode	44, 0
8	10 mA, 8 h instead of 20 mA, 4 h	77
9	30 mA, 3 h instead of 20 mA, 4 h	65
10	No electricity	0

[a] Reaction conditions: C anode, Pt cathode, constant current (20 mA), **1a** (0.3 mmol), **2a** (0.9 mmol), $^nBu_4NBF_4$ (0.3 mmol), CH_3CN (9.0 mL), H_2O (0.5 mL), HOAc (0.5 mL), r.t., 4 h. [b] Isolated yields.

After the optimal conditions were established, our attention was turned toward the substrate scope to explore the versatility of this electrochemical trifluoromethylation protocol. The results are shown in Table 2. Firstly, contrary to previous reports, quinoxalin-2(1*H*)-one without any substituents gave the highest yield (81%, **3a**). Subsequently, a series of quinoxalinones with different *N*-protecting groups, such as ethyl, butyl, hexyl and esteryl (**3b**～**3e**) were tested and afforded the desired products in 52%～75% yields. Pleasingly, quinoxalinones bearing functionally diverse *N*-benzyl groups (CH_2Ar) (**3f**～**3j**) could also react smoothly, however, providing relatively lower corresponding products in 60%～68% yields than *N*-alkyl groups. To our delight, quinoxalinones possessing electron-rich and electron-deficient groups on the benzene ring reacted with CF_3SO_2Na (**2a**) to afford the trifluoromethylation products (**3k**～**3q**). From the results, the yield of substrates with electron-rich groups is generally slightly higher than that of substrates with electron-deficient groups. It is noteworthy that some valuable electrophilic functional groups, such as fluoro, chloro and ester substitutions, are tolerated. Disappointingly, some other heterocycles such as 5,6-diphenyl-5,6-dihydropyrazin-2-ol (**1s**), pyrido[2,3-*b*]pyrazin-2(1*H*)-one (**1t**), 2*H*-benzo[*b*][1,4]-oxazin-2-one (**1u**) failed to react under the optimized conditions and the starting materials were recovered, showing certain limitations of this method.

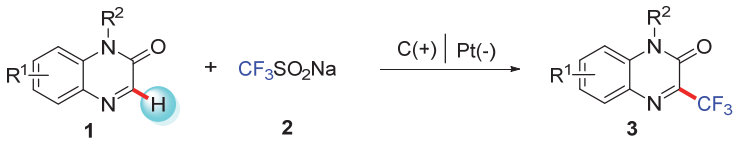
To gain some insight into the mechanism of the electrochemical direct C—H trifluoromethylation of quinoxalin-2(1*H*)-one, control experiments were carried out. When radical scavengers such as 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), 2,4-ditert-butyl-4-methylphenol (BHT) and 1,1-diphenylethylene were introduced to the system, the transformation was strongly inhibited and no desired product was obtained. Moreover, adducts of radical scavengers and CF_3 radical could be detected by HRMS. These results above imply that the reaction involves a radical pathway (Scheme 2).

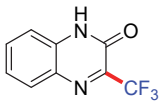
On the basis of these controlled experiments and previous reports, a plausible mechanism is depicted in Scheme 3. When the current is passed, sodium trifluoromethanesulfinate loses an electron at the anode to generate trifluoromethyl radical **B**, and at the same time, quinolinone is protonated to form intermediate **A**. Then intermediate **B** attacks selectively the C(3) position of **A** to form intermediate **C**. Finally, intermediate **C** loses electrons at the anode and deprotonates to obtain product **3a**. Simultaneously, protons get electrons at the cathode and hydrogen evolution reaction occurs.

In order to explain the above experimental results and verify the proposed reaction mechanism, the reaction substrates were first measured by cyclic voltammetry. The initial potential of CF_3SO_2Na is 0.7 V (vs. Ag/AgCl), which is lower than that of quinoxalin-2(1*H*)-one (1.7 V vs. Ag/AgCl), indicating that CF_3SO_2Na is easier to be oxidized on the anode during the reaction (Figure S1). However, it is difficult to explain other phenomena, such as the change of yield and the boundary between reactive and non-reactive substrates. Then, we made CV diagrams of different substrates in the reaction system (Table 2, Table S1).

