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Design, Synthesis, Bioactivity, and Structure−Activity Relationship (SAR) Studies of Novel Benzoylphenylureas Containing Oxime Ether Group

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Novel benzoylphenylureas containing an oxime ether group were designed and synthesized by four schemes. These benzoylphenylureas were identified by ^{1}H NMR spectroscopy and element analysis (or HRMS). The bioactivities of the new compounds were evaluated. These benzoylphenylureas exhibited excellent larvicidal activities against oriental armyworm, some of which were much better in comparison with the commercial Flucycloxuron. In particular, the larvicidal activities against oriental armyworm of compounds **1** and **23** were 5−10 times better than that of Flucycloxuron. Most of these benzoylphenyureas exhibited excellent larvicidal activities against mosquito. At the same time, some of these compounds have good plant growth regulatory activities as well.

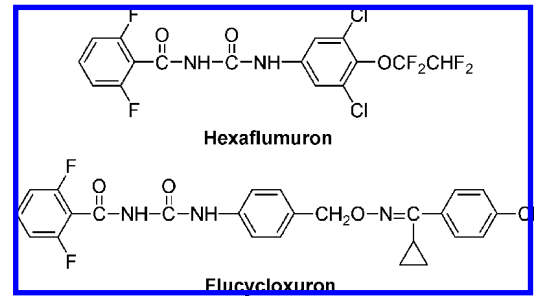
KEYWORDS: Benzoylphenylureas (BPUs); oxime ether; larvivdal activity; plant growth regulatory activity; insect growth regulator; Flucycloxuron

INTRODUCTION

Benzoylphenylureas (BPUs) have been developed as chitin synthesis inhibitor since Dimilin (diflubenzuron) was introduced in the market. A unique mode of action coupled with a high degree of activity on targeted pests and low toxicity to nontarget organisms (including many beneficial arthropods) make benzoylphenylureas a new tool for integrated pest management (IPM) (*1, 2*). Dow AgroSciences LLC won the 2000 "Presidential Green Chemistry Challenge" award for the innovation of Sentricon Termite Colony Elimination System, a new paradigm for termite control, which contains Hexaflumuron as a major active ingredient (*3*). Because of the above advantages, benzoylphenylureas have attracted considerable attention for decades (*4*−*10*).

The oxime ether group is a highly efficient pharmacophore and is widely used in pesticide and drug molecular design. For example, Flucycloxuron discovered by Solvay-Duphar B.V. as insect growth regulator contains an oxime ether group (*11*).

Bioisosterism is an effective way to design bioactive compounds (*12*). A series of general structure **A** first reported by Bayer AG showed high larvicidal activity against pests of *Lepidoptera* and *Hemiptera* (*13*−*16*). Consequently, we designed the general structure **C** through bioisosterism and QSAR (*17*) of benzoylphenylureas. At first, compounds **1** and **2** were synthesized in our laboratory. The results of insecticidal activity showed that compound **1** exhibited much better larvicidal activity against oriental armyworm than compound **2**. For optimizing the active compound **1**, a series of novel benzoylphenylureas containing the oxime ether group were synthesized, and some of them exhibited excellent larvicidal activities against oriental armyworm and mosquito. Interestingly, some compounds showed good plant growth regulatory activities. Herein, we report the synthesis, bioactivity, and SAR of these benzoylphenylureas containing an oxime ether group (**C**) as shown in **Schemes 1**−**5**.



MATERIALS AND METHODS

Instruments. ^{1}H NMR spectra were obtained at 300 MHz using a Bruker AC-P300 spectrometer or at 400 MHz using a Varian Mercury Plus 400 spectrometer in $CDCl_3$ solution with tetramethylsilane as the internal standard. Chemical shift values (δ) are given in parts per million. Elemental analyses were determined on a Yanaca CHN Corder MT-3 elemental analyzer. HRMS data were obtained on an FTICR-MS instrument (Ionspec7.0T). The melting points were determined on an X-4

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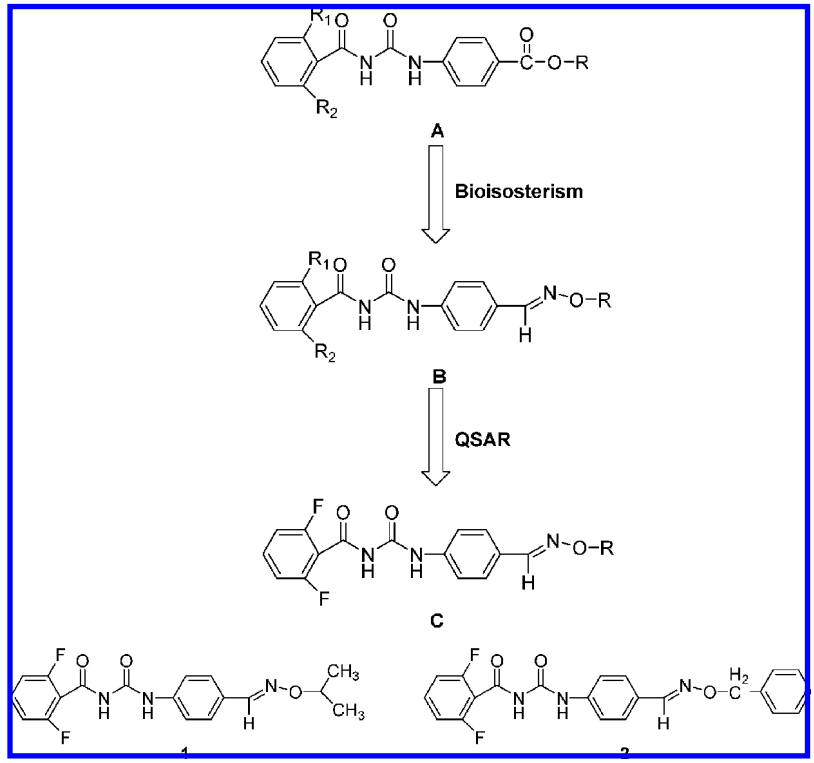


binocular microscope melting point apparatus (Beijing Tech Instruments Co., Beijing, China) and are uncorrected. Yields were not optimized.

General Synthesis. The reagents were all analytically or chemically pure. All anhydrous solvents were dried and purified by standard techniques prior to use. 2,6-Difluorobenzoyl isocyanate was prepared according to the method in the literature (*18*).

