One-Pot Synthesis of Pyrrolo[1,2-c]quinazolinone Derivatives

Matija Petrovčić, Marija Alešković, Kata Mlinarić-Majerski*

Department of Organic Chemistry and Biochemistry, Ruđer Bošković Institute, Bijenička Cesta 54, 10 000 Zagreb, Croatia Fax +385(1)4680195; E-mail: majerski@irb.hr

Received: 25.07.2014; Accepted after revision: 29.08.2014

Abstract: A fast and simple one-pot synthesis of pyrrolo[1,2-*c*]quinazolinones is reported. The tandem Suzuki coupling of *N*-Bocpyrrol-2-yl boronic acid and *ortho*-substituted aminoaryl halogenides with subsequent cyclization of the third ring yields a variety of pyrroloquinazolinone scaffolds in good to moderate yields. The palladium-catalyzed cross-coupling reaction is applicable to a wide range of substituted aminoaryl halogenides.

Key words: pyrrolo[1,2-*c*]quinazolinones, Suzuki coupling, palladium catalysis, tandem reaction, heterocycles

Quinazolines and quinazolinones are common structural motifs found in naturally occurring heterocycles.¹ They are also relevant pharmacophores in medicinal chemistry due to their diverse biological activities such as anti-inflammatory, diuretic, and anticonvulsant properties.² Furthermore, annulation of a pyrrole ring resulting in the structures, such as pyrrolo[1,2-c]quinazolinone, pyrrolo[1,2-c]quinazoline, and pyrrolo[3,2-c]quinoline, leads to additional biological effects, including antihypertensive, cytotoxic, antiviral, antimalarial, and antibacterial properties.³ Despite these interesting activities, to date only a few examples of the pyrrolo[1,2-c]quinazolinone synthesis are known in the literature. They usually involve multistep synthetic procedures with tedious isolation of intermediate compounds. Cotter et al. published a synthesis of 7-hydroxy-2-methylpyrrolo[1,2-c]quinazolinone starting from 2-amino-3-hydroxyacetophenone in three reaction steps.⁴ Later, Bandurco et al. synthesized a series of substituted pyrrolo[1,2-*c*]quinazolinones in extremely variable yields by condensing the appropriate quinazolinone with α -haloketones.^{3a} Two pyrrolo[1,2-*c*]quinazolinone derivatives were prepared from acetylindole in eight reaction steps and were analyzed by X-ray diffraction.⁵ In addition, a pyrrolo[1,2-*c*]quinazolinone derivative was isolated as an intermediate in the synthesis of tricyclic guanidines⁶ or via tandem aza-Wittig–carbodiimide electrocyclization, wherein a key step for the formation of the third ring is a TBAF-promoted intramolecular cyclization.⁷ Recently, Lubell and Dörr published a synthesis of various pyrrolo[1,2-*c*]quinazolinones in five steps starting from *N*-(Boc)anthranilate.⁸

Although it is known that the amino group electronically deactivates the C–Br bond in the oxidative addition to the palladium catalyst,⁹ there are examples of direct Suzuki coupling in the preparation of biaryls and heteroaryls bearing an unprotected NH₂ group.¹⁰ However, to the best of our knowledge, palladium-catalyzed coupling reaction of pyrroles and *ortho*-substituted anilines has not been reported to date.

We have shown that the Suzuki reaction between various *ortho*-substituted arylhalides and *N*-Boc-pyrrol-2-yl boronic acid gives 2-[(2-substituted)phenyl]pyrrole derivatives, and we found that *o*-bromoaniline under the same reaction conditions yields pyrrolo[1,2-c]quinazolinone **1** as a product of cross-coupling reaction followed by intra-



Scheme 1

SYNLETT 2014, 25, 2769–2772 Advanced online publication: 07.10.2014 DOI: 10.1055/s-0034-1379183; Art ID: st-2014-d0627-l © Georg Thieme Verlag Stuttgart · New York molecular cyclization.¹¹ Herein, we demonstrate that the above-mentioned one-pot tandem reaction can be applied to the preparation of a series of new pyrrolo[1,2-c]quinazolinones **1–10** (Scheme 1). The results of the employed tandem reactions are presented in Table 1.