As shown in Figure 1a, the reactivity of the substrate mainly depends on the electrochemical parameters of the second peak. It is well known that the lower the onset voltage is, the easier the reaction is and the more favorable the thermodynamics is. This also explains that Entry 30 (1.57 V vs. Ag/AgCl) and 3U (1.53 V vs. Ag/AgCl) do not react (higher than 1.37 V vs. Ag/AgCl). It is noticed that although Entry 15 has a low onset voltage (1.35 V vs. Ag/AgCl), the yield is only 52%. At this time, we consider its effective voltage (1.75 V vs. Ag/AgCl), and the effective voltage indicates the voltage required for the reaction to reach the same *operando* rate, that is, to reach the rate, a higher effective voltage usually requires a higher driving force and the less products are obtained in the same condition. This parameter can also explain the above non-reactive Entry 30 (1.64 V vs. Ag/AgCl) and Entry 31 (1.65 V vs. Ag/AgCl). For Entry 13 (1.33 V, 1.63 V vs. Ag/AgCl) with lower initial voltage and effective voltage, the theoretical yield should be very high, but the actual yield is 64%. In order to explain this phenomenon, we introduce the electrochemical parameter-Tafel slope, which describes the electrodynamics of electron transfer on the

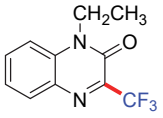
Table 2 Substrate scope and electro-descriptors of different substrates under optimized conditions[a]





