Syntheses and Herbicidal Activity of Pyrazolyl Benzoxazole Derivatives

Na Xue, Yuhan Zhou,* Guowei Wang, Weirong Miao, and Jingping Qu*

State Key Laboratory of Fine Chemicals, Dalian University of Technology,
Dalian 116012, People's Republic of China
*E-mail: zhouyh@dl.cn or qujp@chem.dlut.edu.in

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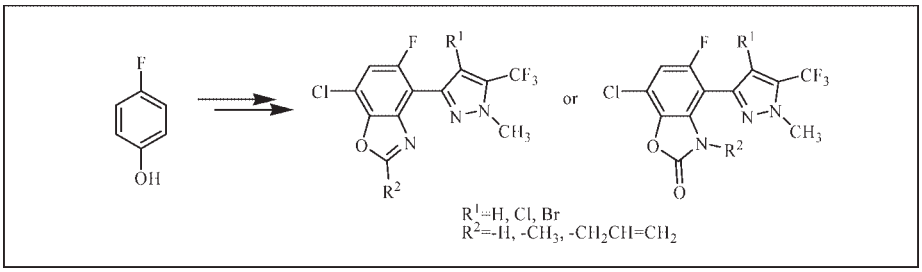

In recent years, protoporphyrinogen oxidase (Protox) inhibitor herbicides are developed rapidly, because of this type of herbicides shows high herbicidal activity and low toxicity. In this paper, we prepared a series of new substituted pyrazolyl benzoxazole derivative, which were synthesized from 4-fluorophenol, via a serial of reactions included chlorination, acylation, condensation, ring closure, methylation, nitration, and so on. All the structures are confirmed by ^{1}H NMR, MS and element analysis. Preliminary bioassay shows that most substituted pyrazolyl benzoxazole derivatives exhibit high herbicidal activity to the tested gramineous weeds and latifoliate weeds.

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INTRODUCTION

Herbicides play an important role in agricultural practices. In recent 30 years, herbicides targeting the enzyme protoporphyrinogen IX oxidase (Protox), which have been used commercially to control annual grasses and weeds in soybean, peanut, cotton, rice, and other crops, are developed rapidly [1–3], because this type of herbicides shows high bioactivity and low toxicity. Diphenyl ether (DPE) herbicides are the first widely used family of Protox inhibitor herbicides. Nitrofen was the leading compound of this kind [4].

The bicyclic nature of diphenyl ethers is similar to the structure of half of protoporphyrinogen IX, which allows competitive inhibition of Protox located in the plastid by occupying the binding site for protoporphyrinogen IX [5–7]. Besides, many other chemical structures belong to this family are reported, such as phenyl heterocycle (Heterocycle including triazolinone, oxazolidone, pyrazole, phthalamide, etc.) and benzoheterocycle. Many of them are commercial and of high bioactivity [8–11]. Some samples of commercial Protox inhibitors are shown in Figure 1.

As the development of Protox inhibitor, many benzoheterocyclic compounds have shown good herbicidal activity, which are effective at controlling grass and broadleaf weeds at low dose [12–14]. In recent years, benzoxazole derivatives were found to be high bioactivities [15–19]. Earlier work at our laboratory involved some pyrazole [20] and isoxazole [21] derivatives with high herbicidal activity. In this article, we described the syntheses and herbicidal activity of pyrazolyl benzoxazole derivatives. Preliminary bioassay showed that most of them had good herbicidal activity.

RESULTS AND DISCUSSION

The syntheses of the compounds are described in the Schemes 1 and 2, and the yields were not optimized. The intermediates **10a–10c** and **11a–11c** were synthesized from 4-fluorophenol, via a serial of reactions included chlorination, acylation, condensation, ring closure, methylation, nitration, and so on (Scheme 1). The title compounds can be obtained through the different ring-close and alkyl reactions from compounds **10a–10c** or **11a–11c** (Scheme 2).

The synthesis of **11** is the key step, which involves reducing nitro group to amino group in the phenyl ring. At the beginning, we used sodium sulfide to reduce nitro group, the yield was only 10%. We also used the method of catalytic hydrogenation with Pt/C, but the selectivity was not good. Finally, we found reduction of **10** with iron and saturated ammonium chloride has the higher yield (86%) and selectivity. For the product **11** is sensitive to air, reaction should be carried out under

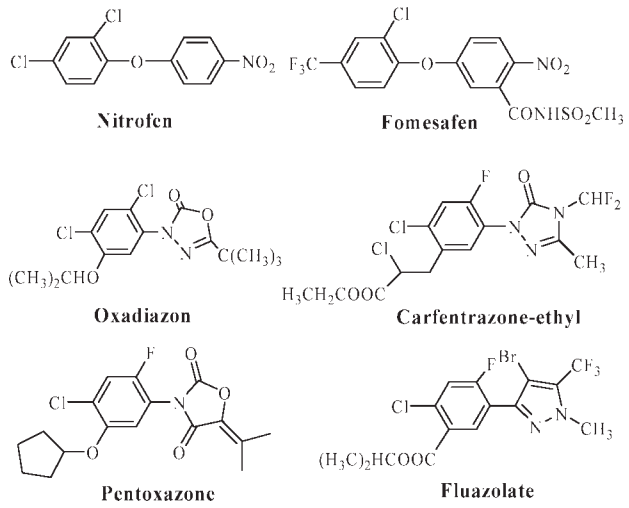


Figure 1. Samples of commercial protox inhibitors.

nitrogen, and the crude product is used directly in the next reaction without further purification.

13 can be synthesized by stirring the mixture of compounds **11** and acetyl chloride or acetic anhydride at room temperature, but the selectivity was not satisfied. So we changed to another pathway. At first, **10** was acetylation to form **12**, then **12** was reduced with iron and subjected to ring-closed in acetic acid. By that way **13** was made in good yield.