 Table 1
 Synthesis of Quinazolinones 1–10 via Suzuki Coupling Reaction and Intramolecular Cyclization Sequence^a

Entry	Aniline	Isolated compounds		
		Recovered aniline (%)	Yield of 1–10 (%)	Yield of 1a–10a (%)
1	12a	21	1 27	1a 22
2	12b	25	2 37	
3	12c	25	3 31	3a 4
4	12d	37	4 29	
5	12e	11	5 23	5a 3
6	12f	35	6 22	
7	12g	15	7 11	7a 8 ^b
8	12h	53	8 11°	8a 7 ^d
9	12i	_	9 80	
10	12j	-	10 38	

^a Isolated yield.

^b Isolated with 10% of impurities.

^c In mixture with **8a**.

^d In mixture with 8.

The best yields were achieved when the reaction was conducted with 5 mol% of Pd(PPh₃)₄ in a 10:1 mixture of toluene and methanol with Cs₂CO₃ as a base.¹² In all experiments, except entries 9 and 10 (Table 1), some starting aniline was recovered together with the quinazolinone product. However, in entries 1, 3, 5, 7, and 8 (Table 1), besides the quinazolinone product and the recovered aniline, the cross-coupling products **1a**, **3a**, **5a**, **7a**, and **8a**, respectively, were formed. Furthermore, in entries 1 and 2 (Table 1) traces of di-*tert*-butyl 1*H*,1'*H*-2,2'-bipyrrole-1,1'dicarboxylate (**13**)¹³ were detected.

The formation of 1–10 involves a palladium-catalyzed cross-coupling reaction between 11 and 12, the formation of intermediates I_1-I_{10} , and subsequent nucleophilic attack of the amino group to the Boc-carbonyl (Scheme 1). Formation of compounds 1a-10a is the result of the Boc deprotection of the intermediate compounds I_1-I_{10} under the basic reaction conditions.¹⁴ Moreover, since the reaction is carried out in refluxing toluene, thermal deprotection is also possible.¹⁵ On the other hand, the byproduct bipyrrole 13 results from a competitive homocoupling reaction that uses up the starting boronic acid 11. To minimize the formation of the byproduct 13, the addition time of 11 to the refluxing reaction mixture was extended to seven hours, with subsequent refluxing for another 17 hours.

Formation of the Boc-protected intermediate through the cross-coupling reaction is most probably the slowest step. The yields of the tandem process vary from moderate to good. Cross-coupling reactions of arylhalogenides substituted with electron-donating groups gave tricyclic products in moderate yields (Table 1, entries 2-4), and in one example, the cross-coupled product that had not undergone the cyclization step was also isolated (Table 1, entry 3). Since its formation was not observed in all cases it is obvious that the electron-donating substituent on the aniline increases the nucleophilicity of the amine and thus helps the cyclization step to occur. On the other hand, in the reactions with electron-withdrawing substituents, that should facilitate the oxidative addition of palladium¹⁶ and enhance yields, it was not observed (Table 1, entries 5-10). However, it is known that very strong electron-withdrawing substituents may enhance the acidity and coordination of the amine group to the palladium catalyst, preventing the oxidative addition and resulting in a lower yield of cross-coupling reaction.^{9,16} Therefore, in the reactions conducted with dihalogen-substituted anilines the vields were very different (Table 1, entries 9 and 10). Thus, in the reaction with 2-bromo-5-chloro-3-fluoroaniline (12i) we isolated 80% of the tricylic product; whereas in the reaction with 2-bromo-3,5-difluoroaniline (12j) it dropped to a moderate yield of 38%. The rather poor yields observed in the cross-coupling reactions with nitro anilines 12e and 12f could be explained by solubility problems (Table 1, entries 5 and 6). During the workup of the reaction in entries 5, 6, and 8 (Table 1), a fine emulsion was formed, resulting in difficulties in isolation of the products.

In conclusion, we have shown that the palladium-catalyzed coupling of *o*-bromoaniline and *N*-Boc-pyrrol-2-yl boronic acid can be applied for the one-pot preparation of a series of pyrrolo[1,2-c]quinazolinones **1–10**. The reaction employs commercially available pyrrole boronic acid and various *o*-bromoanilines, with both electron-withdrawing and electron-donating groups. However, a direct correlation with respect to the substituent influence on cross-coupling and/or cyclization reaction cannot be made. The application of these tandem reactions for the construction of the pyrrolobenzodiazocine or pyrrolobenzodiazepinone derivatives is under current investigation.