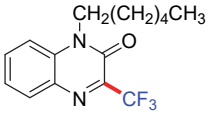
Entry11 **3a**, 81%

E_{onset}	1.37
$E_{effective}$	1.63
Tafel slope	1.00



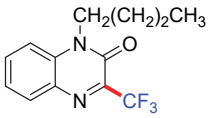
Entry12 **3b**, 75%

E_{onset}	1.41
$E_{effective}$	1.62
Tafel slope	1.30



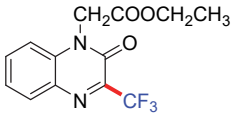
Entry13 **3c**, 64%

E_{onset}	1.33
$E_{effective}$	1.63
Tafel slope	1.04



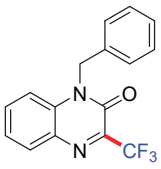
Entry14 **3d**, 71%

E_{onset}	1.34
$E_{effective}$	1.64
Tafel slope	0.93



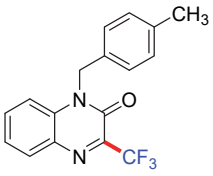
Entry 15 **3e**, 52%

E_{onset}	1.35
$E_{effective}$	1.75
Tafel slope	1.00



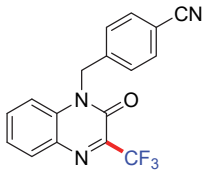
Entry 16 **3f**, 67%

E_{onset}	1.30
$E_{effective}$	1.62
Tafel slope	0.92



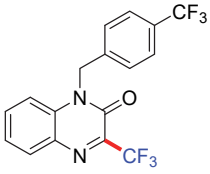
Entry 17 **3g**, 62%

E_{onset}	1.30
$E_{effective}$	1.62
Tafel slope	0.91



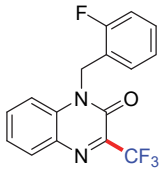
Entry 18 **3h**, 60%

E_{onset}	1.38
$E_{effective}$	1.63
Tafel slope	1.01



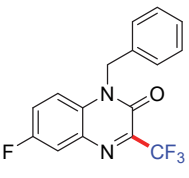
Entry 19 **3i**, 61%

E_{onset}	1.31
$E_{effective}$	1.64
Tafel slope	0.92



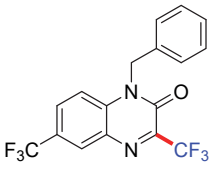
Entry 20 **3j**, 68%

E_{onset}	1.36
$E_{effective}$	1.64
Tafel slope	0.99



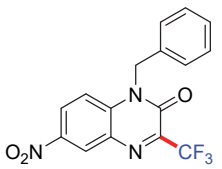
Entry 21 **3k**, 56%

E_{onset}	1.43
$E_{effective}$	1.62
Tafel slope	1.04



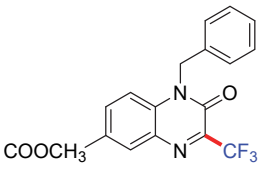
Entry 22 **3l**, 51%

E_{onset}	1.37
$E_{effective}$	1.67
Tafel slope	0.93



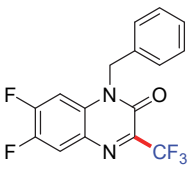
Entry 23 **3m**, 55%

E_{onset}	1.45
$E_{effective}$	1.63
Tafel slope	1.18



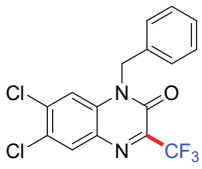
Entry 24 **3n**, 61%

E_{onset}	1.36
$E_{effective}$	1.63
Tafel slope	0.85



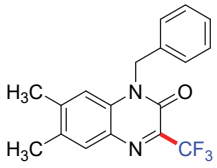
Entry 25 **3o**, 55%

E_{onset}	1.54
$E_{effective}$	1.65
Tafel slope	1.54



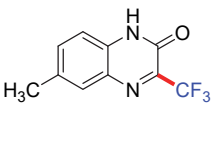
Entry 26 **3p**, 54%

E_{onset}	1.38
$E_{effective}$	1.63
Tafel slope	0.98



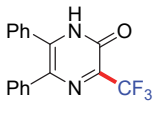
Entry 27 **3q**, 62%

E_{onset}	1.62
$E_{effective}$	1.65
Tafel slope	1.95



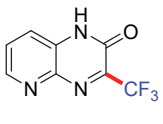
Entry 28 **3r** (3:1) , 74%

E_{onset}	1.39
$E_{effective}$	1.64
Tafel slope	1.07



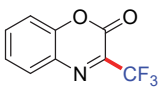
Entry 29 **3s**, 0%

E_{onset}	1.41
$E_{effective}$	1.64
Tafel slope	1.18



Entry 30 **3t**, 0%

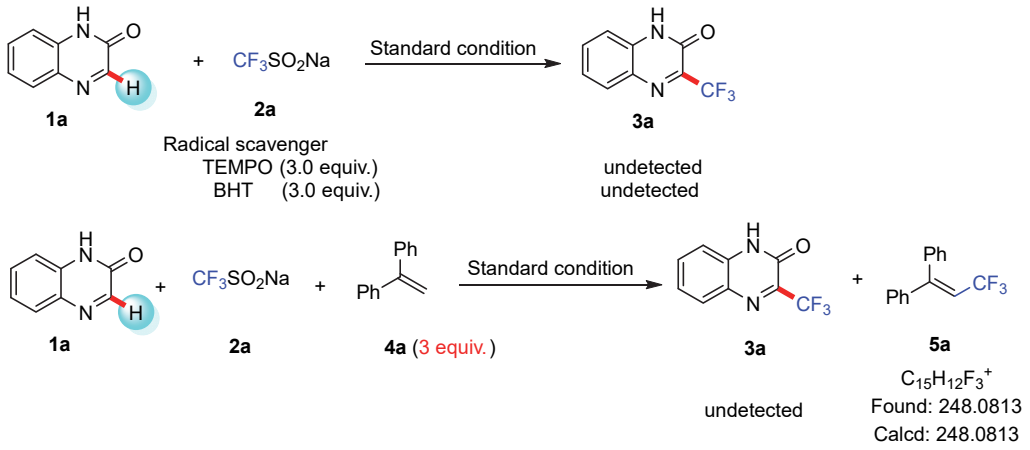
E_{onset}	1.57
$E_{effective}$	1.64
Tafel slope	1.71



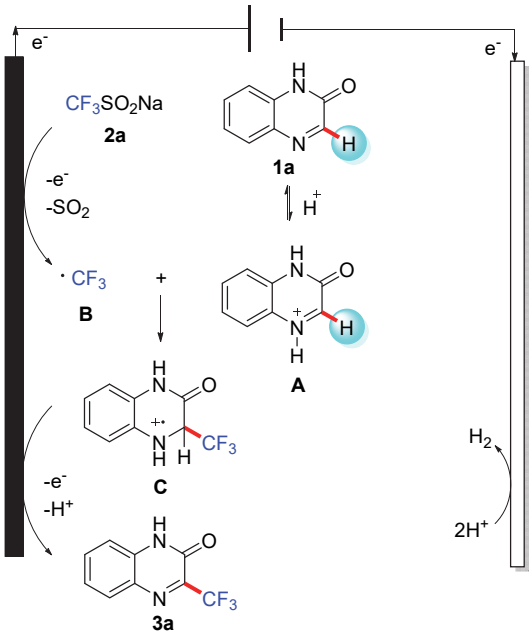
Entry 31 **3u**, 0%

E_{onset}	1.34
$E_{effective}$	1.65
Tafel slope	1.55

[a] Reaction conditions: C anode, Pt cathode, constant current=20 mA, **1a** (0.3 mmol), **2a** (0.9 mmol), $^{n}Bu_4NBF_4$ (0.3 mmol), CH_3CN (9.0 mL), H_2O (0.5 mL), HOAc (0.5 mL), r.t., 4 h.