15 and **16** are isomers. The different reacting conditions lead to different products. When using base such as anhydrous potassium carbonate as the catalyst, and acetone as solvent, alkyl was attached to atom N. But when silver (I) oxide and methylene chloride were employed, alkyl was attached to atom O. The distinguishing of **15** and **16** can be determined by the shift of ^{1}H NMR. For example, **15a:** δ: 3.18 (s, 3H, NCH_3); **16a:** δ: 4.31 (s, 3H, OCH_3).

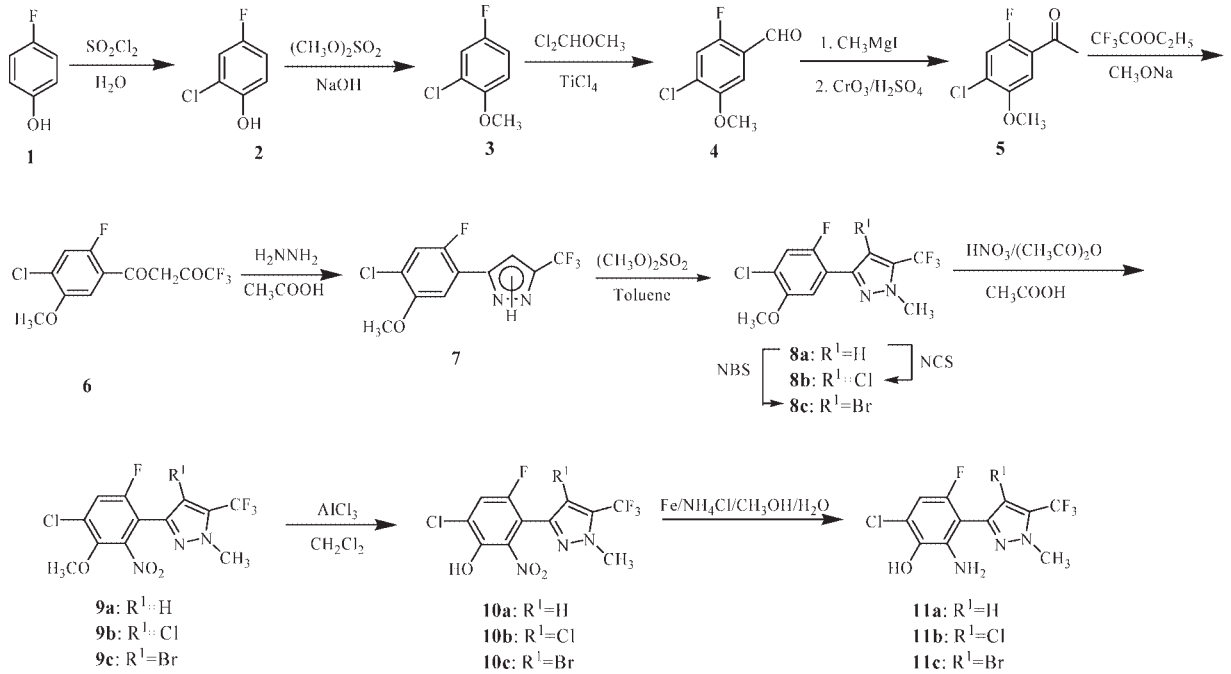
The herbicidal activity of the compounds were tested against *Setaria viridis, Ditaria sanguinalis* (monocot crops) and *Abutilon theophrasti* (dicot crops) using Fomesafen and Fluazolate for comparison. The results shown in Table 1 were the effect visual measurement treat after 10 days.

From Table 1 we can conclude that most of them had good herbicidal activity. When no substituent on pyrazole position 4, there is no herbicidal activity or low activity (**13a, 14a, 15a, 16a, 17a**), but when halogen (such as chlorine or bromine) is on pyrazole, most of them show good herbicidal efficacy. Similar results have been reported by Meazza *et al*. [22]. Their study on pyrroles showed that the halopyrrole nucleus is important for biological activity; if there is only hydrogen on pyrrole the compounds are virtually inactive.

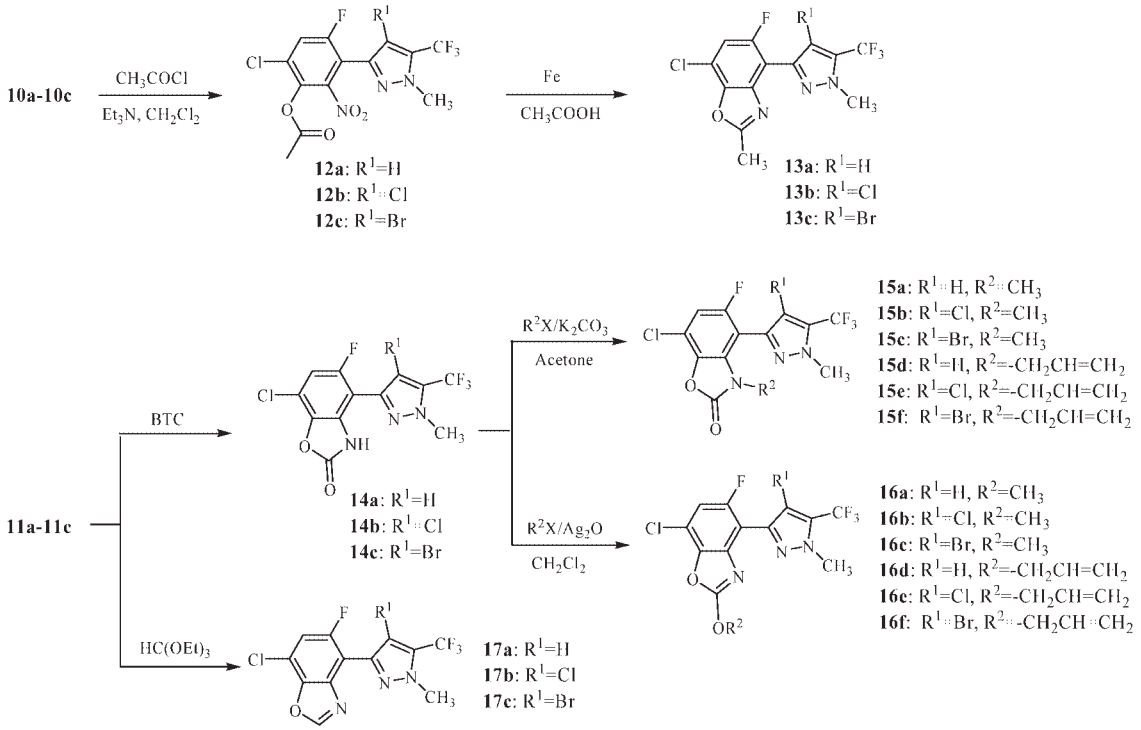
The herbicidal activity of compound **14** is not high, mainly because of its poor lipophilicity. When its lipophilicity is increased by introducing methyl or allyl to N or O atom, which form **15** or **16**, the activity is much increased.