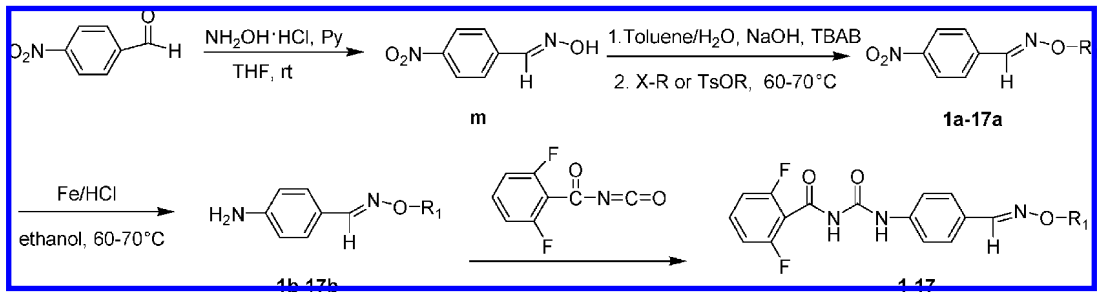
General Synthetic Procedure for the Target Compounds 1−17 (Scheme 1). *Synthesis of (E)-4-Nitrobenzaldehyde Oxime (**m**).* To a mixture of 4-nitrobenzaldehyde (12.08 g, 80 mmol) and hydroxylamine hydrochloride (6.68 g, 96 mmol) in tetrahydrofuran (80 mL) was added dropwise a solution of pyridine (7.58 g, 96 mmol) in tetrahydrofuran (10 mL). Then the mixture was stirred at room temperature. When the reaction was complete, most of the tetrahydrofuran was removed by vacuum distillation, and water was added. The mixture was extracted by ethyl acetate (40 mL × 2). The organic extract was washed with saturated brine (40 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to give a yellow solid. Recrystallization from a mixture of ethyl acetate and petroleum ether (60−90 °C) gave the desired compound **m** as a pale yellow acicular crystal (12.30 g, 92.5%): mp, 135−136 °C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 8.25 (d, 2H, $^3J_{HH}$ = 8.9 Hz, Ar−H), 8.21 (s, 1H, CH═N), 7.82 (s, 1H, N−OH), 7.75 (d, 2H, $^3J_{HH}$ = 8.9 Hz, Ar−H).

*Synthesis of (E)-O-Isopropyl-4-nitrobenzaldehyde Oxime (**1a**).* A mixture of compound **m** (4.98 g, 30 mmol), tetrabutylammonium bromide (TBAB, 1.00 g), NaOH (1.80 g, 45 mmol), toluene (100 mL), and water (20 mL) was heated to 60−70 °C. Then a solution of 2-iodopropane (6.12 g, 36 mmol) in toluene (20 mL) was added dropwise, and the mixture was stirred for 3 h. When the reaction was complete, water (40 mL) was added. The organic layer was washed with saturated brine (50 mL) and dried over anhydrous magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure to give a crude product, which was purified by flash column chromatography on silica gel using a mixture of petroleum ether (60−90 °C) and ethyl acetate (v/v = 10:1) as the eluent to obtain compound **1a** as a yellow solid (5.76 g, 92.3%): mp, 55−56 °C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 8.23 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar−H), 8.10 (s, 1H, CH═N), 7.75 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar−H), 4.50 (septet, 1H, $^3J_{HH}$ = 6.3 Hz, O*CH*$(CH_3)_2$), 1.33 (d, 6H, $^3J_{HH}$ = 6.3 Hz, OCH*$(CH_3)_2$*).

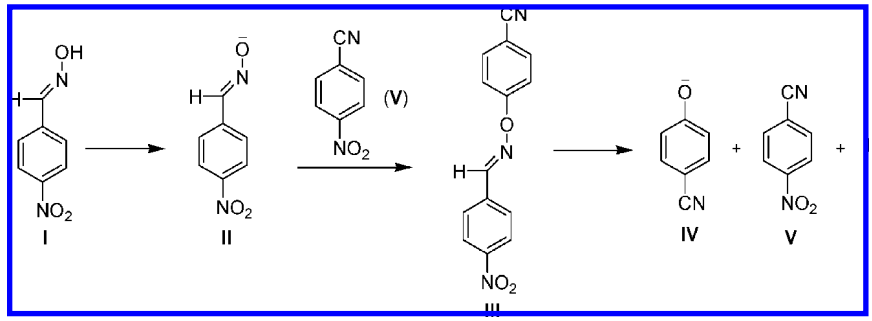
*Synthesis of (E)-O-Isopropyl-4-aminobenzaldehyde Oxime (**1b**).* Compound **1a** (0.62 g, 3 mmol) was dissolved in ethanol (10 mL) and heated to 60−70 °C. Then water (2 mL), concentrated HCl (five drops), and iron powder (0.65 g, 10 mmol) were added. The solution was cooled to room temperature when the reaction was complete. The pH of the reaction mixture was adjusted to near 9 and filtered. To the filtrate was added water (10 mL), and the mixture was extracted by diethyl ether (10 mL × 2). The extract was dried over anhydrous magnesium sulfate and filtered. After removal of the solvent, the residue was purified by flash column chromatography on silica gel using a mixture of petroleum ether (60−90 °C) and ethyl acetate (v/v = 3:1) as the eluent to give compound **1b** as an orange red oil (0.39 g, 73.6%): ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.96 (s, 1H, CH═N), 7.39 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar−H), 6.64 (d, 2H, $^3J_{HH}$ = 8.6 Hz, Ar−H), 4.40 (septet, 1H, $^3J_{HH}$ = 6.2 Hz, O*CH*$(CH_3)_2$), 3.28 (br s, 2H, NH_2), 1.28 (d, 6H, $^3J_{HH}$ = 6.2 Hz, OCH*$(CH_3)_2$*).

Synthesis of the Target Compound 1. A solution of 2,6-difluorobenzoyl isocyanates (0.22 g, 1.2 mmol) in dry dichloromethane (10 mL) was added dropwise to a solution of compound **1b** (0.21 g, 1.2 mmol) in dry dichloromethane (5 mL) at room temperature. The reaction was monitored by TLC using a mixture of petroleum ether (60−90 °C) and ethyl acetate (v/v = 3:1) as the eluent. After the reaction was complete, the solvent was evaporated off under reduced pressure, and the product was purified by flash column chromatography on silica gel using a mixture of petroleum ether (60−90 °C) and ethyl acetate (v/v = 3:1) as the eluent to give compound **1** as a white solid (0.27 g, 62.8%): mp, 174−176 °C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 10.49 (br s, 1H, CONHCO), 8.38 (br s, 1H, CONHAr), 8.03 (s, 1H, CH═N), 7.49−7.59 (m, 5H, Ar−H),

Scheme 1. General Synthetic Route for the Target Compounds **1**−**17**



Scheme 2. Possible Mechanism of Synthesis of 4-Hydroxybenzonitrile



7.06 (t, 2H, $^3J_{HH}$ = 8.6 Hz, Ar−H), 4.45 (septet, 1H, $^3J_{HH}$ = 6.2 Hz, O*CH*$(CH_3)_2$), 1.31 (d, 6H, $^3J_{HH}$ = 6.2 Hz, OCH*$(CH_3)_2$*). Anal. Calcd for $C_{18}H_{17}F_2N_3O_3$: C, 59.83; H, 4.74; N, 11.63. Found: C, 59.67; H, 5.00; N, 11.83.

Intermediates **2a**−**17a**, **2b**−**17b** and the target compounds **2**−**17** were prepared by following the same procedures as for **1a**, **1b**, and **1**, respectively. The physical properties and ^{1}H NMR data of compounds **2a**−**17a** and **2b**−**17b** are listed in **Table 1**. The physical properties, elemental analyses of the target compounds **2**−**17**, and their ^{1}H NMR data are listed in **Tables 2** and **3**, respectively.