Scheme 2 Mechanism experiment and radical trapping



Scheme 3 Possible reaction mechanism of electrochemical oxidative C—H trifluoromethylation

electrode. Generally speaking, the larger the Tafel slope, the slower the electron transfer on the electrode surface and the more unfavorable the kinetics. The larger Tafel slope Entry 13 (1.04) inhibited the reaction. Entry 12 can also be explained in this way. For non-reactive (or 0% yield) Entry 29, although its initial voltage and effective voltage indicate that it can be reacted, its lower Tafel slope relative to Entries 30 and 31 indicates that side reactions may occur and desired products are not obtained. However, it cannot be considered that the smaller the Tafel slope, the more target products can be obtained, such as Entry 13, its onset voltage and effective voltage are very close to Entry 11 with the highest yield, but there is a much smaller Tafel slope (0.85), which indicates that the substrate is oxidized too fast on the anode surface and more side reactions inevitably occur, resulting in the yield of only 61%.

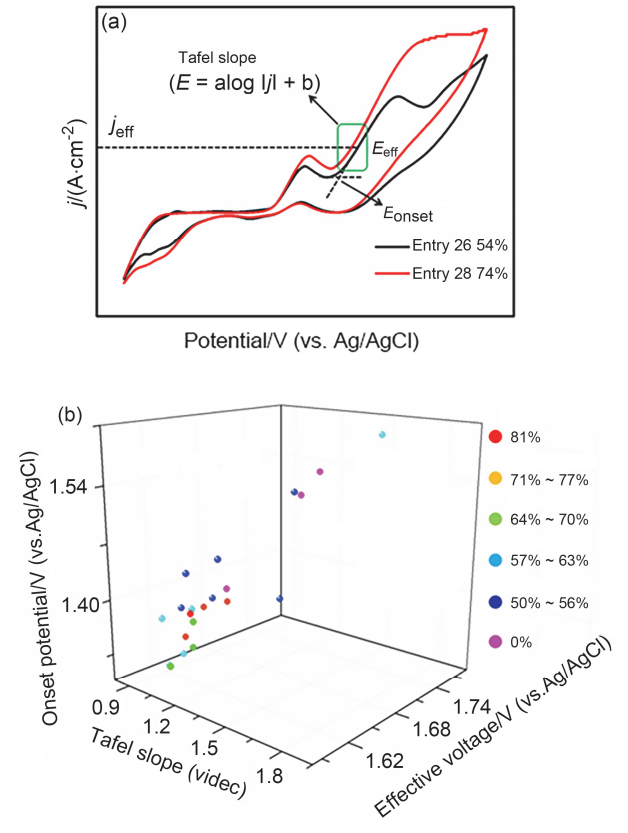


Figure 1 (a) Three electro-descriptors, onset potential, Tafel slope and effective voltage, identified from the CV diagram of Entries 26 and 28; (b) the 3D electro-descriptor-diagram built with three electro-descriptors

From the above results we can see that if only one or two parameters are used to predict the reaction activity (including yield and reactive/non-reactive), it is difficult to get the correct results. Inspired by Ding's group report, we made the CV curve of the reaction system, and fitted the initial potential, Tafel slope and effective voltage to generate a 3D "electric-descriptor-diagram" (Figure 1b). In the reactive region, it can also be seen such a trend, that is, the closer to the red ball (the highest yield), the higher the

yield, indicating that the three parameters are concentrated here, rather than the increase or decrease of some parameters. However, for Entries 25, 27 with acceptable yields, it can be seen from the figure that they are far away from the region of high reactivity, which indicates that there are exceptions when using three-dimensional "electric descriptor diagram" to predict reactivity. It is undeniable that the accuracy of reactivity prediction can be greatly improved by using multidimensional electrical descriptors.

3 Conclusions

In summary, we have developed an electrochemical direct C—H trifluoromethylation of quinoxalin-2(1*H*)-ones in the undivided cell. Quinoxalin-2(1*H*)-ones with a variety of substituents can react and get corresponding products. Especially, by employing the inexpensive, readily available and easy processing CF_3SO_2Na as CF_3 source, as well as no oxidant and catalyst used, this method is more in line with the requirements of green and sustainable development. Finally, by using this 3D "electric-descriptor-diagram" to evaluate the substrates, the reactive/non-reactive boundary and the trend of yield change can be clearly seen. Ongoing research includes extending the method to other heterocyclic aromatic substrates, as well as the applicability and accuracy of a powerful "electric-descriptor-diagram" tool.

