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Synthesis of novel 1,2,3-triazole-containing pyridine–pyrazole amide derivatives based on one-pot click reaction and their evaluation for potent nematicidal activity against *Meloidogyne incognita*

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Abstract In order to find a novel, leading nematicide compound, a series of pyridine–pyrazole amide derivatives containing 1,2,3-triazoles were synthesized via click chemistry in a one-pot reaction. Their structures were characterized by proton nuclear magnetic resonance (^{1}H NMR), ^{13}C NMR, ^{19}F NMR and high-resolution mass spectrometry (HRMS). Preliminary bioassays showed that most of the synthesized compounds exhibited good inhibitory activity in vivo against *Meloidogyne incognita* at 25 mg L^{-1}. Among the tested compounds, **3a**, **3e**, **3f**, **3g**, **3j**, **3m**, **3q**, **3s**, **3t**, **3v** and **3w** exhibited 100 % inhibition rates. Moreover, **3k** displayed a 92.4 % inhibitory activity at 10 mg L^{-1}. This investigation suggested that this pyridine–pyrazole amide containing a 1,2,3-triazole scaffold could be further optimized to explore novel, high-bioactivity nematicidal leads.

Keywords Pyridine–pyrazole amide · 1,2,3-Triazole · Nematicide · Click chemistry

Introduction

Root-knot nematodes (RKNs) are soil worms belonging to the plant-parasitic nematodes [1] that feed on the roots of different crops such as tomato, pepper, watermelons and onions, resulting in an annual crop loss of about 100 billion US dollars around the world. RKNs have become one of the most difficult pests to control [2, 3]. Currently, nematode control is mainly achieved by two groups of

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chemical nematicides. One is the synthetic fumigant nematicides like methyl bromide; however, methyl bromide has now been withdrawn from the market in many countries due to the degradation of the ozone layer [4–6]. Another group is non-fumigant nematicides, including carbamates such as carbofuran and aldicarb, and organophosphates such as fenamiphos and fosthiazate [7]. Recently, newly developed nematicides fluensulfonne [8–10] and tioxazafen [11] were released to the market in 2011 and 2014, respectively. However, with the development of resistance and environment problems caused by carbamates and organophosphates [12, 13], the nematicides available are still limited; as such, it is urgent to develop efficacious alternatives.

Substituted pyridine–pyrazole amide is an important functional group which has been used to act on insecticide targets in ryanodine receptors [14], such as in chlorantraniliprole [15] and cyantraniliprole [16]. What's more, BASF crop science reported in 2007 that the pyridine–pyrazole amide derivative **1–1** can be used as a nematicide [17]. In our group's previous study, Li et al. [18] reported that pyridine–pyrazole amide derivative **1–2** containing a diphenylacetylene scaffold exhibited 100 and 93.9 % inhibition rates against *Meloidogyne incognita* at 25 and 10 mg L^{-1}, respectively. In this study, we tried to use this significant core structure to develop novel nematicides, and the 1,2,3-triazole structure was introduced to the target compound to derive structural diversity (Fig. 1).

In the last 10 years, an exciting development in the synthesis of 1,2,3-triazoles has been click chemistry, discovered by Sharpless [19, 20]. Enlightened by all of the intriguing reasons above, a series of novel 1,2,3-triazole-containing pyridine–pyrazole amide derivatives were designed and synthesized by click reactions (Scheme 1). Their nematicidal activities against *M. incognita* in vivo were evaluated.

Results and discussion

Synthesis

The synthesis of target compounds **3** was illustrated in Scheme 2. In the click reaction, the starting material sodium azide is hazardous and explosive. Recently, click-based, one-pot synthesis of 1,2,3-triazoles without isolation of aryl azides was

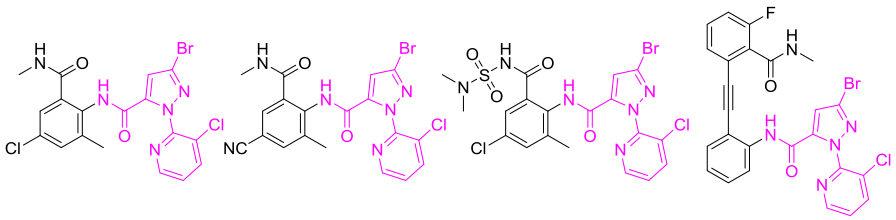
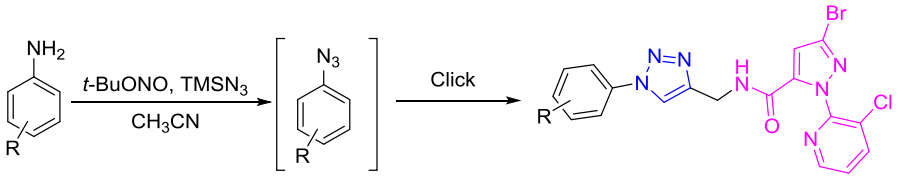
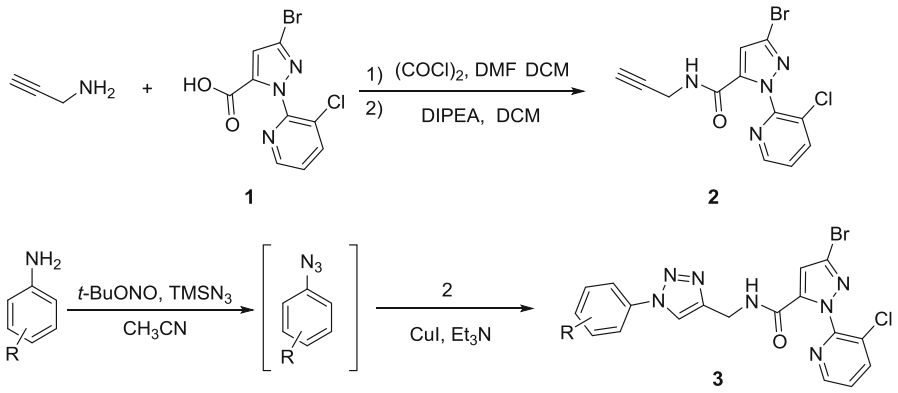


Fig. 1 Some insecticides and nematicides containing pyridine–pyrazole amide structures



Scheme 1 Synthesis of novel pyridine–pyrazole amide derivatives containing 1,2,3-triazoles via click reactions



Scheme 2 General synthetic route for the target compound **3**

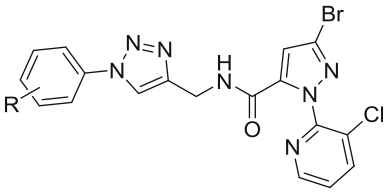
reported [21]. Aryl azides were synthesized from their corresponding amines using stable and non-explosive reagents: tertbutyl nitrite (*t*-BuONO) and azidotrimethylsilane ($TMSN_3$). This provides a mild and safe option for the straightforward preparation of 1,2,3-triazoles in a one-pot reaction. Therefore, we chose this convenient approach to initiate our synthesis.