Compared with corresponding compounds **15** (**b, c, e, f**) and **16** (**b, c, e, f**) , we can find that the herbicidal

Scheme 1. Syntheses of the intermediates.



Scheme 2. Syntheses of the aimed compounds.



activities of the compounds alkyl attached to atom O is higher than that of alkyl attached to atom N. And the activity of **16b** is all 100% even at the usage dose of 37.5 g/hm^2, so it is a valuable compound that fit for dicot crops and monocot crops. **15b** and **15e** are good for dicot crops, reached more than 80% at the usage

Table 1

Herbicidal activity of the title compounds.[a]

	Setaria viridis			*Ditaria sanguinalis*			*Abutilon theophrasti*		
Comp.	37.5[b]	150[b]	600[b]	37.5[b]	150[b]	600[b]	37.5[b]	150[b]	600[b]
13a	0	0	1	0	0	1	0	0	1
13b	4	7	8	5	7	8	6	6	7
13c	2	4	5	1	3	5	2	4	6
14a	0	0	0	0	0	0	0	0	0
14b	1	5	6	1	3	4	2	6	7
14c	0	1	2	0	1	2	1	3	4
15a	0	0	0	0	0	0	0	0	1
15b	1	3	8	1	4	8	9	10	10
15c	3	6	8	3	4	7	5	9	10
15e	2	4	5	2	5	6	8	10	10
15f	2	3	7	5	5	7	7	8	10
16a	1	2	4	3	3	5	3	6	9
16b	10	10	10	10	10	10	10	10	10
16c	10	10	10	9	10	10	10	10	10
16e	5	5	6	3	5	6	5	8	9
16f	8	10	10	8	10	10	10	10	10
17a	0	0	0	0	0	0	0	1	1
17b	3	7	9	5	6	9	7	10	10
17c	8	10	10	7	9	10	10	10	10
Fomesafen	4	9	10	4	9	10	6	9	10
Fluazolate	9	10	10	9	10	10	9	10	10

[a] 0 = no activity and 10 = total kill.
[b] The usage dose of compounds (g a.i./ hm^2).

dose of 37.5 g/hm^2, but for monocot crops, the activity not very high. The activity of **17c** is higher than **17b** for monocot crops, but for dicot crops, they are the same.

The activity of compounds **16b, 16c, 16f,** and **17c** is obviously higher than Fomesafen, **16b** and **16c** is even a little higher than Fluazolate.

EXPERIMENTAL

Melting points were taken on a Micro melting point apparatus (X-6, Beijing Tech Instrument Co. Ltd.) and were uncorrected. ^{1}H NMR spectra were measured in deuterochloroform on a Varian VA400 MHz spectrometer with TMS as an internal standard. Elemental analyses were performed on a Vario EL III (Elementar, German) elemental analysis instrumentation. MS were obtained with a HP1100 high Performance Liquid Chromatography/Mass Selective Detector.

8 were synthesized from 4-Fluorophenol according to the existing methods [23,24].

General procedure for 9a–9c. ***3-(4-Chloro-6-fluoro-3-methoxy-2-nitrophenyl)-1-methyl-5-trifluoromethyl-1H-pyrazole (9a)*** A mixed acid (27 mL, V(acetic anhydride): V(fuming nitric acid)= 2:1) was added dropwise to a solution of **8a** (8 g, 0.026 mol) in acetic acid (25 mL) while maintaining the reaction solution at 0°C, and the resulting mixture was stirred at 0°C for 2 h. The reaction solution was poured into water, filtrated, and washed with water. The crude product was recrystallized with ethanol. **9a** was obtained in 83% yield as a faint yellow solid; m.p. 94.0–96.0°C; MS (API-ES, positive), *m*/*z*: 354 ([M+H]$^+$); **^{1}H NMR**, δ: 7.37 (d, 1H, J = 9.6 Hz, Ph-*H*), 6.94 (d, 1H, J = 3.2 Hz, Pyr-*H*), 4.02 (s, 3H, Pyr-CH_3), 3.98 (s, 3H, OCH_3). Anal. Calcd. for $C_{12}H_8ClF_4N_3O_3$ (353.7): C, 40.75; H, 2.28; N, 11.88. Found: C, 40.87; H, 2. 35; N, 11.67.