4 Experimental section

4.1 General information

Unless otherwise noted, all reagents and solvents were used directly as obtained commercially without further purification. Column chromatography was performed using silica gel (200～300 mesh size) with indicated solvents. Thin-layer chromatography (TLC) was conducted with silica gel GF254 precoated plates (0.25 mm) and visualized with UV light. The instrument for electrolysis is dual display potentiostat (DJS-292) (made in China). Cyclic voltammograms were obtained on a CHI 610E potentiostat. The anodic electrode was graphite rod (ϕ 6 mm) and cathodic electrode was platinum plate (10 mm×10 mm×0.3 mm). All ^{1}H NMR spectra were recorded on 600 MHz spectrometers, and the data are reported using solvents as internal standards ($CDCl_3$ at δ 7.26, DMSO-d_6 at δ 2.50). All proton-decoupled ^{13}C NMR spectra were recorded at 151 MHz, and the data are reported using solvents as internal standards ($CDCl_3$ at δ 77.2, DMSO-d_6 at δ 39.5). All ^{19}F NMR spectra were recorded on 377 MHz spectrometers. HRMS analyses of the compounds were conducted on a Thermo Q Exactive mass spectrometer using electrospray ionization in the positive ion mode.

4.2 General procedure for electrochemical oxidative C—H trifluoromethylation of quinoxalin-2(1*H*)-ones

In an undivided cell (25 mL) was equipped with a carbon anode (ϕ 6 mm) and a platinum electrodes (10 mm×10 mm) as the cathode. Quinoxalin-2(1*H*)-one (**1a**, 0.3 mmol), CF_3SO_2Na (**2a**, 0.9 mmol), $^nBu_4NBF_4$ (0.3 mmol), CH_3CN (9.0 mL), H_2O (0.5 mL), HOAc (0.5 mL) were continuously added. The reaction mixture was stirred and electrolyzed at a constant current of 20 mA under air at room temperature for 4 h. After the reaction was completed, the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel to afford the desired pure product **3a**.

3-(Trifluoromethyl)quinoxalin-2-ol (**3a**): Yellow solid, m.p. 181～182 ℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 13.05 (s, 1H), 7.90 (dd, J=8.1, 0.9 Hz, 1H), 7.75～7.67 (m, 1H), 7.44～7.35 (m, 2H); ^{13}C NMR (151 MHz, DMSO-d_6) δ: 152.11, 134.11, 133.93, 130.31 (d, J=5.0 Hz), 124.62, 121.40, 119.57, 116.29; ^{19}F NMR (377 MHz, DMSO) δ: −68.52. HRMS (Thermo Q Exactive) calcd for $C_9H_6F_3N_2O$ $[M+H]^+$ 215.0427, found 215.0425.

1-Ethyl-3-(trifluoromethyl)quinoxalin-2(1*H*)-one (**3b**): Light yellow solid, m.p. 97～98 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.01 (dd, J=8.1, 1.4 Hz, 1H), 7.73 (ddd, J=8.6, 7.4, 1.5 Hz, 1H), 7.46～7.40 (m, 2H), 4.38 (q, J=7.2 Hz, 2H), 1.42 (t, J=7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 166.32, 151.14, 143.82 (d, J=34.5 Hz), 133.78, 133.63, 132.05, 130.98, 124.74, 120.62, 118.79, 113.51, 62.38, 43.38, 14.05; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −69.99. HRMS (Thermo Q Exactive) calcd for $C_{11}H_{10}F_3N_2O$ $[M+H]^+$ 243.0740, found 243.0739.

1-Hexyl-3-(trifluoromethyl)quinoxalin-2(1*H*)-one (**3c**): Red oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.00 (dd, J=8.1, 1.3 Hz, 1H), 7.75～7.68 (m, 1H), 7.45～7.41 (m, 1H), 7.39 (d, J=8.5 Hz, 1H), 4.30～4.25 (m, 2H), 1.78 (dt, J=15.7, 7.7 Hz, 2H), 1.51～1.44 (m, 2H), 1.36 (ddd, J=10.1, 6.5, 3.0 Hz, 4H), 0.90 (t, J=7.1 Hz, 3H); ^{13}C NMR (151 MHz, CDCl3) δ: 151.31, 143.88 (d, J=34.0 Hz), 133.87, 133.34, 131.95, 131.16, 124.21, 113.95, 42.63, 31.33, 27.14, 26.59, 22.48, 13.94; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −70.03 (s). HRMS (Thermo Q Exactive) calcd for $C_{15}H_{18}F_3N_2O$ $[M+H]^+$ 299.1293, found 299.1290.