Compound **1** was synthesized according to the literature [22]. First, compound **1** was treated with oxalyl chloride to give corresponding acyl chloride, then the corresponding acyl chloride was dissolved in anhydrous dichloromethane (DCM) and added dropwise to a solution of propargylamine in DCM to obtained compound **2** in 75 % yield. Then, a wide range of anilines were dissolved in acetonitrile and reacted in the presence of *t*-BuONO and $TMSN_3$ at 0 °C, with warming to room temperature. After complete consumption of the starting material, catalytic amounts of CuI (0.2 eq), Et_3N (1.2 eq) and compound **2** (1.0 eq) were added directly at room temperature under Argon gas. The target compounds **3** were obtained in moderate to high yields.

Nematicidal activity

The nematicidal activities of **3a**–**3w** against *M. incognita* are listed in Table 1. The preliminary bioassays indicated that most of the target compounds had good inhibitory activity against *M. incognita* at 25 mg L^{-1}. Among the tested

Table 1 Nematicidal activities of compounds **3a–3w** against *M. incognita*



No.	Compound	*R*	Inhibition rate	
			25 mg L^{-1}	10 mg L^{-1}
1	**3a**	*R*=H	100.0 %	16.1 %
2	**3b**	*R*=3-F	88.5 %	n.t.
3	**3c**	*R*=3-Cl	78.1 %	n.t.
4	**3d**	*R*=4-Cl	78.1 %	n.t.
5	**3e**	*R*=2-Br	100.0 %	0.0 %
6	**3f**	*R*=3-Br	100.0 %	60.1 %
7	**3g**	*R*=4-Br	100.0 %	72.2 %
8	**3h**	*R*=2-CH_3	96.7 %	38.9 %
9	**3i**	*R*=3-CH_3	p.t.	75.9 %
10	**3j**	*R*=4-CH_3	100.0 %	66.4 %
11	**3k**	*R*=2-OCH_3	p.t.	92.4 %
12	**3l**	*R*=3-OCH_3	72.2 %	n.t.
13	**3m**	*R*=4-OCH_3	100.0 %	60.8 %
14	**3n**	*R*=4-NO_2	89.1 %	n.t.
15	**3o**	*R*=4-CN	78.1 %	n.t.
16	**3p**	*R*=3-CF_3	72.7 %	n.t.
17	**3q**	*R*=2-F,6-F	100.0 %	43.8 %
18	**3r**	*R*=2-F,4-F	95.5 %	n.t.
19	**3s**	*R*=3-CN,4-F	100.0 %	23.9 %
20	**3t**	*R*=2-F,4-Cl	100.0 %	n.t.
21	**3u**	*R*=2-Br,3-F	90.3 %	n.t.
22	**3v**	*R*=2-Br,6-F	100.0 %	27.2 %
23	**3w**	*R*=3-F,4-OCH_3	100.0 %	60.3 %
24	Fenamiphos	–	–	100.0 %[a]
25	Avermectin	–	–	100.0 %[a]
26	DMF (1.0 %)[b]	–	0.0 %	0.0 %
27	CK	–	–	0.0 %

p.t. plant toxic, *n.t.* not tested

[a] Inhibitory activity at 1 mg L^{-1}

[b] CK with DMF (1.0 %)

compounds, **3a**, **3e**, **3f**, **3g**, **3j**, **3m**, **3q**, **3s**, **3t**, **3v** and **3w** exhibited 100 % inhibition rates; **3i** and **3k** were toxic to the plants and resulted in the death of plants because of their high concentration. Consequently, the compounds with high nematicidal potency or toxicity to plants were investigated further at lower concentrations. The plant toxicity of **3i** and **3k** did not exist when treated at 10 mg L^{-1}, and some of the tested compounds still showed moderate nematicidal activity. Especially, compound **3k** displayed more than a 90 % inhibition rate against *M. incognita* at 10 mg L^{-1}.

When bromine was introduced into the three or four position of the benzene ring, compounds **3f** and **3g** exhibited higher inhibitory activity than other compound bearing halogen-substituted or no substituents in the benzene ring (entries 1–7), which indicated that the bromine group played a positive role in promoting the nematicidal activity of the target compounds. Also, the compounds containing electron-withdrawing ability in the benzene ring caused a large drop in inhibitory activity compared with counterparts when *R* were electron-donating groups (entries 8–15). Meanwhile, the compound **3w** with the existence of 3-F,4-OCH_3 group showed better inhibitory activity than other double position-substituted target compounds (entries 16–22), which confirmed that this electron-donating substituent was the key factor for the maintenance of higher nematicidal activity.

Experimental

Instrumentation and chemicals

Melting points (Mps) of compounds were recorded on a Büchi B540 apparatus (Büchi Labortechnik, Flawil, Switzerland) and are uncorrected. Nuclear magnetic resonance (NMR) spectra were recorded on Bruker AM-400 spectrometer with deuterated chloroform ($CDCl_3$) or deuterated dimethyl sulfoxide (DMSO-d_6) as solvents and tetramethylsilane (TMS) as an internal standard. Two-dimensional (2D) NMR for compound **3d** spectra were recorded on Bruker AM-500 spectrometer with DMSO-d_6 as the solvent and TMS as the internal standard.

Chemical shifts are reported in δ (parts per million). High-resolution electron mass spectra [electrospray ionization time-of-flight (ESI-TOF) or electron ionization TOF (EI-TOF)] were performed on a micromass liquid chromatography (LC)-TOF spectrometer. Unless otherwise noted, reagents and solvents were used as received from commercial suppliers.

Biological assay [23, 24]

In vivo All compounds were dissolved with dimethylformamide (DMF) and diluted with distilled water to obtain concentrations of 25.0 and 10.0 mg L^{-1} for bioassays. The final concentration of DMF in each treatment never exceeded 1 % v/v. The 1-week-old cucumber seedlings were replanted in sterilized sand in test tubes (one seedling per test tube, tube size: 20 × 250 mm), and the roots of each seedling were treated with 3 mL of test solution. Then, approximately 2000 living J2 nematodes were inoculated into the rhizosphere sand of each host plant.