General Synthetic Procedure for the Target Compounds 18−**22 (Scheme 3).** *Synthesis of (E)-O-(1,1,1,3,3,3-Hexafluoro-2-propyl)-4-nitrobenzaldehyde Oxime (**18a**).* A suspension of sodium hydride (0.20 g, 50%, 4.2 mmol) in dry diethyl ether (30 mL) was cooled to −15 °C. Then a solution of 1,1,1,3,3,3-hexafluoro-2-propanol (0.71 g, 4.2 mmol) in dry diethyl ether (30 mL) was added dropwise, and subsequently a solution of *O*-(mesitylsulfonyl)hydroxylamine (**n**) (0.76 g, 3.5 mmol) in diethyl ether (10 mL) was added at −15 °C. The mixture was stirred for 3 h at −10 to 0 °C and filtered. Then to the filtrate were added a solution of 4-nitrobenzaldehyde (0.53 g, 3.5 mmol) in diethyl ether (20 mL) and 5 drops of acetic acid. After stirring at room temperature for 3 h, the reaction mixture was washed successively with water, saturated sodium carbonate solution, and saturated brine. The organic layer was dried over anhydrous magnesium sulfate. The solvent was removed to give a crude product, which was purified by flash column chromatography on silica gel using a mixture of petroleum ether (60−90 °C) and ethyl acetate (v/v = 10:1) as the eluent to obtain compound **18a** as a yellow oil (0.66 g, 60.0%): ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.35 (s, 1H, CH=N), 8.28 (d, 2H, $^3J_{HH}$ = 8.1 Hz, Ar−H), 8.79 (d, 2H, $^3J_{HH}$ = 8.1 Hz, Ar−H), 5.10 (septet, 1H, $^3J_{HF}$ = 6.2 Hz, OCH).

*Synthesis of (E)-O-(1,1,1,3,3,3-Hexafluoro-2-propyl)-4-aminobenzaldehyde Oxime (**18b**).* Compound **18b** was prepared by following the same procedure as for **1b** to give an orange yellow oil (0.35 g, 75.4%): ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.95 (s,

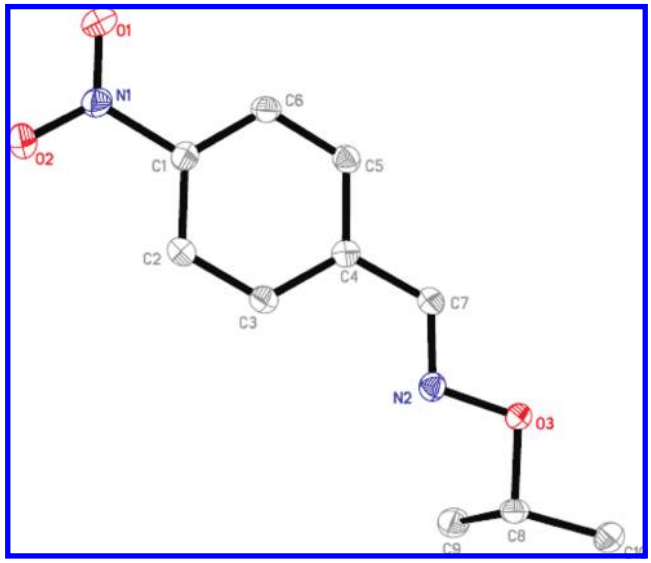


Figure 1. Molecular structure of compound **1a**.

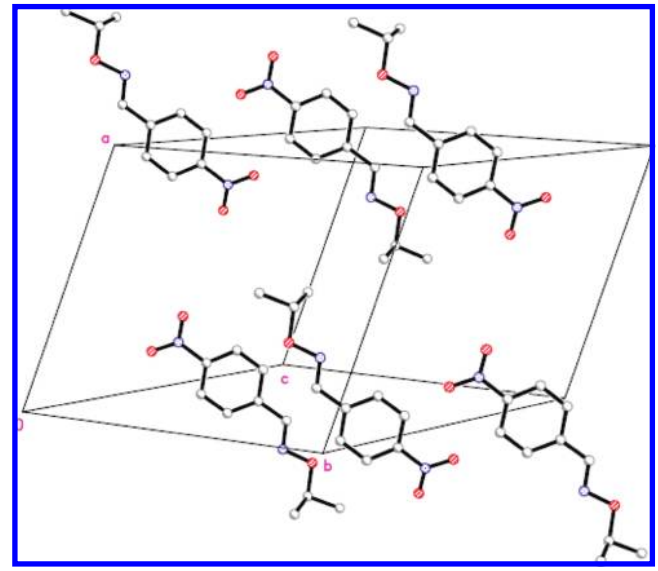


Figure 2. Packing diagram of compound **1a**.

Table 1. Physical Properties and ^{1}H NMR Data of Intermediates **2a**−**17a** and **2b**−**17b**