1-Butyl-3-(trifluoromethyl)quinoxalin-2(1*H*)-one (**3d**): Light yellow solid, m.p. 68～69 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.00 (dd, J=8.1, 1.2 Hz, 1H), 7.74～7.69 (m, 1H), 7.45～7.41 (m, 1H), 7.40 (d, J=8.5 Hz, 1H), 4.33～4.25 (m, 2H), 1.77 (tt, J=7.9, 6.7 Hz, 2H), 1.55～1.47 (m, 2H), 1.02 (t, J=7.4 Hz, 3H); ^{13}C NMR (151 MHz, CDCl3) δ: 151.34, 143.89(d, J=34.1 Hz), 143.78, 133.88, 133.33, 131.97, 131.17, 124.22, 120.83, 119.00, 113.96, 42.39, 29.21, 20.23, 13.67; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −70.04; ^{19}F NMR (377 MHz, CDCl3) δ: −62.74, −69.92. HRMS (Thermo Q Exactive) calcd for $C_{13}H_{14}F_3N_2O$ $[M+H]^+$ 271.1053, found 271.1049.

Ethyl 2-(2-*oxo*-3-(trifluoromethyl)quinoxalin-1(2*H*)-yl)-acetate (**3e**): White solid, m.p. 130～131 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.02 (dd, J=8.0, 1.4 Hz, 1H), 7.70 (ddd, J=8.6, 7.5, 1.5 Hz, 1H), 7.48～7.43 (m, 1H), 7.16 (d, J=8.5 Hz, 1H), 5.07 (d, J=4.6 Hz, 2H), 4.27 (q, J=7.1 Hz, 2H), 1.29 (t, J=7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 166.32, 151.14, 143.82 (d, J=34.3 Hz), 133.78, 133.63, 132.05, 130.98, 124.74, 122.46, 120.62, 118.79, 113.51,

62.38, 43.38, 14.05; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −69.99; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −63.05, −70.19. HRMS (Thermo Q Exactive) calcd for $C_{13}H_{12}F_3N_2O_3$ $[M+H]^+$ 301.0795, found 301.0792.

1-Benzyl-3-(trifluoromethyl)quinoxalin-2(1*H*)-one (**3f**): Light yellow solid, m.p. 114～115 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.03～7.98 (m, 1H), 7.63～7.58 (m, 1H), 7.42～7.38 (m, 1H), 7.38～7.32 (m, 3H), 7.31～7.27 (m, 3H), 5.54 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 151.73, 144.07 (d, J=34.1 Hz), 134.43, 133.99, 133.44, 131.87, 131.18, 129.08, 128.06, 127.03, 124.51, 120.81, 118.98, 114.78, 46.04; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −69.91. HRMS (Thermo Q Exactive) calcd for $C_{16}H_{12}F_3N_2O$ $[M+H]^+$ 305.0896, found 305.0894.

1-(4-Methylbenzyl)-3-(trifluoromethyl)quinoxalin-2(1*H*)- one (**3g**): Light yellow solid, m.p. 145～146 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.03～7.96 (m, 1H), 7.64～7.57 (m, 1H), 7.40 (dd, J=11.6, 4.5 Hz, 2H), 7.18 (d, J=8.1 Hz, 2H), 7.14 (d, J=8.0 Hz, 2H), 5.49 (s, 2H), 2.31 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 151.74, 137.88, 134.02, 133.39, 131.83, 131.43, 131.18, 129.72, 127.08, 124.44, 114.81, 45.84, 21.07; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −69.92. HRMS (Thermo Q Exactive) calcd for $C_{17}H_{14}F_3N_2O$ $[M+H]^+$ 317.0907, found 317.0910.

4-((2-*oxo*-3-(Trifluoromethyl)quinoxalin-1(2*H*)-yl)-methyl)benzonitrile (**3h**): Light yellow solid, m.p. 198～199 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.04 (dd, J=8.0, 1.3 Hz, 1H), 7.63 (dd, J=13.4, 4.9 Hz, 3H), 7.48～7.42 (m, 1H), 7.38 (d, J=8.2 Hz, 2H), 7.23 (d, J=8.4 Hz, 1H), 5.57 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 151.55, 143.06 (d, J=34.2 Hz), 139.67, 133.73, 133.59, 132.91, 132.24, 131.18, 127.72, 124.95, 120.65, 118.82, 118.16, 114.18, 112.25, 45.66; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −69.91. HRMS (Thermo Q Exactive) calcd for $C_{17}H_{11}F_3N_3O$ $[M+H]^+$ 328.0703, found 328.0710.