Fenamiphos and avermectin (B1) at concentrations of 5.0 and 1.0 mg L^{-1}, respectively, served as positive control, and the negative control group was prepared in the same way but lacked the tested compound. Distilled water without nematodes served as blank control. Each treatment was replicated four times and the experiment was repeated three times. All the above test tubes were incubated at 20–25 °C for 20 days, with 10 h in the daylight and 14 h in the dark per day. The number of root knots in each test tube was counted and a score recorded. The inhibition rate on J2 of *M. incognita* was calculated by comparison with the negative control group:

$$\text{Inhibition rate}\,(\%) = [(\text{score of negative control} - \text{score of treatment})/(\text{score of negative control})] \times 100\,\%.$$

Scoring criteria: 0: 0–5 knots; 5: 6–10 knots; 10: 11–20 knots; 20: more than 20 knots.

Synthesis of compound 1

Compound **1** was synthesized according to the literature [22].

Data for compound **1**: yellow solid; Mp: 198.6–199.8 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.99 (s, 1H), 8.57 (s, 1H), 8.26 (d, J = 7.2 Hz, 1H), 7.69 (s, 1H), 7.26 (s, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 158.47, 148.14, 147.32, 139.45, 137.40, 128.04, 127.19, 127.00, 113.36 ppm. HRMS (EI+): m/z $[M]^+$ calcd. for $C_9H_5^{35}Cl^{79}BrN_3O_2^+$, 300.9254, found: 300.9256; calcd. for $C_9H_5^{37}Cl^{79}BrN_3O_2^+$, 302.9224, found: 302.9227; calcd. for $C_9H_5^{35}Cl^{81}BrN_3O_2^+$, 302.9233, found: 302.9277; calcd. for $C_9H_5^{37}Cl^{81}BrN_3O_2^+$, 304.9204, found: 304.9207.

Synthesis of compound 2

A mixture of 3-bromo-1-(3-chloropyridin-2-yl)-1*H*-pyrazole-5-carboxylic acid (**1**, 1.0 mmol), an excess of oxalyl chloride (3 mL) was stirred at room temperature for 10 min, then one drop DMF was added. The reaction mixture was stirred at room temperature for another 3 h and concentrated in vacuo to give corresponding acyl chloride. The corresponding acyl chloride was dissolved in 2 mL of anhydrous dichloromethane (DCM), then added dropwise to a solution of propargylamine (1.0 mmol), N,N-diisopropylethylamine (DIPEA, 1.2 mmol) in 15 mL of anhydrous DCM in an ice bath. The reaction mixture was then stirred at room temperature and monitored by thin layer chromatography (TLC); after completion, the solvent was evaporated under reduced pressure. The residual solid was purified by column chromatography on silica gel with ethyl acetate/petroleum ether as eluent to afford compound **2** in 75 % yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, J = 4.8 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.44 (dd, J = 8.0, 4.4 Hz, 1H), 6.85 (s, 1H), 6.77 (s, 1H), 4.08 (dd, J = 5.2, 2.0 Hz, 2H), 2.17 (t, J = 2.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1, 148.8, 146.7, 139.4, 138.6, 129.3, 128.0, 126.0, 110.2, 78.4, 72.4, 29.3 ppm. HRMS (ESI): m/z $[M + Na]^+$ calcd. for $C_{12}H_8^{35}Cl^{79}BrN_4ONa^+$, 360.9468, found: 360.9463; calcd. for $C_{12}H_8^{35}Cl^{81}BrN_4ONa^+$,

found: 362.9433; calcd. for $C_{12}H_8^{37}Cl^{81}BrN_4ONa^+$, 364.9418, found: 364.9403; calcd. for $C_{12}H_8^{37}Cl^{79}BrN_4ONa^+$, 362.9438, found: 362.9438.

General procedure for the synthesis of target compounds 3

Different aniline (0.75 mmol) was dissolved in CH_3CN (10 mL) in a 25-mL round-bottomed flask and cooled to 0 °C in an ice bath. To this stirred mixture was added *t*-BuONO (1.125 mmol) followed by $TMSN_3$ (0.9 mmol) dropwise. The resulting solution was stirred at room temperature for 2 h. Compound **2** (0.5 mmol), CuI (0.1 mmol) and Et_3N (0.6 mmol) were then added and the reaction was stirred at room temperature. The progress of the reaction was monitored by TLC. After the completion of reaction, the solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography using petroleum ether/ethyl acetate as eluting solution to afford the target compounds **3** [25–29]. The data of **3a**–**3w** are shown as follows. We selected one compound, **3d**, as a representative compound and signal positions of carbon protons were assigned.

Data for **3a**: Yield 55 %; yellow solid; Mp: 204.2–204.5 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.37 (*t*, $J = 5.6$ Hz, 1H), 8.65 (s, 1H), 8.50 (d, $J = 4.4$ Hz, 1H), 8.19 (d, $J = 8.0$ Hz, 1H), 7.88 (d, $J = 8.0$ Hz, 2H), 7.66–7.57 (m, 3H), 7.49 (t, $J = 7.2$ Hz, 1H), 7.29 (s, 1H), 4.49 (d, $J = 5.6$ Hz, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.2, 149.1, 147.5, 145.6, 139.8, 139.7, 137.1, 130.4, 129.1, 128.5, 127.1, 127.1, 121.7, 120.4, 110.6, 34.8 ppm. HRMS (ESI): *m*/*z* $[M - H]^+$ calcd. for $C_{18}H_{12}^{35}Cl^{79}BrN_7O^+$, 455.9975, found: 455.9976; calcd. for $C_{18}H_{12}^{35}Cl^{81}BrN_7O^+$, 457.9955, found: 457.9955; calcd. for $C_{18}H_{12}^{37}Cl^{79}BrN_7O^+$, 457.9946, found: 457.9955; calcd. for $C_{18}H_{12}^{37}Cl^{81}BrN_7O^+$, 459.9925, found: 459.9931.