compd.	R_1	yield	m.p. (°C)	^{1}H NMR δ (ppm)
2a	$PhCH_2$	76.6%	yellow solid 119-121	^{1}H NMR (300 MHz, $CDCl_3$): 8.22 (d, 2H, $^3J_{HH}$ = 8.7 Hz, Ar-H), 8.18 (s, 1H, CH=N), 7.74 (d, 2H, $^3J_{HH}$ = 8.7 Hz, Ar-H), 7.32-7.44 (m, 5H, Ph), 5.26 (s, 2H, CH_2Ph).
2b	$PhCH_2$	42.9%	pale yellow oil	^{1}H NMR (400 MHz, $CDCl_3$): 8.04 (s, 1H, CH=N), 7.28-7.42 (m, 7H, Ar-H), 6.64 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 5.16 (s, 2H, CH_2PH), 3.84 (brs, 2H, NH_2).
3a	CH_3	77.8%	yellow solid 103-106	^{1}H NMR (300 MHz, $CDCl_3$): 8.24 (d, 2H, $^3J_{HH}$ = 8.9 Hz, Ar-H), 8.11 (s, 1H, CH=N), 7.75 (d, 2H, $^3J_{HH}$ = 8.9 Hz, Ar-H), 4.04 (s, 3H, OCH_3).
3b	CH_3	85.2%	pale yellow oil	^{1}H NMR (300 MHz, $CDCl_3$): 7.96 (s, 1H, C =N), 7.38 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 6.65 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 3.93 (s, 3H, OCH_3), 3.86 (brs, 2H, NH_2).
4a	CH_3CH_2	73.7%	yellow solid 106-109	^{1}H NMR (300 MHz, $CDCl_3$): 8.23 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 8.12 (s, 1H, CH=N), 7.75 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 4.29 (q, 2H, $^3J_{HH}$ = 7.1 Hz, OCH_2 CH_3), 1.35 (t, 3H, $^3J_{HH}$ = 7.1 Hz, CH_3CH_2O).
4b	CH_3CH_2	88.9%	orange yellow oil	^{1}H NMR (300 MHz, $CDCl_3$): 7.98 (s, 1H, CH=N), 7.38 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 6.64 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 4.18 (q, 2H, $^3J_{HH}$ = 7.1 Hz, OCH_2CH_3), 3.84 (brs, 2H, NH_2), 1.30 (t, 3H, $^3J_{HH}$ = 7.1 Hz, CH_3CH_2O).
5a	$CH_3CH_2CH_2$	83.7%	pale yellow solid 57-59	^{1}H NMR (300 MHz, $CDCl_3$): 8.23 (d, 2H, $^3J_{HH}$ = 8.9 Hz, Ar-H), 8.13 (s, 1H, CH=N), 7.74 (d, 2H, $^3J_{HH}$ = 8.9 Hz, Ar-H), 4.19 (t, 2H, $^3J_{HH}$ = 6.7 Hz, OCH_2CH_2), 1.70-1.82 (m, 2H, $CH_2CH_2CH_3$), 0.99 (t, 3H, $^3J_{HH}$ = 7.4 Hz, CH_2CH_3).
5b	$CH_3CH_2CH_2$	81.7%	orange yellow oil	^{1}H NMR (300 MHz, $CDCl_3$): 7.98 (s, 1H, CH=N), 7.38 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 6.64 (d, 2H, $^3J_{HH}$ = 8.7 Hz, Ar-H), 4.07 (t, 2H, $^3J_{HH}$ = 6.7 Hz, OCH_2CH_2), 3.83 (brs, 2H, NH_2),1.66-1.82 (m, 2H, $CH_2CH_2CH_3$), 0.99 (t, 3H, $^3J_{HH}$ = 7.4 Hz, CH_2CH_3).
6a	CH_2CH_2Cl	59.1%	pale yellow solid 66-67	^{1}H NMR (300 MHz, $CDCl_3$): 8.24 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 8.20 (s, 1H, CH=N), 7.76 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 4.45 (t, 2H, $^3J_{HH}$ = 5.8 Hz, OCH_2CH_2), 3.80 (t, 3H, $^3J_{HH}$ = 5.8 Hz, CH_2CH_2Cl).
6b	CH_2CH_2Cl	76.4%	orange yellow oil	^{1}H NMR (400 MHz, $CDCl_3$): 8.03 (s, 1H, CH=N), 7.38 (d, 2H, $^3J_{HH}$ = 7.7 Hz, Ar-H), 6.65 (d, 2H, $^3J_{HH}$ = 7.7 Hz, Ar-H), 4.33 (t, 2H, $^3J_{HH}$ = 5.9 Hz, OCH_2CH_2), 3.88 (brs, 2H, NH_2), 3.77 (t, 3H, $^3J_{HH}$ = 5.9 Hz, CH_2CH_2Cl).
7a	CH_2CH_2F	88.5%	yellow solid	^{1}H NMR (300 MHz, $CDCl_3$): 8.24 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 8.20 (s, 1H, CH=N), 7.76 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 4.72 (dt, 2H, $^3J_{HH}$ = 4.1 Hz, $^2J_{HF}$ = 47.5 Hz, CH_2CH_2F), 4.47 (dt, 2H, $^3J_{HH}$ = 4.1 Hz, $^3J_{HF}$ = 28.6 Hz, OCH_2CH_2F).
7b	CH_2CH_2F	55.8%	yellow oil	^{1}H NMR (300 MHz, $CDCl_3$): 8.04 (s, 1H, CH=N), 7.38 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 6.64 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 4.68 (dt, 2H, $^3J_{HH}$ = 4.2 Hz, $^2J_{HF}$ = 47.6 Hz, CH_2CH_2F), 4.38 (dt, 2H, $^3J_{HH}$ = 4.2 Hz, $^3J_{HF}$ = 28.7 Hz, OCH_2CH_2F), 3.87 (brs, 2H, NH_2).
8a	$CH_2CH=CH_2$	77.7%	pale yellow solid 73-75	^{1}H NMR (300 MHz, $CDCl_3$): 8.23 (d, 2H, $^3J_{HH}$ = 8.9 Hz, Ar-H), 8.16 (s, 1H, CH=N), 7.75 (d, 2H, $^3J_{HH}$ = 8.9 Hz, Ar-H), 5.98-6.11 (m, 1H, CH_2CH=CH_2), 5.37 (dq, 1H, $^3J_{HH}$ = 17.2 Hz, CH_2CH=CH_2), 5.28 (dq, 1H, $^3J_{HH}$ = 10.4 Hz, CH_2CH = CH_2), 4.73 (dt, 2H, $^3J_{HH}$ = 5.8 Hz, CH_2CH = CH_2).
8b	$CH_2CH=CH_2$	95.4%	orange yellow oil	^{1}H NMR (300 MHz, $CDCl_3$): 8.01 (s, 1H, CH=N), 7.38 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 6.64 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 5.98-6.11 (m, 1H, CH_2CH=CH_2), 5.30-5.38 (m, 1H, CH_2CH=CH_2), 5.23 (dd, 1H, J = 10.4, 1.3 Hz, CH_2CH=CH_2), 4.62-4.69 (m, 2H, CH_2CH=CH_2), 3.84 (brs, 2H, NH_2).