4-Chloro-3-(4-chloro-6-fluoro-3-methoxy-2-nitrophenyl)-1-methyl-5-trifluoromethyl-1H-pyrazole (9b). The compound was orange pasty matter and was used directly in the next reaction without purification; MS (API-ES, positive), *m*/*z*: 388 ([M+H]$^+$); **^{1}H NMR**, δ: 7.42 (d, 1H, J = 7.6 Hz, Ph-*H*), 4.02 (s, 3H, Pyr-CH_3), 4.01 (s, 3H, OCH_3). Anal. Calcd. for $C_{12}H_7Cl_2F_4N_3O_3$ (388.1): C, 37.14; H, 1.82; N, 10.83. Found: C, 36.87; H, 1.63; N, 10.67.

4-Bromo-3-(4-chloro-6-fluoro-3-methoxy-2-nitrophenyl)-1-methyl-5-trifluoromethyl-1H-pyrazole (9c). The compound was orange pasty matter and was used directly in the next reaction without purification; MS (API-ES, positive), *m*/*z*: 432 ([M+H]$^+$); **^{1}H NMR**, δ: 7.42 (d, 1H, J = 7.6 Hz, Ph-*H*), 4.03 (s, 3H, Pyr-CH_3), 4.01 (s, 3H, OCH_3). Anal. Calcd. for $C_{12}H_7BrClF_4N_3O_3$ (432.6): C, 33.32; H, 1.63; N, 9.71. Found: C, 32.99; H, 1.60; N, 9.62.

General procedure for 10a-10c. ***6-Chloro-4-fluoro-3-(1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-2-nitrophenol (10a).*** A mixture of **9a** (3.9 g, 11 mmol), anhydrous aluminium chloride (3.7 g, 27.7 mmol) and dichloromethane (70 mL) were stirred at room temperature for 2 h. The reaction solution was poured into icy hydrochloric acid and extracted with dichloromethane (20 mL × 3). The combined organic layer was washed with water, dried over anhydrous magnesium sulfate and concentrated under vacuum. **10a** was obtained in 100% yield as a yellow powder and was used directly in the next reaction without purification. A sample suiting for analysis was obtained by recrystallization with a mixture of petroleum ether and ethyl acetate (3:1); m.p. 94.0–97.0°C; MS (API-ES, negative), *m*/*z*: 338 ([M-H]$^-$); ^{1}H NMR, δ: 7.53 (d, 1H, J = 9.6 Hz, Ph-*H*), 6.95 (d, 1H, J = 3.2 Hz, Pyr-*H*), 4.01 (s, 3H, Pyr-CH_3). Anal. Calcd. for $C_{11}H_6ClF_4N_3O_3$ (339.6): C, 38.90; H, 1.78; N, 12.37. Found: C, 38.84; H, 1.71; N, 12.42.

6-Chloro-3-(4-chloro-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-4-fluoro-2-nitrophenol (10b). The compound was a light yellow powder and was used directly in the next reaction without purification. The yield of two steps was 82%. A sample suiting for analysis was obtained by recrystallization with a mixture of petroleum ether and ethyl acetate (3:1); m.p. 85.2–87.1°C; MS (API-ES, negative), *m*/*z*: 372 ([M-H]$^-$); **^{1}H NMR**, δ: 7.58 (d, 1H, J = 8.4 Hz, Ph-*H*), 4.03 (s, 3H, Pyr-CH_3). Anal. Calcd. for $C_{11}H_5Cl_2F_4N_3O_3$ (374.1): C, 35.32; H, 1.35; N, 11.23. Found: C, 35.64; H, 1.43; N, 11.42.

3-(4-Bromo-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-6-chloro-4-fluoro-2-nitrophenol (10c). The compound was a yellow powder and was used directly in the next reaction without purification. The yield of two steps was 83%. A sample suiting for analysis was obtained by recrystallization with a mixture of petroleum ether and ethyl acetate (3:1); m.p. 86.3–88.6°C; MS (API-ES, negative), *m*/*z*: 416 ([M-H]$^-$); **^{1}H NMR**, δ: 7.58 (d, 1H, J = 8.4 Hz, Ph-*H*), 4.04 (s, 3H, Pyr-CH_3). Anal. Calcd. for $C_{11}H_5BrClF_4N_3O_3$ (418.5): C, 31.57; H, 1.20; N, 10.04. Found: C, 31.69; H, 1.23; N, 10.25.

General procedure for 11a–11c. ***2-Amino-6-chloro-4-fluoro-3-(1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)phenol (11a).*** Under nitrogen a mixture of **10a** (3.7 g, 10.9 mmol), iron (3.8 g, 0.068 mol), a solution of saturated ammonium chloride (120 mL) and methanol (80 mL) were stirred at 55°C for 6 h. Then methanol was removed under vacuum. The reaction solution was filtrated and the filtrate was extracted with ethyl acetate (40 mL × 3). The combined organic layer was washed with water, dried over anhydrous magnesium sulfate and concentrated under vacuum. **11a** was obtained in 86% yield as a brown solid and was used directly in the next reaction without purification.

2-Amino-6-chloro-3-(4-chloro-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-4-fluorophenol (11b). The crude product was obtained as brown paste and was used directly in the next reaction without purification. The yield of crude product was 95%.

2-Amino-3-(4-bromo-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-6-chloro-4-fluorophenol (11c). The crude product was obtained as brown paste and was used directly in the next reaction without purification. The yield of crude product was 90%.