Data for **3b**: Yield 68 %; yellow solid; Mp: 173.6–174.1 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.41 (t, $J = 5.6$ Hz, 1H), 8.74 (s, 1H), 8.50 (dd, $J = 4.8$, 1.2 Hz, 1H), 8.20 (dd, $J = 8.0$, 1.2 Hz, 1H), 7.85 (dt, $J = 10.0$, 2.0 Hz, 1H), 7.80 (dd, $J = 8.0$, 1.2 Hz, 1H), 7.68–7.61 (m, 2H), 7.35 (td, $J = 8.8$, 2.4 Hz, 1H), 7.30 (s, 1H), 4.49 (d, $J = 5.6$ Hz, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.9 ($J = 243.6$ Hz), 157.2, 149.1, 147.5, 145.9, 139.8, 139.7, 138.3 ($J = 10.7$ Hz), 132.3 ($J = 9.1$ Hz), 128.5, 127.1, 127.1, 121.9, 116.30 ($J = 3.0$ Hz), 115.8 ($J = 20.9$ Hz), 110.6, 107.9 ($J = 25.6$ Hz), 34.69 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ −110.5 (m) ppm. HRMS (ESI): *m*/*z* $[M - H]^+$ calcd. for $C_{18}H_{11}F^{35}Cl^{79}BrN_7O^+$, 473.9881, found: 473.9880; calcd. for $C_{18}H_{11}F^{35}Cl^{81}BrN_7O^+$, 475.9861, found: 475.9859; calcd. for $C_{18}H_{11}F^{37}Cl^{79}BrN_7O^+$, 475.9852, found: 475.9859; calcd. for $C_{18}H_{11}F^{37}Cl^{81}BrN_7O^+$, 477.9831, found: 477.9838.

Data for **3c**: Yield 76 %; yellow solid; Mp: 169.6–170.0 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.40 (t, $J = 5.6$ Hz, 1H), 8.76 (s, 1H), 8.50 (d, $J = 3.6$ Hz, 1H), 8.20 (d, $J = 8.0$ Hz, 1H), 8.04 (s, 1H), 7.92 (d, $J = 8.0$ Hz, 1H), 7.66–7.54 (m, 3H), 7.30 (s, 1H), 4.49 (d, $J = 5.6$ Hz, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.2, 149.1, 147.5, 145.9, 139.8, 139.7, 138.1, 134.7, 132.1, 128.9, 128.5, 127.1, 127.1, 121.9, 120.2, 119.0, 110.6, 34.7 ppm. HRMS (ESI): *m*/*z* $[M - H]^+$ calcd. for $C_{18}H_{11}^{35}Cl_2^{79}BrN_7O^+$, 489.9586, found: 489.9590; calcd. for $C_{18}H_{11}^{35}Cl^{37}Cl^{79}BrN_7O^+$,

491.9556, found: 491.9566; calcd. for $C_{18}H_{11}^{35}Cl_2^{81}BrN_7O^+$, 491.9565, found: 491.9566; calcd. for $C_{18}H_{11}^{37}Cl_2^{79}BrN_7O^+$, 493.9527, found: 493.9539; calcd. for $C_{18}H_{11}^{35}Cl^{37}Cl^{81}BrN_7O^+$, 493.9536, found: 493.9539; calcd. for $C_{18}H_{11}^{37}Cl_2^{81}BrN_7O^+$, 495.9505, found: 495.9510.

Data for **3d**: Yield 66 %; yellow solid; Mp: 210.0–210.6 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.39 (t, J = 5.5 Hz, 1H, NH), 8.69 (s, 1H, NCH=C), 8.50 (dd, J = 5.0, 1.5 Hz, 1H, ArCH), 8.19 (dd, J = 8.0, 1.5 Hz, 1H, ArCH), 7.97–7.90 (m, 2H, ArCH), 7.64–7.72 (m, 3H, ArCH), 7.29 (s, 1H, COC=CH=C), 4.49 (d, J = 5.5 Hz, 2H, CH_2) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 157.10 (C=O), 149.04 (ArCH), 147.41 (ArCH), 145.76 (CH=C-CH_2), 139.70 (COC=CH), 139.60 (ArCH), 135.75 (ArCH), 133.26 (ArCH), 130.22 (ArCH), 128.36 (ArCH), 127.02 (C-Br), 126.95 (ArCH), 121.99 (ArCH), 121.75 (N-CH=C-CH_2), 110.49 (C=CH-CBr), 34.64 (CH_2) ppm. HRMS (ESI): m/z $[M - H]^+$ calcd. for $C_{18}H_{11}^{35}Cl_2^{79}BrN_7O^+$, 489.9586, found: 489.9574; calcd. for $C_{18}H_{11}^{35}Cl^{37}Cl^{79}BrN_7O^+$, 491.9556, found: 491.9555; calcd. for $C_{18}H_{11}^{35}Cl_2^{81}BrN_7O^+$, 491.9565, found: 491.9555; calcd. for $C_{18}H_{11}^{37}Cl_2^{79}BrN_7O^+$, 493.9527, found: 493.9530; calcd. for $C_{18}H_{11}^{35}Cl^{37}Cl^{81}BrN_7O^+$, 493.9536, found: 493.9530; calcd. for $C_{18}H_{11}^{37}Cl_2^{81}BrN_7O^+$, 495.9505, found: 495.9502.

Data for **3e**: Yield 62 %; yellow solid; Mp: 212.5–212.9 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.41 (t, J = 5.6 Hz, 1H), 8.50 (d, J = 4.8 Hz, 1H), 8.35 (s, 1H), 8.19 (d, J = 8.0 Hz, 1H), 7.91 (d, J = 7.6 Hz, 1H), 7.66–7.53 (m, 4H), 7.29 (s, 1H), 4.51 (d, J = 5.6 Hz, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.2 149.1, 147.5, 144.6 139.8, 139.7, 136.7 134.1, 132.4 129.4, 129.1 128.5 127.1, 127.1 125.7 119.2 110.6 34.6 ppm. HRMS (ESI): m/z $[M - H]^+$ calcd. for $C_{18}H_{11}^{35}Cl^{79}Br_2N_7O^+$, 533.9080, found: 533.9075; calcd. for $C_{18}H_{11}^{35}Cl^{79}Br^{81}BrN_7O^+$, 535.9060, found: 535.9056; calcd. for $C_{18}H_{11}^{37}Cl^{79}Br_2N_7O^+$, 535.9051, found: 535.9056; calcd. for $C_{18}H_{11}^{35}Cl^{81}Br_2N_7O^+$, 537.9039, found: 537.9039; calcd. for $C_{18}H_{11}^{37}Cl^{79}Br^{81}BrN_7O^+$, 537.9030, found: 537.9039; calcd. for $C_{18}H_{11}^{37}Cl^{81}Br_2N_7O^+$, 539.9010, found: 539.9016.