Table 1. Continued

compd.	R_1	yield	m.p. (°C)	^{1}H NMR δ (ppm)
9a	H_2C—≡—H	80.4%	pale yellow solid	^{1}H NMR (400 MHz, $CDCl_3$): 8.24 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 8.18 (s, 1H, CH=N), 7.78 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 4.83 (d, 2H, $^4J_{HH}$ = 2.3 Hz, OCH_2), 2.54 (t, H, $^4J_{HH}$ = 2.3 Hz,CH).
9b	H_2C—≡—H	57.1%	orange yellow solid 68-70	^{1}H NMR (300 MHz, $CDCl_3$): 8.02 (s, 1H, CH=N), 7.40 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 6.64 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 4.72 (d, 2H, $^4J_{HH}$ = 2.4 Hz, OCH_2), 3.87 (brs, 2H, NH_2), 2.48 (t, H, $^4J_{HH}$ = 2.4 Hz, CH).
10a	$ClH_2CO_2CH_3$	73.4%	pale yellow solid 101-102	^{1}H NMR (300 MHz, $CDCl_3$): 8.20 (s, 1H, CH=N), 8.17 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 7.69 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 4.72 (s, 2H, $OCH_2CO_2CH_3$), 3.74 (s, 3H, CO_2CH_3).
10b	$ClH_2CO_2CH_3$	26.7%	yellow solid	^{1}H NMR (300 MHz, $CDCl_3$): 8.09 (s, 1H, CH=N), 7.37 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 6.64 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 4.68 (s, 2H, $OCH_2CO_2CH_3$), 3.88 (brs, 2H, NH_2), 3.78 (s, 3H, CO_2CH_3).
11a	$ClH_2ClH_2OCH_3$	68.7%	pale yellow solid 77-79	^{1}H NMR (300 MHz, $CDCl_3$): 8.23 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 8.19 (s, 1H, CH=N), 7.75 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 4.39 (t, 2H, $^3J_{HH}$ = 4.6 Hz, OCH_2CH_2), 3.71 (t, 2H, $^3J_{HH}$ = 4.6 Hz, OCH_2CH_2), 3.43 (s, 3H, CH_2OCH_3).
11b	$CH_2CH_2OCH_3$	84.9%	orange yellow oil	^{1}H NMR (300 MHz, $CDCl_3$): 8.23 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 8.19 (s, 1H, CH=N), 7.75 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 4.39 (t, 2H, $^3J_{HH}$ = 4.6 Hz, OCH_2CH_2), 3.86 (brs, 2H, NH_2), 3.71 (t, 2H, $^3J_{HH}$ = 4.6 Hz, OCH_2CH_2), 3.43 (s, 3H, CH_2OCH_3).
12a	$CH_2CH_2CH_2CH_3$	85.0%	yellow solid 38-39	^{1}H NMR (300 MHz, $CDCl_3$): 8.23 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 8.12 (s, 1H, CH=N), 7.74 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 4.23 (t, 2H, $^3J_{HH}$ = 6.7 Hz, OCH_2CH_2), 1.67-1.76 (m, 2H, OCH_2CH_2), 1.38-1.50 (m, 2H, $CH_2CH_2CH_3$), 0.97 (t, 3H, $^3J_{HH}$ = 7.3 Hz, $CH_2CH_2CH_3$).
12b	$CH_2CH_2CH_2CH_3$	82.3%	orange yellow oil	^{1}H NMR (300 MHz, $CDCl_3$): 7.98 (s, 1H, CH=N), 7.38 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 6.64 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 4.12 (t, 2H, $^3J_{HH}$ = 6.7 Hz, OCH_2CH_2), 3.83 (brs, 2H, NH_2),1.63-1.73 (m, 2H, OCH_2CH_2), 1.36-1.48 (m, 2H, $CH_2CH_2CH_3$), 0.95 (t, 3H, $^3J_{HH}$ = 7.3 Hz, $CH_2CH_2CH_3$).
13a	$CH(CH_3)CH_2CH_3$	56.8%	yellow solid	^{1}H NMR (300 MHz, $CDCl_3$): 8.23 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 8.11 (s, 1H, CH=N), 7.75 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 4.23-4.36 (m, 1H, $OCH(CH_3)$), 1.53-1.81 (m, 2H, $OCH(CH_3)CH_2$), 1.30 (d, 3H, $^3J_{HH}$ = 6.3 Hz, $OCH(CH_3)$), 0.97 (t, 3H, $^3J_{HH}$ = 7.5 Hz, CH_2CH_3).
13b	$CH(CH_3)CH_2CH_3$	47.9%	orange yellow oil	^{1}H NMR (300 MHz, $CDCl_3$):7.97 (s, 1H, CH=N), 7.39 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 6.65 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 4.10-4.24 (m, 1H, $OCH(CH_3)$), 3.82 (brs, 2H, NH_2), 1.46-1.80 (m, 2H, $OCH(CH_3)CH_2$), 1.26 (d, 3H, $^3J_{HH}$ = 6.3 Hz, $OCH(CH_3)$), 0.95 (t, 3H, $^3J_{HH}$ = 7.5 Hz, CH_2CH_3).
14a	$CH(CH_3)(CH_2)_2CH_3$	85.3%	yellow oil	^{1}H NMR (300 MHz, $CDCl_3$): 8.22 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 8.10 (s, 1H, CH=N), 7.74 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 4.32-4.43 (m, 1H, $CH(CH_3)CH_2$), 1.60-1.79 (m, 2H, $CH(CH_3)CH_2CH_2$), 1.38-1.55 (m, 1H, $CH_2CH_2CH_3$), 1.31 (d, 3H, $^3J_{HH}$ = 6.3 Hz, $CH(CH_3)CH_2$), 0.96 (t, 3H, $^3J_{HH}$ = 7.4 Hz, $CH_2CH_2CH_3$).
14b	$CH(CH_3)(CH_2)_2CH_3$	40.0%	pale yellow oil	^{1}H NMR (300 MHz, $CDCl_3$): 7.96 (s, 1H, CH=N), 7.38 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 6.65 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 4.21-4.33 (m, 1H, $CH(CH_3)CH_2$), 3.84 (brs, 2H, NH_2), 1.60-1.77 (m, 2H, $CH(CH_3)CH_2CH_2$), 1.37-1.54 (m, 1H, $CH_2CH_2CH_3$), 1.26 (d, 3H, $^3J_{HH}$ = 6.3 Hz, $CH(CH_3)CH_2$), 0.94 (t, 3H, $^3J_{HH}$ = 7.4 Hz, $CH_2CH_2CH_3$).
15a	$CH_2CH(CH_3)_2$	80.9%	pale yellow solid 47-49	^{1}H NMR (300 MHz, $CDCl_3$): 8.23 (d, 2H, $^3J_{HH}$ = 8.9 Hz, Ar-H), 8.11 (s, 1H, CH=N), 7.75 (d, 2H, $^3J_{HH}$ = 8.9 Hz, Ar-H), 3.91 (d, 2H, $^3J_{HH}$ = 6.7 Hz OCH_2), 1.99-2.15 (m, 1H, $CH_2CH(CH_3)_2$), 0.97 (d, 6H, $^3J_{HH}$ = 6.7 Hz, $CH(CH_3)_2$).

Table 1. Continued

compd.	R_1	yield	m.p. (°C)	^{1}H NMR δ (ppm)
15b	$CH_2CH(CH_3)_2$	83.0%	pale yellow solid	^{1}H NMR (300 MHz, $CDCl_3$): 7.99 (s, 1H, CH=N), 7.38 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 6.63 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 3.89 (d, 2H, $^3J_{HH}$ = 6.7 Hz OCH_2), 3.83 (brs, 2H, NH_2),1.97-2.10 (m, 1H, $CH_2CH(CH_3)_2$), 0.95 (d, 6H, $^3J_{HH}$ = 6.7 Hz, $CH(CH_3)_2$).
16a	$CH_2(CH_2)_3CH_3$	79.6%	yellow solid	^{1}H NMR (300 MHz, $CDCl_3$): 8.23 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 8.09 (s, 1H, CH=N), 7.75 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 4.11 (t, 2H, $^3J_{HH}$ = 6.8 Hz OCH_2), 1.65-1.74 (m, 2H, OCH_2CH_2), 1.34-1.39 (m, 4H, $OCH_2(CH_2)_2$), 0.90 (t, 3H, $^3J_{HH}$ = 7.2 Hz).
16b	$CH_2(CH_2)_3CH_3$	87.0%	pale yellow oil	^{1}H NMR (300 MHz, $CDCl_3$): 7.98 (s, 1H, CH=N), 7.38 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 6.64 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 4.11 (t, 2H, $^3J_{HH}$ = 6.8 Hz OCH_2), 3.82 (brs, 2H, NH_2), 1.65-1.74 (m, 2H, OCH_2CH_2), 1.34-1.39 (m, 4H, $OCH_2(CH_2)_2$), 0.90 (t, 3H, $^3J_{HH}$ = 7.2 Hz).
17a	cyclopentyl	86.0%	yellow solid	^{1}H NMR (300 MHz, $CDCl_3$): 8.22 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 8.08 (s, 1H, CH=N), 7.74 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 4.81-4.87 (m, 1H), 1.56-1.89 (m, 8H).
17b	cyclopentyl	54.2%	orange yellow oil	^{1}H NMR (300 MHz, $CDCl_3$): 7.94 (s, 1H, CH=N), 7.38 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 6.65 (d, 2H, $^3J_{HH}$ = 8.8 Hz, Ar-H), 4.81-4.87 (m, 1H), 3.88 (brs, 2H, NH_2), 1.56-1.90 (m, 8H).

1H, CH=N), 7.52 (d, 2H, $^3J_{HH}$ = 8.1 Hz, Ar—H), 6.65 (d, 2H, $^3J_{HH}$ = 8.1 Hz, Ar—H), 4.95 (septet, 1H, $^3J_{HF}$ = 6.2 Hz, OCH), 3.82 (br s, 2H, NH_2).

Synthesis of the Target Compound 18. Compound **18** was prepared by following the same procedure as for **1** to give a white solid (0.33 g, 63.4%): mp, 186−188 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 10.62 (br s, 1H, CONHCO), 9.06 (br s, 1H, CONHAr), 8.23 (s, 1H, CH=N), 7.48−7.59 (m, 5H, Ar—H), 7.07 (t, 2H, $^3J_{HH}$ = 9.0 Hz, Ar—H), 5.06 (septet, 1H, $^3J_{HF}$ = 6.2 Hz, OCH). Anal. Calcd for $C_{18}H_{11}F_8N_3O_3$: C, 46.01; H, 2.36; N, 8.95. Found: C, 46.09; H, 2.38; N, 8.96.