General procedure for 12a–12c. ***6-Chloro-4-fluoro-3-(1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-2-nitrophenyl acetate (12a).*** A mixture of **10a** (650 mg, 1.91 mmol), acetyl chloride (0.2 mL, 2.96 mmol), triethylamine (0.3 mL, 2.16 mmol) and methylene chloride (25 mL) was stirred at 40°C for 1 h. The reaction solution was poured into water. The organic layer was washed with a solution of 5% sodium bicarbonate and water, dried over anhydrous magnesium sulfate and concentrated under vacuum. The crude product was recrystallized with ethanol. **12a** was obtained in 85% yield as a white powder; m.p. 137.5–139.2°C; MS (API-ES, positive), *m*/*z*: 382 ([M+H]$^+$), 404 ([M+Na]$^+$); **^{1}H NMR** δ: 7.45 (d, J = 9.6 Hz, 1H, Ph-*H*),

6.95 (d, J = 3.2 Hz, 1H, Pyr-*H*), 4.00 (s, 3H, Pyr-CH_3), 2.36 (s, 3H, COCH_3). Anal. Calcd. for $C_{13}H_8ClF_4N_3O_4$ (381.7): C, 40.91; H, 2.11; N, 11.01. Found: C, 40.62; H, 2.20; N, 11.25.

6-Chloro-3-(4-chloro-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-4-fluoro-2-nitrophenyl acetate (12b). The compound was obtained in 75% yield as a light brown powder; m.p. 103.8–105.3°C; MS (API-ES, positive), *m*/*z*: 416 ([M+H]$^+$), 438 ([M+Na]$^+$); **^{1}H NMR** δ: 7.51 (d, J = 8.4 Hz, 1H, Ph-*H*), 4.02 (s, 3H, Pyr-CH_3), 2.37 (s, 3H, COCH_3). Anal. Calcd. for $C_{13}H_7Cl_2F_4N_3O_4$ (416.1): C, 37.52; H, 1.70; N, 10.10. Found: C, 37.69; H, 1.73; N, 10.27.

3-(4-Bromo-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-6-chloro-4-fluoro-2-nitrophenyl acetate (12c). The compound was obtained in 72% yield as a brown powder; m.p. 107.9–109.0°C; MS (API-ES, positive), *m*/*z*: 460 ([M+H]$^+$); **^{1}H NMR** δ: 7.51 (d, J = 8.0 Hz, 1H, Ph-*H*), 4.04 (s, 3H, Pyr-CH_3), 2.37 (s, 3H, COCH_3). Anal. Calcd. for $C_{13}H_7BrClF_4N_3O_4$ (460.6): C, 33.90; H, 1.53; N, 9.12. Found: C, 34.02; H, 1.68; N, 8.91.

General procedure for 13a–13c. ***7-chloro-5-fluoro-2-methyl-4-(1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-benzoxazole (13a).*** Under nitrogen a mixture of **12a** (680 mg, 1.78 mmol), iron (1.0 g, 0.017 mol), and acetic acid (35 mL) were stirred at 80°C for 3 h. The reaction solution was filtrated and the filtrate was poured into water, filtrated, and washed with water, recrystallized with ethanol. **13a** was obtained in 74% yield as a white solid; m.p. 124.9–126.9°C; MS (API-ES, positive), *m*/*z*: 334 ([M+H]$^+$), 356 ([M+Na]$^+$); **^{1}H NMR** δ: 7.27 (s, 1H, Pyr-*H*), 7.21 (d, J = 10.8 Hz, 1H, Ph-*H*), 4.14 (s, 3H, Pyr-CH_3), 2.73 (s, 3H, Oxa-CH_3). Anal. Calcd. for $C_{13}H_8ClF_4N_3O$ (333.7): C, 46.79; H, 2.42; N, 12.59. Found: C, 46.84; H, 2.41; N, 12.72.

7-Chloro-4-(4-chloro-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-5-fluoro-2-methyl-benzoxazole (13b). The compound was obtained in 70% yield as a light yellow paste; MS (API-ES, positive), *m*/*z*: 368 ([M+H]$^+$), 390 ([M+Na]$^+$); **^{1}H NMR** δ: 7.23 (d, J = 9.6 Hz, 1H, Ph-*H*), 4.11 (s, 3H, Pyr-CH_3), 2.70 (s, 3H, Oxa-CH_3). Anal. Calcd. for $C_{13}H_7Cl_2F_4N_3O$ (368.1): C, 42.42; H, 1.92; N, 11.41. Found: C, 42.53; H, 1.94; N, 11.40.

4-(4-Bromo-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-7-chloro-5-fluoro-2-methyl-benzoxazole (13c). The compound was obtained in 74% yield as a white powder; m.p. 139.4–140.9°C; MS (API-ES, positive), *m*/*z*: 412 ([M+H]$^+$); **^{1}H NMR** δ: 7.23 (d, J = 9.6 Hz, 1H, Ph-*H*), 4.13 (s, 3H, Pyr-CH_3), 2.70 (s, 3H, Oxa-CH_3). Anal. Calcd. for $C_{13}H_7BrClF_4N_3O$ (412.6): C, 37.85; H, 1.71; N, 10.19. Found: C, 38.08; H, 1.71; N, 10.32.

General procedure for 14a–14c. ***7-Chloro-5-fluoro-4-(1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-3H-benzoxazol-2-one (14a).*** A solution of **11a** (600 mg, 1.94 mmol) in toluene (6 mL) was added dropwise to a solution of triphosgene (210 mg, 0.71 mmol) in toluene (2 mL). After the reaction solution was stirred at room temperature for 1 h, triethylamine (0.2 mL) was added. Stirred for 0.5 h, the reaction solution was poured into water. The organic layer was washed with a solution of 5% sodium bicarbonate and water, dried over anhydrous magnesium sulfate and concentrated under vacuum. After recrystallization with ethanol, **14a** was obtained in 69% yield as a light brown powder; m.p. 213.6–215.2°C; MS (API-ES, positive), *m*/*z*: 336 ([M+H]$^+$), 358 ([M+Na]$^+$); **^{1}H NMR** δ: 9.48 (s, 1H, N-*H*), 7.16 (d, J = 3.6 Hz, 1H, Pyr-*H*), 6.97 (d, J = 11.6 Hz, 1H, Ph-*H*), 4.11 (s, 3H, Pyr-CH_3). Anal. Calcd. for $C_{12}H_6ClF_4N_3O_2$ (335.6): C, 42.94; H, 1.80; N, 12.52. Found: C, 43.12; H, 1.95; N, 12.58.