Data for **3f**: Yield 63 %; yellow solid; Mp: 166.0–166.4 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.36 (t, J = 5.2 Hz, 1H), 8.74 (s, 1H), 8.50 (dd, J = 4.8 Hz, 1.2 Hz, 1H), 8.19(d, 8.0 Hz, 1H), 8.15 (s, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.63 (dd, J = 8.0, 4.8 Hz, 1H), 7.55 (t, J = 8.0 Hz, 1H), 7.29 (s, 1H), 4.49 (d, J = 5.2 Hz, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 156.7, 148.6, 147.0, 145.4, 139.3, 139.2, 137.7, 131.8, 131.3, 128.0, 126.6, 126.6, 122.4, 122.3, 121.4, 118.9, 110.1, 34.2 ppm. HRMS (ESI): m/z $[M - H]^+$ calcd. for $C_{18}H_{11}^{35}Cl^{79}Br_2N_7O^+$, 533.9080, found: 533.9084; calcd. for $C_{18}H_{11}^{35}Cl^{79}Br^{81}BrN_7O^+$, 535.9060, found: 535.9061; calcd. for $C_{18}H_{11}^{37}Cl^{79}Br_2\ N_7O^+$, 535.9051, found: 535.9061; calcd. for $C_{18}H_{11}^{35}Cl^{81}Br_2N_7O^+$, 537.9039, found: 537.9039; calcd. for $C_{18}H_{11}^{37}Cl^{79}Br^{81}BrN_7O^+$, 537.9030, found: 537.9039; calcd. for $C_{18}H_{11}^{37}Cl^{81}Br_2N_7O^+$, 539.9010, found: 539.9019.

Data for **3g**: Yield 58 %; yellow solid; Mp: 216.6–217.2 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.36 (t, J = 5.6 Hz, 1H), 8.68 (s, 1H), 8.50 (dd, J = 4.8, 1.2 Hz, 1H), 8.19 (dd, J = 8.0, 1.2 Hz, 1H), 7.87 (d, J = 8.8 Hz, 2H), 7.79 (d, J = 8.8 Hz, 2H), 7.63 (dd, J = 8.0, 4.8 Hz, 1H), 7.28 (s, 1H), 4.49 (d, J = 5.6 Hz, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 156.7, 148.6, 147.0,

145.4, 139.3, 139.2, 135.8, 132.8, 128.0, 126.6, 126.6, 121.9, 121.3, 121.2, 110.1, 34.3 ppm. HRMS (ESI): *m/z* $[M - H]^+$ calcd. for $C_{18}H_{11}^{35}Cl^{79}Br_2N_7O^+$, 533.9080, found: 533.9080; calcd. for $C_{18}H_{11}^{35}Cl^{79}Br^{81}BrN_7O^+$, 535.9060, found: 535.9060; calcd. for $C_{18}H_{11}^{37}Cl^{79}Br_2N_7O^+$, 535.9051, found: 535.9060; calcd. for $C_{18}H_{11}^{35}Cl^{81}Br_2N_7O^+$, 537.9039, found: 537.9041; calcd. for $C_{18}H_{11}^{37}Cl^{79}Br^{81}BrN_7O^+$, 537.9030, found: 537.9041; calcd. for $C_{18}H_{11}^{37}Cl^{81}Br_2N_7O^+$, 539.9010, found: 539.9001.

Data for **3h**: Yield 49 %; yellow solid; Mp: 184.7–185.1 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.66 (t, $J = 5.2$ Hz, 1H), 8.49 (d, $J = 3.6$ Hz, 1H), 8.32 (s, 1H), 8.19 (d, $J = 8.0$ Hz, 1H), 7.64 (dd, $J = 8.0$, 4.8 Hz, 1H), 7.51–7.46 (m, 3H), 7.43–7.37 (m, 2H), 4.48 (d, $J = 5.6$ Hz, 2H), 2.13 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 156.7, 148.7, 147.0, 144.2, 139.4, 139.2, 136.2, 132.9, 131.3, 129.7, 128.0, 126.9, 126.6, 126.6, 125.9, 124.8, 110.3, 34.2, 17.4 ppm. HRMS (ESI): *m/z* $[M - H]^+$ calcd. for $C_{19}H_{14}^{35}Cl^{79}BrN_7O^+$, 470.0132, found: 470.0128; calcd. for $C_{19}H_{14}^{35}Cl^{81}BrN_7O^+$, 472.0111, found: 472.0110; calcd. for $C_{19}H_{14}^{37}Cl^{79}BrN_7O^+$, 472.0102, found: 472.0110; calcd. for $C_{19}H_{14}^{37}Cl^{81}BrN_7O^+$, 474.0082, found: 474.0089.

Data for **3i**: Yield 56 %; yellow solid; Mp: 170.2–170.5 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.36 (t, $J = 5.6$ Hz, 1H), 8.61 (s, 1H), 8.50 (dd, $J = 4.8$, 1.2 Hz, 1H), 8.19 (dd, $J = 8.0$, 1.2 Hz, 1H), 7.72 (s, 1H), 7.68–7.61 (m, 2H), 7.46 (t, $J = 8.0$ Hz, 1H), 7.30–7.28 (m, 2H), 4.49 (d, $J = 5.6$ Hz, 2H), 2.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 156.7, 148.7, 147.0, 145.07, 139.6, 139.3, 139.2, 136.6, 129.6, 129.2, 128.0, 126.6, 126.6, 121.2, 120.3, 117.0, 110.1, 34.3, 20.9 ppm. HRMS (ESI): *m/z* $[M - H]^+$ calcd. for $C_{19}H_{14}^{35}Cl^{79}BrN_7O^+$, 470.0132, found: 470.0131; calcd. for $C_{19}H_{14}^{35}Cl^{81}BrN_7O^+$, 472.0111, found: 472.0110; calcd. for $C_{19}H_{14}^{37}Cl^{79}BrN_7O^+$, 472.0102, found: 472.0110; calcd. for $C_{19}H_{14}^{37}Cl^{81}BrN_7O^+$, 474.0082, found: 474.0085.