Intermediates **19a**−**22a**, **19b**−**22b**, and the target compounds **19**−**22** were prepared by following the same procedures as for **18a**, **18b**, and **1**, respectively. The physical properties and ^{1}H NMR data of compounds **19a**−**22a** and **19b**−**22b** are listed in **Table 4**. The physical properties, elemental analyses of the target compounds **19**−**22**, and their ^{1}H NMR data are listed in **Tables 5** and **6**, respectively.

Synthetic Procedure for the Target Compound 23 (Scheme 4). *Synthesis of (E)-O-tert-Butyl-4-nitrobenzaldehyde Oxime (23a).* A solution of **m** (0.83 g, 5 mmol) in chloroform (20 mL) was heated to 50−60 °C, and isobutylene was bubbled into the solution. Then, 0.5 mL of concentrated H_2SO_4 was added into the mixture. The mixture was washed successively with water, saturated sodium carbonate solution, and saturated brine when the reaction was complete (monitored by TLC using a mixture of petroleum ether (60−90 °C) and ethyl acetate (v/v = 10:1) as the eluent). The organic layer was dried over anhydrous magnesium sulfate and filtered. The solvent was removed to give a crude product, which was purified by flash column chromatography on silica gel using petroleum ether (60−90 °C) as the eluent to obtain compound **23a** as a yellow solid (0.80 g, 72.1%): mp, 59−61 °C.; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.22 (d, 2H, $^3J_{HH}$ = 8.7 Hz, Ar—H), 8.09 (s, 1H, CH=N), 7.75 (d, 2H, $^3J_{HH}$ = 8.7 Hz, Ar—H), 1.38 (s, 9H, OC $(CH_3)_3$).

Synthesis of (E)-O-tert-Butyl-4-aminobenzaldehyde Oxime (23b). Compound **23b** was prepared by following the same procedure as for **1b** to give an orange-yellow oil (1.06 g, 81.5%): ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.95 (s, 1H, CH=N), 7.40 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar—H), 6.65 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar—H), 3.81 (br s, 2H, NH_2), 1.34 (s, 9H, OC$(CH_3)_3$).

Synthesis of the Target Compound **23.** Compound **23** was prepared by following the same procedure as for **1** to give a white solid (1.90 g, 63.4%): mp, 171−173 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 10.48 (br s, 1H, CONHCO), 8.44 (br s, 1H, CONHAr), 8.02 (s, 1H, CH=N), 7.49−7.59 (m, 5H, Ar—H), 7.07 (t, 2H, $^3J_{HH}$ = 8.8 Hz, Ar—H), 1.37 (s, 9H, OC $(CH_3)_3$). Anal. Calcd for $C_{19}H_{19}F_2N_3O_3$: C, 60.79; H, 5.10; N, 11.19. Found: C, 60.89; H, 5.22; N, 11.19.

Synthetic Procedure for the Target Compound 24 (Scheme 5). *Synthesis of 4-Aminobenzaldehyde.* 4-Aminobenzaldehyde was prepared according to the literature (*18*). The product was not purified to be used in the next step because of its easy self-condensation. ^{1}H NMR (400 MHz, $CDCl_3$), δ 9.76 (s, 1H, CHO), 7.69 (d, 2H, $^3J_{HH}$ = 8.4 Hz, Ar—H), 4.25 (br s, 2H, NH_2).

Synthesis of 1-(2,6-Difluorobenzoyl)-3-(4-formylphenyl)urea (24a). A solution of 2,6-difluorobenzoyl isocyanates (1.51 g, 8.3 mmol) in dichloromethane (20 mL) was added dropwise to a solution of 4-aminobenzaldehyde in dichloromethane (20 mL) at room temperature. Then the mixture was stirred overnight, and the solvent was removed under reduced pressure. The product was purified by flash column chromatography on silica gel using a mixture of petroleum ether (60−90 °C) and ethyl acetate (v/v = 3:1) as the eluent to give compound **24a** as a white solid (0.66 g, 20.6%, yield of two steps): mp, 205−206 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 10.75 (br s, 1H, CONHCO), 9.76 (s, 1H, CHO), 9.02 (br s, 1H, CONHAr), 7.86 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar—H), 7.68 (d, 2H, $^3J_{HH}$ = 8.4 Hz, Ar—H),7.47−7.60 (m, 1H, Ar—H), 7.08 (t, 2H, $^3J_{HH}$ = 8.4 Hz, Ar—H).

Synthesis of (E)-1-(2,6-Difluorobenzoyl)-3-(4-((hydroxyimino)methyl)phenyl)urea (24b). Compound **24b** was prepared by following the same procedure as for **m** to give a white solid (98.4%): mp, 201−203 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.47 (brs, 1H, CONHCO), 11.15 (s, 1H, N-OH), 10.27 (brs, 1H, CONHAr), 8.10 (s, 1H, CH=N), 7.56−7.67 (m, 5H, Ar—H), 7.26 (t, 2H, $^3J_{HH}$ = 8.3 Hz, Ar—H).

Table 2. Physical Properties and Elemental Analyses of the Target Compounds **2**−**17**

compd.	R_1	yield	m.p. (°C)	Element analysis (%, calc.)		
				C	H	N
2	$PhCH_2$	50.23%	white solid 174-176	64.44 (64.54)	4.27 (4.19)	10.27 (10.26)
3	CH_3	32.5%	white solid 179-181	57.54(57.66)	4.02 (3.93)	12.59 (12.61)
4	CH_3CH_2	46.9%	white solid 174-176	58.66 (58.79)	4.41 (4.35)	12.15 (12.10)
5	$CH_2CH_2CH_2$	50.6%	white solid 171-173	59.81 (59.83)	4.85 (4.74)	11.78 (11.63)
6	CH_2CH_2Cl	37.3%	white solid 184-186	53.41 (53.48)	3.75 (3.70)	11.19 (11.01)
7	CH_2CH_2F	47.4%	white solid 175-176	55.79 (55.89)	3.74 (3.70)	11.12 (11.01)
8	$CH_2CH{=}CH_2$	79.4%	white solid 165-167	60.01 (60.17)	4.11 (4.21)	11.58 (11.69)
9	$H_2C{\equiv}{\equiv}H$	30.5%	white solid 183-184	60.68 (60.51)	3.64 (3.67)	11.76 (11.76)
10	$CH_2CO_2CH_3$	46.9%	white solid 175-177	55.12 (55.25)	3.95 (3.86)	11.00 (10.74)
11	$CH_2CH_2OCH_3$	60.5%	white solid 161-163	57.11 (57.29)	4.53 (4.54)	11.27 (11.14)
12	$CH_2CH_2CH_2CH_3$	34.0%	white solid 164-166	60.69 (60.79)	5.25 (5.10)	11.18 (11.19)
13	$CH(CH_3)CH_2CH_3$	64.3%	white solid 167-169	60.52 (60.79)	5.07 (5.10)	11.39 (11.19)
14	$CH(CH_3)(CH_2)_2CH_3$	64.5%	white solid 154-155	HRMS (ESI) *m/z* calcd for $C_{20}H_{21}F_2N_3O_3$ $(M+Na)^+$ 412.1443, found 412.1444		
15	$CH_2CH(CH_3)_2$	53.6%	white solid 181-182	60.97 (60.79)	5.17 (5.10)	11.08 (11.19)
16	$CH_2(CH_2)_3CH_3$	51.0%	white solid 153-155	61.50 (61.69)	5.33 (5.44)	10.74 (10.79)
17	cyclopentyl	43.2%	white solid 185-187	62.09 (62.01)	5.00 (4.94)	10.80 (10.85)