Acknowledgment

We thank the Ministry of Science Education and Sports of the Republic of Croatia (grant No. 098-0982933-2911, KMM) and the Croatian Academy of Sciences and Arts (grant awarded to M.A.) for financial support. The authors also thank Dr. N. Basarić for helpful discussion.

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(12) General Procedure

To a stirred solution of the corresponding aniline (1 mmol), Cs_2CO_3 (2 mmol), and Pd(PPh₃)₄ (5 mol%) in toluene (20 mL) at reflux and under nitrogen atmosphere, a solution of *N*-Boc-pyrrol-2-yl boronic acid¹⁷ (1 mmol) in a mixture of toluene (10 mL) and MeOH (3 mL) was added over 7 h. The mixture was stirred at reflux for 17 h, cooled, and the MeOH was removed under reduced pressure. To the resultant toluene suspension H₂O (30 mL) was added, and the layers were separated. The water layer was extracted with CH₂Cl₂ (3 × 25 mL; or EtOAc for compound **5**), the combined organic extracts were washed with H₂O (30 mL), dried over MgSO₄, filtered, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel using a suitable eluent as indicated below.

Pyrrolo[1,2-*c*]quinazolin-5(6*H*)-one (1) and 2-(1*H*-Pyrrol-2-yl)aniline (1a)¹¹

Purified by chromatography with a mixture of *n*-hexane– Et_2O (3:2).

Analytical Data

Compound 1: grey powder. ¹H NMR (300 MHz, DMSO- d_6): $\delta = 6.67$ (t, J = 3.3 Hz, 1 H), 7.01 (dd, $J_1 = 3.5$ Hz, $J_2 = 1.5$ Hz, 1 H), 7.18–7.36 (m, 3 H), 7.59 (dd, $J_1 = 3.1$ Hz, $J_2 = 1.5$ Hz, 1 H), 7.89–7.92 (m, 1 H), 11.48 (br s, 1 H). Compound **1a**: white crystals. ¹H NMR (600 MHz, CDCl₃): $\delta = 3.94$ (s, 2 H), 6.30–6.33 (m, 1 H), 6.40–6.44 (m, 1 H), 6.75–6.77 (m, 1 H), 6.79–6.83 (m, 1 H), 6.85–6.87 (m, 1 H), 7.06–7.10 (m, 1 H), 7.24 (s, 1 H), 8.58 (br s, 1 H). **9-Methylpyrrolo[1,2-c]quinazolin-5(6H)-one (2)** Purified by chromatography with a mixture CH₂Cl₂–MeOH (98:2). Fractions were rechromatographed using 0 \rightarrow 35% Et₂O in CH₂Cl₂ as eluent to obtain analytically pure **2**. **Analytical Data** Grey powder; mp 255–258 °C; IR (KBr): v = 2921, 1701,

Grey powder; mp 255–258 °C; IR (KBr): v = 2921, 1/01, 1508, 1411, 721 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 2.35$ (s, 3 H), 6.66 (t, J = 3.3 Hz, 1 H), 6.97 (dd, $J_1 = 3.5$ Hz, $J_2 =$ 1.5 Hz, 1 H), 7.13–7.16 (m, 2 H), 7.58 (dd, $J_1 = 3.0$ Hz, $J_2 =$ 1.5 Hz, 1 H), 7.73 (s, 1 H), 11.40 (br s, 1 H). ¹³C NMR (75 MHz, CDCl₃): $\delta = 20.5$ (CH₃), 104.3 (CH), 113.7 (CH), 114.1 (C), 115.3 (CH), 115.4 (CH), 122.0 (CH), 128.8 (CH), 129.2 (C), 130.3 (C), 132.1 (C), 145.4 (C). HRMS: m/z [M]⁺ calcd for C₁₂H₁₀N₂O: 198.0788; found: 198.0788. **9-Isopropylpyrrolo[1,2-***c***]quinazolin-5(6***H***)-one (3) and**

4-Isopropyl-2-(1*H***-pyrrol-2-yl)aniline (3a)**

Purified by chromatography with a mixture CH_2Cl_2 –MeOH (99:1). Fractions were rechromatographed using CH_2Cl_2 – Et_2O (7:3) as eluent to obtain analytically pure compounds. **Analytical Data**