Data for **3j**: Yield 25 %; yellow solid; Mp: 172.3–173.0 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.37 (t, $J = 5.6$ Hz, 1H), 8.60 (s, 1H), 8.50 (dd, $J = 4.4$, 1.6 Hz, 1H), 8.19 (dd, $J = 8.0$, 1.6 Hz, 1H), 7.76 (d, $J = 8.4$ Hz, 2H), 7.64 (dd, $J = 8.0$, 4.8 Hz, 2H), 7.39 (d, $J = 8.4$ Hz, 2H), 7.29 (s, 1H), 4.48 (d, $J = 5.6$ Hz, 2H), 2.38 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.1, 149.1, 147.5, 145.5, 139.8, 139.7, 138.7, 134.8, 130.7, 128.4, 127.1, 127.1, 121.6, 120.3, 110.6, 34.8, 21.0 ppm. HRMS (ESI): *m/z* $[M - H]^+$ calcd. for $C_{19}H_{14}^{35}Cl^{79}BrN_7O^+$, 470.0132, found: 470.0140; calcd. for $C_{19}H_{14}^{35}Cl^{81}BrN_7O^+$, 472.0111, found: 472.0108; calcd. for $C_{19}H_{14}^{37}Cl^{79}BrN_7O^+$, 472.0102, found: 472.0108; calcd. for $C_{19}H_{14}^{37}Cl^{81}BrN_7O^+$, 474.0082, found: 474.0076.

Data for **3k**: Yield 52 %; yellow solid; Mp: 195.6–196.2 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.35 (t, $J = 5.2$ Hz, 1H), 8.49 (d, $J = 4.4$ Hz, 1H), 8.25 (s, 1H), 8.19 (d, $J = 8.0$ Hz, 1H), 7.63 (dd, $J = 8.0$, 4.8 Hz, 1H), 7.59 (d, $J = 8.0$ Hz, 1H), 7.52 (t, $J = 8.0$ Hz, 1H), 7.31 (d, $J = 8.4$ Hz, 1H), 7.28 (s, 1H), 7.14 (t, $J = 7.6$ Hz, 1H), 4.49 (d, $J = 5.6$ Hz, 2H), 3.84 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 156.7, 151.5, 148.7, 147.0, 143.8, 139.4, 139.2, 130.6, 128.0, 126.6, 126.5, 125.7, 125.6, 124.9, 120.9, 113.1, 110.0, 56.1, 34.2 ppm. HRMS (ESI): *m/z* $[M - H]^+$ calcd. for $C_{19}H_{14}^{35}Cl^{79}BrN_7O_2^+$, 486.0085, found: 486.0082; calcd. for $C_{19}H_{14}^{35}Cl^{81}BrN_7O_2^+$, 488.0060, found: 488.0060; calcd. for

$C_{19}H_{14}^{37}Cl^{79}BrN_7O_2^+$, 488.0051, found: 488.0060; calcd. for $C_{19}H_{14}^{37}Cl^{79}BrN_7O_2^+$, 490.0031, found: 490.0039.

Data for **3l**: Yield 42 %; white solid; Mp: 175.4–175.6 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.38 (t, J = 5.6 Hz, 1H), 8.69 (s, 1H), 8.50 (dd, J = 4.8, 1.6 Hz, 1H), 8.19 (dd, J = 8.0, 1.6 Hz, 1H), 7.64 (dd, J = 8.0, 4.8 Hz, 1H), 7.55–7.45 (m, 3H), 7.29 (s, 1H), 7.07–7.03 (m, 1H), 4.48 (d, J = 5.6 Hz, 2H), 3.85 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.7, 157.2, 149.2, 147.5, 145.6, 139.8, 139.7, 138.1, 131.3, 128.5, 127.1, 127.1, 121.9, 114.8, 112.4, 110.6, 106.0, 56.1, 34.7 ppm. HRMS (ESI): m/z $[M - H]^+$ calcd. for $C_{19}H_{16}^{35}Cl^{79}BrN_7O_2^+$, 488.0237, found: 488.0238; calcd. for $C_{19}H_{16}^{35}Cl^{81}BrN_7O_2^+$, 490.0217, found: 490.0218; calcd. for $C_{19}H_{16}^{37}Cl^{79}BrN_7O_2^+$, 492.0187, found: 492.0193.

Data for **3m**: Yield 59 %; yellow solid; Mp: 187.3–187.5 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.33 (t, J = 5.6 Hz, 1H), 8.52 (s, 1H), 8.50 (dd, J = 4.8, 1.2 Hz, 1H), 8.18 (dd, J = 8.0, 1.2 Hz, 1H), 7.78 (d, J = 8.8 Hz, 2H), 7.63 (dd, J = 8.0, 4.8 Hz, 1H), 7.29 (s, 1H), 7.12 (d, J = 8.8 Hz, 2H), 4.47 (d, J = 5.6 Hz, 2H), 3.83 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.2, 156.7, 148.7, 147.0, 144.9, 139.4, 139.2, 130.0, 128.0, 126.6, 126.5, 121.6, 121.2, 114.9, 110.1, 55.5, 34.3 ppm. HRMS (ESI): m/z $[M - H]^+$ calcd. for $C_{19}H_{14}^{35}Cl^{79}BrN_7O_2^+$, 486.0081, found: 486.0082; calcd. for $C_{19}H_{14}^{35}Cl^{81}BrN_7O_2^+$, 488.0060, found: 488.0061; calcd. for $C_{19}H_{14}^{37}Cl^{79}BrN_7O_2^+$, 488.0051, found: 488.0061; calcd. for $C_{19}H_{14}^{37}Cl^{79}BrN_7O_2^+$, 490.0031, found: 490.0039.

Data for **3n**: Yield 62 %; yellow solid; Mp: 254.6–255.1 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.43 (t, J = 5.6 Hz, 1H), 8.89 (s, 1H), 8.50 (dd, J = 4.8, 1.6 Hz, 1H), 8.45 (d, J = 8.8 Hz, 2H), 8.24–8.18 (m, 3H), 7.64 (dd, J = 8.0, 4.8 Hz, 1H), 7.30 (s, 1H), 4.51 (d, J = 5.6 Hz, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.2, 149.1, 147.6, 147.1, 146.4, 141.3, 139.7, 128.5, 127.1, 127.1, 126.1, 122.2, 120.9, 110.6, 34.7 ppm. HRMS (ESI): m/z $[M - H]^+$ calcd. for $C_{18}H_{11}^{35}Cl^{79}BrN_8O_3^+$, 500.9826, found: 500.9827; calcd. for $C_{18}H_{11}^{35}Cl^{81}BrN_8O_3^+$, 502.9806, found: 502.9806; calcd. for $C_{18}H_{11}^{37}Cl^{79}BrN_8O_3^+$, 502.9797, found: 502.9806; calcd. for $C_{18}H_{11}^{37}Cl^{81}BrN_8O_3^+$, 504.9776, found: 504.9782.