*Synthesis of the Target Compound **24**.* Compound **24b** (0.32 g, 1 mmol) was dissolved in a mixture of tetrahydrofuran (6 mL) and diethyl ether (25 mL), and then a solution of chlorotrimethylsilane (0.13 g, 1.2 mmol) in diethyl ether (5 mL) was added dropwise. The mixture was stirred overnight at room temperature. Then triethylamine (0.12 g, 1.2 mmol) was added and filtered. The solvent was evaporated off under reduced pressure, and the product was purified by flash column chromatography on silica gel using a mixture of petroleum ether (60−90 °C) and ethyl acetate (v/v = 3:1) as the eluent to give compound **24** as a white solid (0.18 g, 47.4%): mp, 182−184 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 10.53 (br s, 1H,CONHCO), 8.77 (br s, 1H, CONHAr), 8.16 (s, 1H, CH=N), 7.47−7.59 (m, 5H, Ar−H), 7.06 (t, 2H, $^3J_{HH}$ = 8.5 Hz, Ar−H), 0.29 (s, 9H, Si $(CH_3)_3$). HRMS (ESI) *m/z* calcd for $C_{18}H_{19}F_2N_3O_3Si$ $(M + H)^+$ 392.1237, found 392.1246.

Biological Assay. All bioassays were performed on representative test organisms reared in the laboratory. The bioassay was repeated at 25 ± 1 °C according to statistical requirements. Assessments were made on a dead/alive basis, and mortality rates were corrected using Abbott's formula (*19*). Evaluations are based on a percentage scale of 0−100 in which 0 = no activity and 100 = total kill.

Larvicidal Activity against Oriental Armyworm (Mythimna separata). The larvicidal activities of the target compounds **1**−**24** against oriental armyworm were evaluated by foliar application using the reported procedure (*20*−*22*). For the foliar armyworm tests, individual corn leaves were placed on moistened pieces of filter paper in Petri dishes. The leaves were then sprayed with the test solution and allowed to dry. The dishes were infested with 10 fourth-instar oriental armyworm larvae. Percentage mortalities were evaluated 4 days after treatment. Each treatment was performed three times. For comparative purposes, Flucycloxuron was tested under the same condition.

Larvicidal Activity against Mosquito (Culex pipiens pallens). The larvicidal activities of the target compounds **1**−**24** against mosquito were evaluated by using the reported procedure (*23*). The compounds **1**−**24** were prepared to different concentrations by dissolving **1**−**24** in acetone and adding distilled water. Then 20 fourth-instar mosquito larvae were put into 10 mL of the test solution and raised for 8 days. The results were expressed by death percentage. For comparative purposes, Flucycloxuron was tested under the same condition.

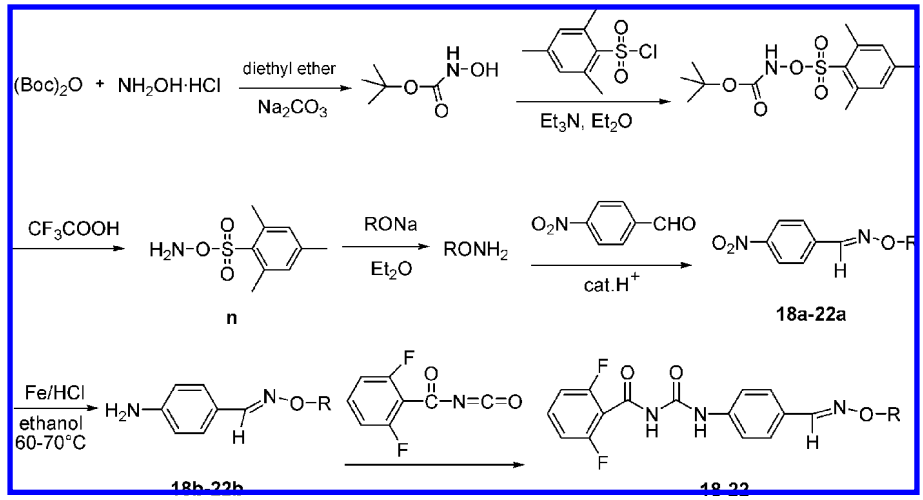
Plant Growth Regulatory Activity Assay. The plant growth regulatory activities of the target compounds **1**−**4**, **6**−**8**, **11**, **12**, and **14**−**17** were evaluated using previously reported

procedures (*24*−*26*). Seeds of cucumber were incubated at 26 °C in the dark for 72 h, and 10 cotyledons were cut off. *N*,*N*-Dimethylformamide solutions of the test compounds were prepared at concentrations of 10 mg/L. The experiments were conducted in sterile Petri dishes (6 cm diameter) lined with a sheet of filter paper. To each dish was added 0.3 mL of the test solution, and the solvent was evaporated before addition of 3 mL of water, followed by the above cotyledons. Assays were carried out at 26 °C in the dark in an incubator for 5 days. The number of roots was counted, and the growth regulatory activities were evaluated. Controls were performed under the same conditions, using only water. Each treatment was performed in triplicate.