Compound **3**: grey powder; mp 170–173 °C. IR (KBr): v = 2954, 1701, 1508, 1407, 715 cm⁻¹. ¹H NMR (300 MHz, DMSO- d_6): $\delta = 1.23$ (s, 3 H), 1.26 (s, 3 H), 2.94 (sept, J = 6.9 Hz, 1 H), 6.66 (t, J = 3.3 Hz, 1 H), 7.03 (dd, $J_1 = 3.5$ Hz, $J_2 = 1.5$ Hz, 1 H), 7.15–7.24 (m, 2 H), 7.57 (dd, $J_1 = 3.0$ Hz, $J_2 = 1.5$ Hz, 1 H), 7.76–7.78 (m, 1 H), 11.40 (br s, 1 H). ¹³C NMR (75 MHz, DMSO- d_6): $\delta = 23.9$, 33.1, 104.3, 113.7, 114.2, 115.3, 115.5, 119.4, 125.9, 129.4, 130.7, 143.3, 145.5. HRMS: m/z [M]⁺ calcd for C₁₄H₁₄N₂O: 226.11; found: 226.1101.

Compound **3a**: white crystals; mp 90–91 °C. IR (KBr): $v = 3384, 3305, 3178, 2962, 1500, 825, 725 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): <math>\delta = 1.21$ (s, 3 H), 1.23 (s, 3 H), 2.82 (sept, J = 6.9 Hz, 1 H), 3.81 (br s, 2 H), 6.31 (dd, $J_1 = 5.8$ Hz, $J_2 = 2.8$ Hz, 1 H), 6.39–6.45 (m, 1 H), 6.71 (d, J = 8.2 Hz, 1 H), 6.84–6.88 (m, 1 H), 6.96 (dd, $J_1 = 2.2$ Hz, $J_2 = 8.2$ Hz, 1 H), 7.11 (d, J = 2.2 Hz, 1 H), 8.68 (br s, 1 H). ¹³C NMR (75 MHz, CDCl₃): $\delta = 24.1$ (2 × CH₃), 33.2 (CH), 107.2 (CH), 109.2 (CH), 116.7 (CH), 117.7 (CH), 119.6 (C), 125.7 (CH), 126.3 (CH), 129.9 (C), 139.7 (C), 140.9 (C). HRMS: m/z [M]⁺ calcd for C₁₃H₁₆N₂: 200.1308; found: 200.1311. **7,9-Dimethylpyrrolo[1,2-c]quinazolin-5(6H)-one (4)** Purified by chromatography with a mixture CH₂Cl₂–Et₂O (7:3).

Analytical Data

Grey powder; mp 254–256 °C. IR (KBr): v = 3224, 2916, 1689, 1498, 1348, 719 cm⁻¹. ¹H NMR (300 MHz, DMSO d_6): $\delta = 2.30$ (s, 3 H), 2.37 (s, 3 H), 6.65 (t, J = 3.3 Hz, 1 H), 6.94 (dd, $J_1 = 3.5$ Hz, $J_2 = 1.5$ Hz, 1 H), 6.98 (s, 1 H), 7.56– 7.59 (m, 2 H), 10.55 (br s, 1 H). ¹³C NMR (75 MHz, DMSO d_6): $\delta = 17.5$ (CH₃), 20.4 (CH₃), 104.1 (CH), 113.9 (CH), 114.2 (C), 115.2 (CH), 119.9 (CH), 123.9 (C), 128.7 (C), 129.4 (C), 130.1 (CH), 131.8 (C), 145.8 (C). HRMS: m/z[M]⁺ calcd for C₁₃H₁₂N₂O: 212.0944; found: 212.0936. **8-Nitropyrrolo[1,2-c]quinazolin-5(6H)-one (5) and 5-Nitro-2-(1H-pyrrol-2-yl)aniline (5a)**

The general workup procedure was slightly changed because of solubility problems. In this case, product **5a** was extracted from the water layer with CH_2Cl_2 and **5** with EtOAc. Chromatography with a mixture CH_2Cl_2 –MeOH (99:1) furnished analytically pure **5a** and chromatography with a mixture CH_2Cl_2 –EtOAc (9:1) furnished pure **5**.