Data for **3o**: Yield 69 %; yellow solid; Mp: 245.4–246.1 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.42 (t, J = 5.6 Hz, 1H), 8.84 (s, 1H), 8.50 (dd, J = 4.8, 1.6 Hz, 1H), 8.19 (dd, J = 8.0, 1.6 Hz, 1H), 8.15 (d, J = 8.8 Hz, 2H), 8.09 (d, J = 8.8 Hz, 2H), 7.63 (dd, J = 8.0, 4.8 Hz, 1H), 7.29 (s, 1H), 4.51 (d, J = 5.6 Hz, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.2, 149.1, 147.5, 146.2, 139.9, 139.7, 139.7, 134.8, 128.4, 127.1, 127.1, 122.0, 120.8, 118.6, 111.5, 110.6, 34.7 ppm. HRMS (ESI): m/z $[M - H]^+$ calcd. for $C_{19}H_{11}^{35}Cl^{79}BrN_8O^+$, 480.9928, found: 480.9926; calcd. for $C_{19}H_{11}^{35}Cl^{81}BrN_8O^+$, 482.9907, found: 482.9905; calcd. for $C_{19}H_{11}^{37}Cl^{79}BrN_8O^+$, 482.9898, found: 482.9905; calcd. for $C_{19}H_{11}^{37}Cl^{81}BrN_8O^+$, 484.9878, found: 484.9881.

Data for **3p**: Yield 74 %; yellow solid; Mp: 182.1–182.5 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.42 (t, J = 5.6 Hz, 1H), 8.87 (s, 1H), 8.50 (dd, J = 4.8, 1.2 Hz, 1H), 8.31–8.22 (m, 2H), 8.19 (dd, J = 8.0, 1.6 Hz, 1H), 7.93–7.76 (m, 2H), 7.63 (dd, J = 8.0, 4.8 Hz, 1H), 7.30 (s, 1H), 4.51 (d, J = 5.6 Hz, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.2, 149.1, 147.5, 146.0, 139.7, 139.6, 137.5,

131.0 (q, $J = 32.3$ Hz), 130.5, 128.5, 127.1, 127.1, 125.6 (q, $J = 4.1$ Hz), 124.3, 124.0 (q, $J = 271.0$ Hz), 122.1, 117.0 (q, $J = 3.8$ Hz) 110.6, 34.7 ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ −61.22(s) ppm. HRMS (ESI): m/z $[M - H]^+$ calcd. for $C_{19}H_{11}F_3^{35}Cl^{79}BrN_7O^+$, 523.9849, found: 523.9847; calcd. for $C_{19}H_{11}F_3^{35}Cl^{81}BrN_7O^+$, 525.9829, found: 525.9829; calcd. for $C_{19}H_{11}F_3^{37}Cl^{79}BrN_7O^+$, 425.9820, found: 425.9829; calcd. for $C_{19}H_{11}F_3^{37}Cl^{81}BrN_7O^+$, 527.9799, found: 527.9806.

Data for **3q**: Yield 42 %; yellow solid; Mp: 184.5–184.8 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.42 (t, $J = 5.2$ Hz, 1H), 8.50 (dd, $J = 4.4$, 1.2 Hz, 1H), 8.44 (s, 1H), 8.19 (d, $J = 8.0$ Hz, 1.2 Hz, 1H), 7.77–7.69 (m, 1H), 7.64 (dd, $J = 8.0$, 4.4 Hz, 1H), 7.46 (t, $J = 8.8$ Hz, 2H), 7.29 (s, 1H), 4.53 (d, $J = 5.2$ Hz, 2H) ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ −120.51 to −120.55 (m) ppm. HRMS (ESI): m/z $[M - H]^+$ calcd. for $C_{18}H_{10}F_2^{35}Cl^{79}BrN_7O^+$, 491.9787, found: 491.9792; calcd. for $C_{18}H_{10}F_2^{35}Cl^{81}BrN_7O^+$, 493.9766, found: 493.9772; calcd. for $C_{18}H_{10}F_2^{37}Cl^{79}BrN_7O^+$, 493.9757, found: 493.9772; calcd. for $C_{18}H_{10}F_2^{37}Cl^{81}BrN_7O^+$, 495.9735, found: 495.9736.

Data for **3r**: Yield 54 %; yellow solid; Mp: 190.1–190.4 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.39 (t, $J = 5.6$ Hz, 1H), 8.50 (dd, $J = 4.8$, 1.6 Hz, 1H), 8.40 (d, $J = 2.0$ Hz, 1H), 8.19 (dd, $J = 8.0$, 1.6 Hz, 1H), 7.87 (td, $J = 8.8$, 6.0 Hz, 1H), 7.71–7.64 (m, 1H), 7.64 (dd, $J = 8.0$, 4.8 Hz, 1H), 7.38–7.32 (m, 1H), 7.28 (s, 1H), 4.50 (d, $J = 5.6$ Hz, 2H) ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ −107.53 to −108.61 (m), −118.94 to −119.03 (m) ppm. HRMS (ESI): m/z $[M - H]^+$ calcd. for $C_{18}H_{10}F_2^{35}Cl^{79}BrN_7O^+$, 491.9787, found: 491.9790; calcd. for $C_{18}H_{10}F_2^{35}Cl^{81}BrN_7O^+$, 493.9766, found: 493.9772; calcd. for $C_{18}H_{10}F_2^{37}Cl^{79}BrN_7O^+$, 493.9757, found: 493.9772; calcd. for $C_{18}H_{10}F_2^{37}Cl^{81}BrN_7O^+$, 495.9735, found: 495.9750.

Data for **3s**: Yield 59 %; yellow solid; Mp: 226.4–226.9 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.43 (t, $J = 5.6$ Hz, 1H), 8.73 (s, 1H), 8.54 (dd, $J = 5.6$, 2.8 Hz, 1H), 8.50 (dd, $J = 4.2$, 1.6 Hz, 1H), 8.34 (ddd, $J = 9.2$, 4.4, 2.8 Hz, 1H), 8.19 (dd, $J = 8.0$, 1.6 Hz, 1H), 7.78 (t, $J = 9.2$ Hz, 1H), 7.64 (dd, $J = 8.0$, 4.8 Hz, 1H), 7.29 (s, 1H), 4.50 (d, $J = 5.6$ Hz, 2H) ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ −108.73 to −108.91 (m) ppm. HRMS (ESI): m/z $[M - H]^+$ calcd. for $C_{19}H_{10}F^{35}Cl^{79}BrN_8O^+$, 498.9834, found: 498.9837; calcd. for $C_{19}H_{10}F^{35}Cl^{81}BrN_8O^+$, 500.9813, found: 500.9814; calcd. for $C_{19}H_{10}F^{37}Cl^{79}BrN_8O^+$, 500.9804, found: 500.9814; calcd. for $C_{19}H_{10}F^{37}Cl^{81}BrN_8O^+$, 502.9784, found: 502.9793