3-(Trifluoromethyl)-1-(4-(trifluoromethyl)benzyl)quinoxalin-2(1*H*)-one (**3i**): White solid, m.p. 121～122 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.03 (dd, J=8.1, 1.4 Hz, 1H), 7.65～7.58 (m, 3H), 7.45～7.42 (m, 1H), 7.39 (d, J=8.1 Hz, 2H), 7.29～7.26 (m, 1H), 5.58 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 151.61, 144.07 (d, J=34.1 Hz), 138.39, 133.69 (d, J=8.7 Hz), 132.12, 131.18, 130.88, 130.58, 130.36, 128.81, 127.35, 126.11 (q, J=3.7 Hz), 124.81, 124.67, 122.87, 120.71, 118.88, 114.37, 45.61; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −62.74, −69.92. HRMS (Thermo Q Exactive) calcd for $C_{17}H_{11}F_6N_2O$ $[M+H]^+$ 371.0625, found 371.0627.

1-(2-Fluorobenzyl)-3-(trifluoromethyl)quinoxalin-2(1*H*)-one (**3j**): Light yellow solid, m.p. 107～108 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.01 (dd, J=8.1, 1.3 Hz, 1H), 7.66～7.62 (m, 1H), 7.44～7.40 (m, 1H), 7.37 (d, J=8.5 Hz, 1H), 7.29 (dd, J=11.4, 4.2 Hz, 1H), 7.15～7.10 (m, 2H), 7.09～7.04 (m, 1H), 5.59 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 161.07, 159.44, 151.88, 133.67, 131.92, 131.15, 129.91 (d, J=8.2 Hz), 128.86 (d, J=3.3 Hz), 124.90 (d, J=3.6 Hz), 124.67 (s), 121.57 (d, J=13.5 Hz), 120.77, 118.93, 115.74, 115.60, 114.37 (d, J=3.1 Hz), 109.99, 39.40 (d, J=5.1 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ: −69.94, −118.13. HRMS (Thermo Q Exactive) calcd for $C_{16}H_{11}F_4N_2O$ $[M+H]^+$ 323.0802, found 323.0804.

1-Benzyl-6-fluoro-3-(trifluoromethyl)quinoxalin-2(1*H*)-one (**3k**): Yellow solid, m.p. 161～162 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.99 (dd, J=8.9, 5.9 Hz, 1H), 7.36 (t, J=7.3 Hz, 2H), 7.31 (t, J=7.3 Hz, 1H), 7.29～7.26 (m, 2H), 7.12 (td, J=8.9, 2.5 Hz, 1H), 7.03 (dd, J=9.9, 2.5 Hz, 1H), 5.47 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 166.05, 164.36, 151.58, 135.81 (d, J=12.0 Hz), 134.15 (d, J=11.1 Hz), 133.82, 129.23, 128.30, 127.98, 127.20, 127.03, 120.74, 118.91, 112.95 (d, J=24.0 Hz), 101.78 (d, J=28.3 Hz), 46.38; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −69.87, −100.93. HRMS (Thermo Q Exactive) calcd for $C_{16}H_{11}F_4N_2O$ $[M+H]^+$ 323.0802, found 323.0802.

1-Benzyl-3,6-bis(trifluoromethyl)quinoxalin-2(1*H*)-one (**3l**): Yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.11 (t, J=7.3 Hz, 1H), 7.64 (s, 1H), 7.61 (dd, J=7.5, 6.1 Hz, 1H), 7.3～7.33 (m, 2H), 7.30 (dq, J=13.9, 7.0 Hz, 3H), 5.53 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 151.32, 134.56(d, J=33.7 Hz), 133.87(d, J=26.65 Hz), 132.72, 129.30, 128.48, 127.25, 120.91 (d, J=3.5 Hz), 112.22 (d, J=4.2 Hz), 109.99, 46.32; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −63.05, −70.19. HRMS (Thermo Q Exactive) calcd for $C_{17}H_{11}F_6N_2O$ $[M+H]^+$ 373.0770, found373.0764 .

1-Benzyl-6-nitro-3-(trifluoromethyl)quinoxalin-2(1*H*)-one (**3m**): Red oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.88 (d, J=2.6 Hz, 1H), 8.42 (dd, J=9.3, 2.6 Hz, 1H), 7.48 (d, J=9.3 Hz, 1H), 7.39～7.35 (m, 2H), 7.34～7.31 (m, 1H), 7.26 (d, J=5.8 Hz, 2H), 5.56 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 151.18, 138.20, 133.38, 130.88, 130.18, 129.39, 128.81, 128.59, 127.48 (d, J=3.9 Hz), 126.92, 115.67, 46.65; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −70.21. HRMS (Thermo Q Exactive) calcd for $C_{16}H_{11}F_3N_3O_3$ $[M+H]^+$ 350.0747, found 350.0744.