7-Chloro-4-(4-chloro-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-5-fluoro-3H-benzoxazol-2-one (14b). The compound was obtained in 59% yield as a white powder; m.p. 217.2–218.5°C; MS (API-ES, positive), *m*/*z*: 392 ([M+Na]$^+$); **^{1}H NMR** δ: 8.86 (s, 1H, N-*H*), 7.01 (d, J = 10.4 Hz, 1H, Ph-*H*), 4.13 (s, 3H, Pyr-CH_3). Anal. Calcd. for $C_{12}H_5Cl_2F_4N_3O_2$ (370.1): C, 38.94; H, 1.36; N, 11.35. Found: C, 38.78; H, 1.42; N, 11.36.

4-(4-Bromo-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-7-chloro-5-fluoro-3H-benzoxazol-2-one (14c). The compound was obtained in 84% yield as a brown powder; m.p. 217.1–219.8°C; MS (API-ES, negative), *m*/*z*: 412 ([M-H]$^-$), 450 ([M+Cl]$^-$); **^{1}H NMR** δ: 8.67 (s, 1H, N-*H*), 7.01 (d, J = 10.4 Hz, 1H, Ph-*H*), 4.15 (s, 3H, Pyr-CH_3). Anal. Calcd. for $C_{12}H_5BrClF_4N_3O_2$ (414.5): C, 34.77; H, 1.22; N, 10.14. Found: C, 35.03; H, 1.31; N, 10.32.

General procedure for 15a–15f. A mixture of Compound **14a** (600 mg, 1.62 mmol), a small amount of anhydrous potassium carbonate, dimethyl sulfate (0.5 mL, 5 mmol) or bromoallylene (0.3 mL, 3.1 mmol)and acetone (15 mL) was stirred at ambient temperature for 3 h. The reaction solution was poured into water and extracted with ethyl acetate (10 mL × 3). The combined organic layer was washed with water, dried over anhydrous magnesium sulfate and concentrated under vacuum. The crude product was purified by silica gel chromatography with eluent (petroleum ether:ethyl acetate = 6:1).

7-Chloro-5-fluoro-3-methyl-4-(1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-3H-benzoxazol-2-one (15a). The Compound was obtained in 34% yield as a light yellow powder; m.p. 194–198°C; MS (API-ES, positive), *m*/*z*: 350 ([M+H]$^+$), 372 ([M+Na]$^+$); **^{1}H NMR** δ: 6.97 (d, J = 10.0 Hz, 1H, Ph-*H*), 6.85 (s, 1H, Pyr-*H*), 4.09 (s, 3H, Pyr-CH_3), 3.18 (s, 3H, NCH_3). Anal. Calcd. for $C_{13}H_8ClF_4N_3O_2$ (349.7): C, 44.65; H, 2.31; N, 12.02. Found: C, 44.58; H, 2.45; N, 12.01.

7-Chloro-4-(4-chloro-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-5-fluoro-3-methy-3H-benzoxazol-2-one (15b). The compound was obtained in 29% yield as a light brown powder; m.p. 103.1–104.8°C; MS (API-ES, positive), *m*/*z*: 384 ([M+H]$^+$), 406 ([M+Na]$^+$); **^{1}H NMR** δ: 7.00 (d, J = 10.0 Hz, 1H, Ph-*H*), 4.11 (s, 3H, Pyr-CH_3), 3.08 (s, 3H, NCH_3). Anal. Calcd. for $C_{13}H_7Cl_2F_4N_3O_2$ (384.1): C, 40.65; H, 1.84; N, 10.94. Found: C, 40.97; H, 2.00; N, 10.28.

4-(4-Bromo-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-7-chloro-5-fluoro-3-methy-3H-benzoxazol-2-one (15c). The compound was obtained in 28% yield as a light yellow powder; m.p. 126.8–128.9°C; MS (API-ES, positive), *m*/*z*: 428 ([M+H]$^+$), 450 ([M+Na]$^+$); **^{1}H NMR** δ: 6.99 (d, J = 9.6 Hz, 1H, Ph-*H*), 4.13 (s, 3H, Pyr-CH_3), 3.05 (s, 3H, NCH_3). Anal. Calcd. for $C_{13}H_7BrClF_4N_3O_2$ (428.6): C, 36.43; H, 1.65; N, 9.80. Found: C, 36.46; H, 1.68; N, 9.55.

3-Allyl-7-chloro-5-fluoro-4-(1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-3H-benzoxazol-2-one (15d). The compound was obtained in 33% yield as a white powder; m.p. 93.3–95.2°C; MS (API-ES, positive), *m*/*z*: 376 ([M+H]$^+$), 398 ([M+Na]$^+$); **^{1}H NMR** δ: 6.98 (d, J = 10.0 Hz, 1H, Ph-*H*), 6.80 (s, 1H, Pyr-*H*), 5.44 (m, 1H, C*H*=CH$_2$), 4.96 (d, J = 10.4 Hz, 1H, 1/2 CH_2=), 4.68 (d, J = 17.2 Hz, 1H, 1/2 CH_2=), 4.47 (d, J =

5.2 Hz, 2H, N-CH_2), 4.09 (s, 3H, Pyr-CH_3). Anal. Calcd. for $C_{15}H_{10}ClF_4N_3O_2$ (375.7): C, 47.95; H, 2.68; N, 11.18. Found: C, 48.11; H, 2.69; N, 11.09.