Data for **3t**: Yield 50 %; yellow solid; Mp: 137.6–138.2 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.41 (t, $J = 5.6$ Hz, 1H), 8.50 (dd, $J = 4.8$, 1.6 Hz, 1H), 8.45 (d, $J = 1.6$ Hz, 1H), 8.19 (dd, $J = 8.0$, 1.6 Hz, 1H), 7.96 (dd, $J = 6.4$, 2.4 Hz, 1H), 7.71–7.61 (m, 3H), 7.28 (s, 1H), 4.51 (d, $J = 5.6$ Hz, 2H) ppm. ^{19}F NMR (376 MHz, DMSO) δ −125.08 to −125.15 (m) ppm. HRMS (ESI): m/z $[M - H]^+$ calcd. for $C_{18}H_{10}F^{35}Cl_2^{79}BrN_7O^+$, 507.9491, found: 507.9490; calcd. for $C_{18}H_{10}F^{35}Cl^{37}Cl^{79}BrN_7O^+$, 509.9471, found: 509.9469; calcd. for $C_{18}H_{10}F^{35}Cl_2^{81}BrN_7O^+$, 509.9462, found: 509.9469; calcd. for $C_{18}H_{10}F^{37}Cl_2^{79}BrN_7O^+$, 511.9441, found: 511.9446; calcd. for $C_{18}H_{10}F^{35}Cl^{37}Cl^{81}BrN_7O^+$, 511.9432, found: 511.9446; calcd. for $C_{18}H_{10}F^{37}Cl_2^{81}BrN_7O^+$, 513.9412, found: 513.9427.

Data for **3u**: Yield 64 %; yellow solid; Mp: 142.1–142.5 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.42 (t, $J = 5.6$ Hz, 1H), 8.50 (dd, $J = 4.8$, 1.6 Hz, 1H), 8.40 (s, 1H), 8.20 (dd, $J = 8.0$, 1.6 Hz, 1H), 7.68–7.62 (m, 3H), 7.50–7.47 (m, 1H), 7.29 (s, 1H), 4.52 (d, $J = 5.6$ Hz, 2H) ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ −103.71 to −103.75 (m) ppm. HRMS (ESI): m/z $[M - H]^+$ calcd. for $C_{18}H_{10}F^{35}Cl^{79}Br_2N_7O^+$, 551.8996, found: 551.8990; calcd. for $C_{18}H_{10}F^{35}Cl^{79}Br^{81}BrN_7O^+$, 553.8966, found: 553.8968; calcd. for $C_{18}H_{10}F^{37}Cl^{79}Br_2N_7O^+$, 553.8957, found: 553.8968; calcd. for $C_{18}H_{10}F^{35}Cl^{81}Br_2N_7O^+$, 555.8945, found: 555.8940; calcd. for $C_{18}H_{10}F^{37}Cl^{79}Br^{81}BrN_7O^+$, 555.8936, found: 555.8940; calcd. for $C_{18}H_{10}F^{37}Cl^{81}Br_2N_7O^+$, 557.8916, found: 557.8926.

Data for **3v**: Yield 35 %; yellow solid; Mp: 206.2–206.7 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.44 (t, $J = 5.6$ Hz, 1H), 8.50 (dd, $J = 4.8$, 1.6 Hz, 1H), 8.39 (s, 1H), 8.19 (dd, $J = 8.0$, 1.6 Hz, 1H), 7.77 (d, $J = 7.6$ Hz, 1H), 7.68–7.58 (m, 3H), 7.29 (s, 1H), 4.52 (d, $J = 5.6$ Hz, 2H) ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ −117.98 to −118.23 (m) ppm. HRMS (ESI): m/z $[M - H]^+$ calcd. for $C_{18}H_{10}F^{35}Cl^{79}Br_2N_7O^+$, 551.8996, found: 551.8996; calcd. for $C_{18}H_{10}F^{35}Cl^{79}Br^{81}BrN_7O^+$, 553.8966, found: 553.8970; calcd. for $C_{18}H_{10}F^{37}Cl^{79}Br_2N_7O^+$, 553.8957, found: 553.8970; calcd. for $C_{18}H_{10}F^{35}Cl^{81}Br_2N_7O^+$, 555.8945, found: 555.8945; calcd. for $C_{18}H_{10}F^{37}Cl^{79}Br^{81}BrN_7O^+$, 555.8936, found: 555.8945; calcd. for $C_{18}H_{10}F^{37}Cl^{81}Br_2N_7O^+$, 557.8916, found: 557.8920.

Data for **3w**: Yield 68 %; white solid; Mp: 216.5–217.0 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.37 (t, $J = 5.6$ Hz, 1H), 8.61 (s, 1H), 8.50 (dd, $J = 4.8$, 1.2 Hz, 1H), 8.19 (dd, $J = 8.0$, 1.2 Hz, 1H), 7.85 (dd, $J = 12.0$, 2.4 Hz, 1H), 7.70 (d, $J = 8.8$ Hz, 1H), 7.64 (dd, $J = 8.0$, 4.8 Hz, 1H), 7.37 (t, $J = 9.2$ Hz, 1H), 7.29 (s, 1H), 4.47 (d, $J = 5.6$ Hz, 2H) ppm. ^{19}F NMR (376 MHz, DMSO-d_6) δ −126.19 to −137.40 (m) ppm. HRMS (ESI): m/z $[M - H]^+$ calcd. for $C_{19}H_{13}F^{35}Cl^{79}BrN_7O_2^+$, 503.9987, found: 503.9990; calcd. for $C_{19}H_{13}F^{35}Cl^{81}BrN_7O_2^+$, 505.9966, found: 505.9969; calcd. for $C_{19}H_{13}F^{37}Cl^{79}BrN_7O_2^+$, 505.9957, found: 505.9969; calcd. for $C_{19}H_{13}F^{37}Cl^{81}BrN_7O_2^+$, 507.9937, found: 507.9946.

Conclusions

In conclusion, 22 novel pyridine–pyrazole amide derivatives containing 1,2,3-triazoles were synthesized via click chemistry in a one-pot reaction and their nematicidal activities against *M. incognita* in vivo were evaluated. Some of the tested compounds showed good nematicidal activity against *M. incognita* at 25 mg L^{-1}. Among them, compound **3k** displayed a 92.4 % inhibition rate at 10 mg L^{-1}, which might be developed as a potential lead compound for further optimization.

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