Analytical Data

Compound 5: yellow crystals; mp 312-313 °C. IR (KBr): v = 3255, 1720, 1521, 1340, 723 cm⁻¹. ¹H NMR (300 MHz, DMSO- d_6): $\delta = 6.78 (dd, J_1 = 3.1 Hz, J_2 = 3.6 Hz, 1 H), 7.30$ $(dd, J_1 = 3.6 Hz, J_2 = 1.5 Hz, 1 H), 7.74 (dd, J_1 = 3.1 Hz, J_2)$ = 1.5 Hz, 1 H), 8.01 (dd, $J_1 = 8.7$ Hz, $J_2 = 2.2$ Hz, 1 H), 8.06-8.08 (m, 1 H), 8.14 (d, J = 8.7 Hz, 1 H), 11.87 (br s, 1 H).¹³C NMR (75 MHz, DMSO- d_6): $\delta = 108.6, 110.7, 114.7, 117.8,$ 117.9, 119.8, 122.9, 127.6, 132.6, 145.0, 145.4. HRMS: m/z $[M + H]^+$ calcd for $C_{11}H_8N_3O_3$: 230.0561; found: 230.0565. Compound **5a**: red crystals; mp 159–161 °C. IR (KBr): v =3392, 1618, 1514, 1336, 877, 744 cm⁻¹. ¹H NMR (600 MHz, DMSO- d_6): $\delta = 5.57$ (s, 2 H), 6.21–6.23 (m, 1 H), 6.57–6.60 (m, 1 H), 6.94–6.96 (m, 1 H), 7.41–7.46 (m, 2 H), 7.65 (d, J = 2.2 Hz, 1 H), 11.27 (s, 1 H). ¹³C NMR (150 MHz, DMSO d_6): $\delta = 108.9, 109.1, 109.3, 111.1, 120.2, 124.2, 127.0,$ 127.5, 145.1; 145.6. HRMS: *m*/*z* [M]⁺ calcd for C₁₀H₉N₃O₂: 203.0688; found: 203.0691.

7,9-Dinitropyrrolo[**1,2-***c*]**quinazolin-5(***6H***)-one (6)** Purified by chromatography with CH₂Cl₂

Analytical Data

Orange crystals; mp 291–293 °C. IR (KBr): $v = 3436, 3257, 1718, 1612, 1529, 1307, 750 \text{ cm}^{-1}.$ ¹H NMR (300 MHz, DMSO- d_6): $\delta = 6.83$ (t, J = 3.3 Hz, 1 H), 7.58 (dd, $J_1 = 3.6$ Hz, $J_2 = 1.5$ Hz, 1 H), 7.77 (dd, $J_1 = 3.0$ Hz, $J_2 = 1.5$ Hz, 1 H), 9.14 (d, J = 2.4 Hz, 1 H), 11.18 (br s, 1 H). ¹³C NMR (75 MHz, DMSO- d_6): $\delta = 109.4$ (CH), 115.3 (CH), 117.8 (CH), 117.9 (C), 118.5 (CH), 122.2 (CH), 126.4 (C), 131.0 (C), 134.6 (C), 141.4 (C), 143.9 (C). HRMS: m/z [M]⁺ calcd for C₁₁H₆N₄O₅: 274.0338; found: 274.0333.

8-Chloropyrrolo[1,2-*c*]quinazolin-5(6*H*)-one (7) and 5-Chloro-2-(1*H*-pyrrol-2-yl)aniline (7a)

Purified by chromatography with a CH₂Cl₂-EtOAc (96:4). Analytical Data

Compound 7: dark grey powder; mp 257–259 °C. IR (KBr): $v = 2360, 1710, 1587, 1409, 721 \text{ cm}^{-1}.$ ¹H NMR (300 MHz, DMSO- d_6): $\delta = 6.69$ (t, J = 3.3 Hz, 1 H), 7.05 (dd, $J_1 = 3.5 \text{ Hz}, J_2 = 1.5 \text{ Hz}, 1 \text{ H}$), 7.22–7.27 (m, 2 H), 7.60 (dd, $J_1 = 3.1 \text{ Hz}, J_2 = 1.5 \text{ Hz}, 1 \text{ H}$), 7.95 (d, J = 8.2 Hz, 1 H), 11.57 (br s, 1 H). ¹³C NMR (75 MHz, DMSO- d_6): $\delta = 105.2$ (CH), 113.3 (C), 114.0 (CH), 114.8 (CH), 115.9 (CH), 122.9 (CH), 123.9 (CH), 128.3 (C), 131.2 (C), 133.6 (C), 145.2 (C). HRMS: m/z [M]⁺ calcd for C₁₁H₇ClN₂O: 218.0242; found: 218.0249. 7-Chloro-9-nitropyrrolo[1,2-*c*]quinazolin-5(6*H*)-one (8) and 2-Chloro-4-nitro-6-(1*H*-pyrrol-2-yl)aniline (8a)

Separation of products **8** and **8a** was unsuccessful even after several repeated chromatography. The yields were estimated from ¹H NMR spectroscopic analysis of the mixture of **8** (11%) and **8a** (8%).