3-Allyl-7-chloro-4-(4-chloro-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-5-fluoro-3H-benzoxazol-2-one (15e). The compound was obtained in 36% yield as a light brown powder; m.p. 89.4–91.3°C; MS (API-ES, positive), *m*/*z*: 410 ([M+H]$^+$), 432 ([M+Na]$^+$); **^{1}H NMR** δ: 7.02 (d, *J* = 10.0 Hz, 1H, Ph-*H*), 5.44 (m, 1H, C*H*=CH$_2$), 4.99 (d, *J* = 10.4 Hz, 1H, 1/2 CH_2=), 4.67 (d, *J* = 16.8 Hz, 1H, 1/2 CH_2=), 4.31 (d, *J* = 17.2 Hz, 2H, N-CH_2), 4.10 (s, 3H, Pyr-CH_3). Anal. Calcd. for $C_{15}H_9Cl_2F_4N_3O_2$ (410.2): C, 43.93; H, 2.21; N, 10.25. Found: C, 44.33; H, 2.49; N, 9.86.

3-Allyl-4-(4-bromo-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-7-chloro-5-fluoro-3H-benzoxazol-2-one (15f). The compound was obtained in 42% yield as a white powder; m.p. 130.2–132.0°C; MS (API-ES, positive), *m*/*z*: 454 ([M+H]$^+$), 476 ([M+Na]$^+$); **^{1}H NMR** δ: 7.01 (d, *J* = 9.6 Hz, 1H, Ph-*H*), 5.42 (m, 1H, C*H*=CH$_2$), 5.00 (d, *J* = 10.4 Hz, 1H, 1/2 CH_2=), 4.69 (d, *J* = 16.8 Hz, 1H, 1/2 CH_2=), 4.37 (m, 1H,1/2 N-CH_2), 4.19 (m, 1H,1/2 N-CH_2), 4.12 (s, 3H, Pyr-CH_3). Anal. Calcd. for $C_{15}H_9BrClF_4N_3O_2$ (454.6): C, 39.63; H, 2.00; N, 9.24. Found: C, 39.41; H, 1.98; N, 9.19.

General procedure for 16a–16f. A mixture of **14a** (600 mg, 1.62 mmol), methyl iodide (0.51 g, 3 mmol), and sliver(I) oxide (417 mg, 1.80 mmol) in methylene chloride (50 mL) was stirred at ambient temperature for 24 h. Sliver(I) oxide was filtered and filtrate was concentrated under vacuum. The crude product was purified by silica gel chromatography with eluent (petroleum ether:ethyl acetate = 6:1).

7-Chloro-5-fluoro-2-methoxy-4-(1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-benzoxazole (16a). The compound was obtained in 42% yield as a light yellow powder; m.p. 129.7–132.1°C; MS (API-ES, positive), *m*/*z*: 350 ([M+H]$^+$), 372 ([M+Na]$^+$); **^{1}H NMR** δ: 7.31 (s, 1H, Pyr-*H*), 7.08 (d, *J* = 11.6 Hz, 1H, Ph-*H*), 4.31 (s, 3H, OCH_3), 4.12 (s, 3H, Pyr-CH_3). Anal. Calcd. for $C_{13}H_8ClF_4N_3O_2$ (349.7): C, 44.65; H, 2.31; N, 12.02. Found: C, 44.58; H, 2.45; N, 12.01.

7-Chloro-4-(4-chloro-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-5-fluoro-2-methoxy-benzoxazole (16b). The compound was obtained in 19% yield as a light yellow pasty matter. MS (API-ES, positive), *m*/*z*: 384 ([M+H]$^+$), 406 ([M+Na]$^+$); **^{1}H NMR** δ: 7.08 (d, *J* = 10.0 Hz, 1H, Ph-*H*), 4.24 (s, 3H, OCH_3), 4.10 (s, 3H, Pyr-CH_3). Anal. Calcd. for $C_{13}H_7Cl_2F_4N_3O_2$ (384.1): C, 40.65; H, 1.84; N, 10.94. Found: C, 40.41; H, 1.89; N, 10.51.

4-(4-Bromo-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-7-chloro-5-fluoro-2-methoxy-benzoxazole (16c). The compound was obtained in 45% yield as a light yellow pasty matter. MS (API-ES, positive), *m*/*z*: 428 ([M+H]$^+$), 450 ([M+Na]$^+$); **^{1}H NMR** δ: 7.08 (d, *J* = 10.0 Hz, 1H, Ph-*H*), 4.24 (s, 3H, OCH_3), 4.13 (s, 3H, Pyr-CH_3). Anal. Calcd. for $C_{13}H_7BrClF_4N_3O_2$ (428.6): C, 36.43; H, 1.65; N, 9.80. Found: C, 36.73; H, 1.79; N, 9.58.

2-(Allyloxy)-7-chloro-5-fluoro-4-(1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)benzoxazole (16d). The compound was obtained in 19% yield as a white powder; m.p. 122.4–123.4°C; MS (API-ES, positive), *m*/*z*: 376 ([M+H]$^+$), 398 ([M+Na]$^+$); **^{1}H NMR** δ: 7.32 (s, 1H, Pyr-*H*), 7.08 (d, *J* = 11.2 Hz, 1H, Ph-*H*), 6.09 (m, 1H, C*H*=CH$_2$), 5.55 (d, *J* = 16.8 Hz, 1H, 1/2 CH_2=), 5.42 (d, *J* = 10.4 Hz, 1H, 1/2 CH_2=), 5.13 (d, *J* = 6.0 Hz, 2H, O-CH_2), 4.11 (s, 3H, Pyr-CH_3). Anal. Calcd. for $C_{15}H_{10}ClF_4N_3O_2$ (375.7): C, 47.95; H, 2.68; N, 11.18. Found: C, 48.24; H, 2.86; N, 10.79.