Methyl 1-benzyl-2-oxo-3-(trifluoromethyl)-1,2-dihydroquinoxaline-6-carboxylate (**3n**): White solid, m.p. 195～196 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.67 (d, J=1.9 Hz, 1H), 8.23 (dd, J=8.9, 1.9 Hz, 1H), 7.41 (d, J=8.9 Hz, 1H), 7.34 (t, J=7.3 Hz, 2H), 7.30 (dd, J=8.6, 5.9 Hz, 1H), 7.26 (d, J=5.8 Hz, 2H), 5.54 (s, 2H), 3.95 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 165.24, 151.54, 145.10 (q, J=74.3 Hz), 136.99, 133.90 (d, J=11.5 Hz), 133.61 (s), 130.51, 129.20, 128.29, 127.01, 126.55, 120.54, 118.71, 114.92, 52.56, 46.29, 29.69; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −70.07. HRMS (Thermo Q Exactive) calcd for $C_{18}H_{14}F_3N_2O_3$ $[M+H]^+$ 363.0951, found 363.0949.

1-Benzyl-6,7-difluoro-3-(trifluoromethyl)quinoxalin-2(1*H*)-one (**3o**): Yellow solid, m.p. 105～106 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.82 (dd, J=9.5, 8.2 Hz, 1H), 7.39～7.35 (m, 2H), 7.35～7.31 (m, 1H), 7.26～7.24 (m, 2H), 7.17～7.12 (m, 1H), 5.47 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 151.26, 133.56, 129.35, 128.46, 126.94, 119.28 (dd, J=18.1, 2.8 Hz), 118.70), 109.99, 103.58, 103.43, 46.65; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −70.03 (s), −123.71～−124.13 (m), −139.28 (dt, J=15.8, 7.6 Hz). HRMS (Thermo Q Exactive) calcd for $C_{16}H_{10}F_5N_2O$

$[M+H]^+$ 341.0708, found 341.0706.

1-Benzyl-6,7-dichloro-3-(trifluoromethyl)quinoxalin-2(1*H*)-one (**3p**): Yellow solid, m.p. 183～184 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.09 (s, 1H), 7.46 (s, 1H), 7.37 (t, J=7.4 Hz, 2H), 7.32 (t, J=7.2 Hz, 1H), 7.26 (t, J=3.7 Hz, 2H), 5.46 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 151.08, 138.11, 133.59, 133.17, 132.40, 130.04, 129.34, 128.79, 128.46, 127.01, 120.43, 118.59, 116.23, 46.35; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −70.04. HRMS (Thermo Q Exactive) calcd for $C_{16}H_{10}Cl_2F_3N_2O$ $[M+H]^+$ 373.0117, found 373.0122.

1-Benzyl-6,7-dimethyl-3-(trifluoromethyl)quinoxalin-2(1*H*)-one (**3q**): Light yellow solid, m.p. 188～189 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.74 (s, 1H), 7.33 (t, J=7.3 Hz, 2H), 7.30～7.26 (m, 3H), 7.12 (s, 1H), 5.50 (s, 2H), 2.35 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 151.85, 144.17, 134.69, 133.86, 132.16, 131.61, 129.71, 129.03, 127.93, 127.02, 115.07, 45.86, 21.00, 19.10; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −69.71. HRMS (Thermo Q Exactive) calcd for $C_{18}H_{16}F_3N_2O$ $[M+H]^+$ 333.1209, found 333.1210.

6-Methyl-3-(trifluoromethyl)quinoxalin-2(1*H*)-one (**3r**) and 7-methyl-3-(trifluoromethyl)quinoxalin-2(1*H*)-one (**3r'**): Light yellow solid, m.p. 193～194 ℃; ^{1}H NMR (600 MHz, DMSO-d_6, **3r**) δ: 13.00 (s, 1H), 7.79 (d, J=8.3 Hz, 1H), 7.24 (d, J=8.3 Hz, 1H), 7.17 (s, 1H), 2.45 (s, 3H); ^{1}H NMR (600 MHz, DMSO-d_6, **3r'**) δ: 13.00 (s, 1H), 7.72 (s, 1H), 7.56 (d, J=8.6 Hz, 1H), 7.30 (d, J=8.4 Hz, 1H), 2.40 (s, 1H); ^{13}C NMR (151 MHz, DMSO-d_6) δ: 152.27, 144.88, 135.28, 134.14, 130.03, 129.62, 128.67, 126.19, 121.55, 115.99, 115.70, 109.99, 21.98, 20.68; ^{19}F NMR (377 MHz, DMSO-d_6) δ: −62.74, −69.92. HRMS (Thermo Q Exactive) calcd for $C_{10}H_8F_3N_2O$ $[M+H]^+$ 229.0583, found 229.0581.

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Supporting Information Experimental procedures, full spectroscopic data for **3**. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn/.

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