7-(Chloro-9-fluoropyrrolo[1,2-*c*]quinazolin-5(6*H*)-one (9)

Purified by chromatography with CH₂Cl₂.

Analytical Data

White crystals; mp 236–238 °C. IR (KBr): v = 3247, 1698, 1573, 1499, 724 cm⁻¹. ¹H NMR (300 MHz, DMSO- d_6): $\delta = 6.73$ (t, J = 3.3 Hz, 1 H), 7.17 (dd, $J_1 = 3.6$ Hz, $J_2 = 1.5$ Hz, 1 H), 7.44 (dd, $J_{1(HF)} = 8.5$ Hz, $J_2 = 2.7$ Hz, 1 H), 7.67 (dd, $J_1 = 3.1$ Hz, $J_2 = 1.5$ Hz, 1 H), 7.87 (dd, $J_{1(HF)} = 9.1$ Hz, $J_2 = 2.7$ Hz, 1 H), 10.91 (br s, 1 H). ¹³C NMR (75 MHz, DMSO- d_6): $\delta = 107.0$ (CH), 107.4 (d, $J_{CF} = 24.6$ Hz, CH), 114.4 (CH), 115.1 (d, $J_{CF} = 27.2$ Hz, CH), 116.7 (CH), 116.7 (d, $J_{CF} = 2.2$ Hz, C), 127.6 (d, $J_{CF} = 3.5$ Hz, C), 145.0 (C), 157.2 (d, $J_{CF} = 241.6$ Hz, C). HRMS: m/z [M]⁺ calcd for C₁₁H₆CIFN₂O: 236.0153; found: 236.0148.

7,9-Difluoropyrrolo[1,2-c]quinazolin-5(6H)-one (10)

Purified by chromatography with a mixture CH_2Cl_2 –MeOH (99.5:0.5). Fractions were rechromatographed using CH_2Cl_2 –EtOAc (97:3) as eluent to obtain analytically pure **10**.

Analytical Data

White crystals; mp 270–271 °C. IR (KBr): v = 3087, 1697, 1510, 1400, 1301, 727 cm⁻¹. ¹H NMR (600 MHz, DMSOd₆): $\delta = 6.71$ (t, J = 3.3 Hz, 1 H), 7.14 (dd, $J_1 = 3.5$ Hz, $J_2 = 1.5$ Hz, 1 H), 7.26–7.30 (m, 1 H), 7.67 (dd, $J_1 = 3.0$ Hz, $J_2 = 1.5$ Hz, 1 H), 7.26–7.30 (m, 1 H), 11.56 (br s, 1 H). ¹³C NMR (150 MHz, DMSO-d₆): $\delta = 102.2$ [dd, $J_{1(CF)} = 28.2$ Hz, $J_{2(CF)} = 22.0$ Hz, CH], 103.8 [dd, $J_{1(CF)} = 24.7$ Hz, $J_{2(CF)} = 3.2$ Hz, CH], 106.7 (CH), 114.0 (CH), 116.7 [dd, $J_{1(CF)} = 11.2$ Hz, $J_{2(CF)} = 4.7$ Hz, C], 117.8 (CH), 117.8 [dd, $J_{1(CF)} = 14.2$ Hz, $J_{1(CF)} = 24.8$ Hz, C], 127.7 (t, $J_{CF} = 3.5$ Hz, C), 144.8 (C), 148.8 [dd, $J_{1(CF)} = 248.4$ Hz, $J_{2(CF)} = 13.3$ Hz, C], 156.6 [dd, $J_{1(CF)} = 240.5$ Hz, $J_{2(CF)} = 11.4$ Hz, C]. ¹⁹F NMR (565 MHz, DMSO-d₆): $\delta = -106.6$ (dt, $J_1 = 9.2$ Hz, $J_2 = 4.5$ Hz, 1 F), -114.4 (m, 1 F). HRMS: m/z [M]⁺ calcd for C₁₁H₆F₂N₂O: 220.0443; found: 220.0448.

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