2-(Allyloxy)-7-chloro-4-(4-chloro-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-5-fluoro-benzoxazole (16e). The compound was obtained in 13% yield as transparent pasty matter. MS (API-ES, positive), *m*/*z*: 410 ([M+H]$^+$); **^{1}H NMR** δ: 7.08 (d, *J* = 10.0 Hz, 1H, Ph-*H*), 6.05 (m, 1H, C*H*=CH$_2$), 5.50 (d, *J* = 14.8 Hz, 1H, 1/2 CH_2=), 5.39 (d, *J* = 9.6 Hz, 1H, 1/2 CH_2=), 5.05 (d, *J* = 6.0 Hz, 2H, O-CH_2), 4.10 (s, 3H, Pyr-CH_3). Anal. Calcd. for $C_{15}H_9Cl_2F_4N_3O_2$ (410.2): C, 43.93; H, 2.21; N, 10.25. Found: C, 44.00; H, 2.07; N, 9.84.

2-(Allyloxy)-4-(4-bromo-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-7-chloro-5-fluoro-benzoxazole (16f). The compound was obtained in 16% yield as transparent pasty matter. MS (API-ES, positive), *m*/*z*: 454 ([M+H]$^+$), 476 ([M+Na]$^+$); **^{1}H NMR** δ: 7.08 (d, *J* = 10.0 Hz, 1H, Ph-*H*), 6.06 (m, 1H, C*H*=CH$_2$), 5.50 (d, *J* = 17.2 Hz, 1H, 1/2 CH_2=), 5.38 (d, *J* = 10.4 Hz, 1H, 1/2 CH_2=), 5.05 (d, *J* = 6.0 Hz, 2H, O-CH_2), 4.12 (s, 3H, Pyr-CH_3). Anal. Calcd. for $C_{15}H_9BrClF_4N_3O_2$ (454.6): C, 39.63; H, 2.00; N, 9.24. Found: C, 39.72; H, 1.93; N, 9.09.

General procedure for 17a–17c. ***7-Chloro-5-fluoro-4-(1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)benzoxazole (17a).*** A mixture of **11a** (500 mg, 1.62 mmol), ethylorthoformate (0.4 mL, 2.42 mmol), Celite (160 mg) and toluene (15 mL) was stirred under nitrogen at 110°C for 18 h. Celite was filtered and filtrate was concentrated under vacuum. The crude product was purified by silica gel chromatography with eluent (petroleum ether:ethyl acetate = 6:1). **17a** was obtained in 42% yield as a light yellow powder; m.p. 158.3–160.5°C; MS (API-ES, positive), *m*/*z*: 320 ([M+H]$^+$), 342 ([M+Na]$^+$); **^{1}H NMR** δ: 8.25 (s, 1H, Oxa-*H*), 7.35 (s, 1H, Pyr-*H*), 7.33 (d, *J* = 10.0 Hz, 1H, Ph-*H*), 4.15 (s, 3H, Pyr-CH_3). Anal. Calcd. for $C_{12}H_6ClF_4N_3O$ (319.6): C, 45.09; H, 1.89; N, 13.15. Found: C, 45.42; H, 2.04; N, 12.75.

7-Chloro-4-(4-chloro-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-5-fluoro-benzoxazole (17b). The compound was obtained in 30% yield as a light brown powder; m.p. 110.7–112.1°C; MS (API-ES, positive), *m*/*z*: 354 ([M+H]$^+$); **^{1}H NMR** δ: 8.22 (s, 1H, Oxa-*H*), 7.35 (d, *J* = 9.6 Hz, 1H, Ph-*H*), 4.13 (s, 3H, Pyr-CH_3). Anal. Calcd. for $C_{12}H_5Cl_2F_4N_3O$ (354.1): C, 40.70; H, 1.42; N, 11.87. Found: C, 40.34; H, 1.67; N, 11.54.

4-(4-Bromo-1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-7-chloro-5-fluoro-benzoxazole (17c). The compound was obtained in 23% yield as a light yellow powder; m.p. 92.1–93.3°C; MS (API-ES, positive), *m*/*z*: 398 ([M+H]$^+$); **^{1}H NMR** δ: 8.21 (s, 1H, Oxa-*H*), 7.35 (d, *J* = 9.6 Hz, 1H, Ph-*H*), 4.14 (s, 3H, Pyr-CH_3). Anal. Calcd. for $C_{12}H_5BrClF_4N_3O$ (398.5): C, 36.16; H, 1.26; N, 10.54. Found: C, 36.43; H, 1.56; N, 10.45.

Herbicidal activity test. The target plants for the test were *Setaria viridis* (Linn.), *Digitaria sanguinalis* (Linn.) Scop. and *Abutilon theophrasti* Medic.A solution of new compounds or check sample (Fomesafen or Fluazolate) in a small amount of acetone was diluted with stewing tap water which containing 0.1% Tween 80. The solution of the compound to be tested was prepared. Weeds (*Setaria viridis* (Linn.), *Digitaria sanguinalis* (Linn.) Scop. and *Abutilon theophrasti* Medic., two or three leaf stage) which growth well and the same leaf stage were selected, and were spray treated with atomizing machine. The amount of spray was 600 L/hm^2. After that the weeds

were aeration-drying and then were cultured at room temperature. Weeds treated with water were the blank test. The herbicidal activity of the compounds was determined after 10 days of treatment. Evaluations were based on a score of 0–10 in which 0 = no activity and 10 = total kill.

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