Table 3. ^{1}H NMR of the Target Compounds **2**−**17**

compd.	^{1}H NMR δ (ppm)
2	^{1}H NMR (300 MHz, $CDCl_3$): 10.50 (brs, 1H, CONHCO), 8.43 (brs, 1H, CONHAr), 8.11 (s, 1H, CH=N), 7.29-7.56 (m, 9H, Ar), 7.06 (t, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 5.21 (s, 2H, CH_2Ph).
3	^{1}H NMR (300 MHz, $CDCl_3$): 10.53 (brs, 1H, CONHCO), 8.92 (brs, 1H, CONHAr), 8.04 (s, 1H, CH=N), 7.50-7.59 (m, 5H, Ar), 7.06 (t, 2H, $^3J_{HH}$ = 8.4 Hz, Ar-H), 3.98 (s, 3H, OCH_3).
4	^{1}H NMR (300 MHz, $CDCl_3$): 10.52 (brs, 1H, CONHCO), 8.93 (brs, 1H, CONHAr), 8.05 (s, 1H, CH=N), 7.50-7.59 (m, 5H, Ar), 7.06 (t, 2H, $^3J_{HH}$ = 8.4 Hz, Ar-H), 4.23 (q, 2H, $^3J_{HH}$ = 7.1 Hz, OCH_2 CH_3), 1.33 (t, 3H, $^3J_{HH}$ = 7.1 Hz, CH_3CH_2O).
5	^{1}H NMR (300 MHz, $CDCl_3$): 10.51 (brs, 1H, CONHCO), 9.08 (brs, 1H, CONHAr), 8.05 (s, 1H, CH=N), 7.47-7.58 (m, 5H, Ar), 7.05 (t, 2H, $^3J_{HH}$ = 8.3 Hz, Ar-H), 4.13 (t, 2H, $^3J_{HH}$ = 6.7 Hz, OCH_2CH_2), 1.69-1.81 (m, 2H, $CH_2CH_2CH_3$), 0.99 (t, 3H, $^3J_{HH}$ = 7.4 Hz, CH_2CH_3).
6	^{1}H NMR (300 MHz, $CDCl_3$): 10.51 (brs, 1H, CONHCO), 8.88 (brs, 1H, CONHAr), 8.11 (s, 1H, CH=N), 7.48-7.58 (m, 5H, Ar), 7.05 (t, 2H, $^3J_{HH}$ = 8.4 Hz, Ar-H), 4.33 (t, 2H, $^3J_{HH}$ = 4.7 Hz, OCH_2CH_2), 3.70 (t, 3H, $^3J_{HH}$ = 4.7 Hz, CH_2CH_2Cl).
7	^{1}H NMR (300 MHz, $CDCl_3$): 10.55 (brs, 1H, CONHCO), 9.40 (brs, 1H, CONHAr), 8.11 (s, 1H, CH=N), 7.46-7.58 (m, 5H, Ar), 7.04 (t, 2H, $^3J_{HH}$ = 8.3 Hz, Ar-H), 4.70 (dt, 2H, $^3J_{HH}$ = 4.1 Hz, $^2J_{HF}$ = 47.6 Hz, CH_2CH_2F), 4.41 (dt, 2H, $^3J_{HH}$ = 4.1 Hz, $^3J_{HF}$ = 28.5 Hz, OCH_2CH_2F).
8	^{1}H NMR (300 MHz, $CDCl_3$): 10.53 (brs, 1H, CONHCO), 8.24 (brs, 1H, CONHAr), 8.09 (s, 1H, CH=N), 7.47-7.58 (m, 5H, Ar), 7.05 (t, 2H, $^3J_{HH}$ = 8.3 Hz, Ar-H), 6.00-6.13 (m, 1H, CH_2CH=CH_2), 5.36 (dq, 1H, $^3J_{HH}$ = 17.3 Hz, CH_2CH=CH_2), 5.26 (dq, 1H, $^3J_{HH}$ = 10.4 Hz, CH_2CH=CH_2), 4.68 (dt, 2H, $^3J_{HH}$ = 5.8 Hz, CH_2CH=CH_2).
9	^{1}H NMR (300 MHz, $CDCl_3$): 10.52 (brs, 1H, CONHCO), 8.52 (brs, 1H, CONHAr), 8.10 (s, 1H, CH=N), 7.49-7.60 (m, 5H, Ar), 7.06 (t, 2H, $^3J_{HH}$ = 8.4 Hz, Ar-H), 4.77 (d, 2H, $^4J_{HH}$ = 2.4 Hz, OCH_2), 2.50 (t, H, $^4J_{HH}$ = 2.4 Hz,CH).
10	^{1}H NMR (400 MHz, $CDCl_3$): 10.53 (brs, 1H, CONHCO), 8.58 (brs, 1H, CONHAr), 8.17 (s, 1H, CH=N), 7.50-7.58 (m, 5H, Ar), 7.06 (t, 2H, $^3J_{HH}$ = 8.4 Hz, Ar-H), 4.73 (s, 2H, $OCH_2CO_2CH_3$), 3.80 (s, 3H, CO_2CH_3).
11	^{1}H NMR (300 MHz, $CDCl_3$): 10.50 (brs, 1H, CONHCO), 8.58 (brs, 1H, CONHAr), 8.11 (s, 1H, CH=N), 7.48-7.58 (m, 5H, Ar), 7.06 (t, 2H, $^3J_{HH}$ = 8.4 Hz, Ar-H), 4.33 (t, 2H, $^3J_{HH}$ = 4.7 Hz, OCH_2CH_2), 3.70 (t, 2H, $^3J_{HH}$ = 4.7 Hz, OCH_2CH_2), 3.43 (s, 3H, CH_2OCH_3).
12	^{1}H NMR (300 MHz, $CDCl_3$): 10.52 (brs, 1H, CONHCO), 8.85 (brs, 1H, CONHAr), 8.05 (s, 1H, CH=N), 7.50-7.59 (m, 5H, Ar), 7.06 (t, 2H, $^3J_{HH}$ = 8.4 Hz, Ar-H), 4.18 (t, 2H, $^3J_{HH}$ = 6.7 Hz, OCH_2CH_2), 1.66-1.75 (m, 2H,OCH_2CH_2),1.38-1.50 (m, 2H, $CH_2CH_2CH_3$), 0.97 (t, 3H, $^3J_{HH}$ = 7.3 Hz, $CH_2CH_2CH_3$).
13	^{1}H NMR (400 MHz, $CDCl_3$): 10.53 (brs, 1H, CONHCO), 9.24 (brs, 1H, CONHAr), 8.03 (s, 1H, CH=N), 7.46-7.57 (m, 5H, Ar), 7.05 (t, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 4.20-4.28 (m, 1H, OCH (CH_3)), 1.54-1.80 (m, 2H, OCH (CH_3)CH_2), 1.28 (d, 3H, $^3J_{HH}$ = 6.3 Hz, OCH (CH_3)), 0.96 (t, 3H, $^3J_{HH}$ = 7.5 Hz, CH_2CH_3).
14	^{1}H NMR (300 MHz, $CDCl_3$): 10.51 (brs, 1H, CONHCO), 8.87 (brs, 1H, CONHAr), 8.03 (s, 1H, CH=N), 7.49-7.56 (m, 5H, Ar), 7.06 (t, 2H, $^3J_{HH}$ = 8.4 Hz, Ar-H), 4.26-4.35 (m, 1H, OCH (CH_3)CH_2), 1.62-1.75 (m, 2H, OCH (CH_3)CH_2CH_2), 1.35-1.51 (m, 2H, $CH_2CH_2CH_2$), 1.30 (d, 3H, $^3J_{HH}$ = 6.3 Hz, OCH (CH_3)CH_2), 0.96 (t, 3H, $^3J_{HH}$ = 7.5 Hz, CH_2CH_3).
15	^{1}H NMR (300 MHz, $CDCl_3$): 10.52 (brs, 1H, CONHCO), 8.80 (brs, 1H, CONHAr), 8.07 (s, 1H, CH=N), 7.49-7.59 (m, 5H, Ar), 7.06 (t, 2H, $^3J_{HH}$ = 8.4 Hz, Ar-H), 3.94 (d, 2H, $^3J_{HH}$ = 6.8 Hz, OCH_2), 1.99-2.13 (m, 1H, CH_2CH (CH_3)$_2$), 0.95 (d, 6H, $^3J_{HH}$ = 6.7 Hz, CH (CH_3)$_2$).
16	^{1}H NMR (300 MHz, $CDCl_3$): 10.52 (brs, 1H, CONHCO), 9.12 (brs, 1H, CONHAr), 8.04 (s, 1H, CH=N), 7.47-7.58 (m, 5H, Ar), 7.04 (t, 2H, $^3J_{HH}$ = 8.4 Hz, Ar-H), 4.16 (t, 2H, $^3J_{HH}$ = 6.7 Hz OCH_2), 1.68-1.75 (m, 2H, OCH_2CH_2), 1.37-1.41 (m, 4H, OCH_2 $(CH_2)_2$), 0.93 (t, 3H, $^3J_{HH}$ 6.8 Hz).
17	^{1}H NMR (300 MHz, $CDCl_3$): 10.52 (brs, 1H, CONHCO), 9.04 (brs, 1H, CONHAr), 8.01 (s, 1H, CH=N), 7.48-7.58 (m, 5H, Ar), 7.04 (t, 2H, $^3J_{HH}$ = 8.4 Hz, Ar-H), 4.76-4.82 (m, 1H), 1.58-1.88 (m, 8H).

Scheme 3. General Synthetic Route for the Target Compounds **18**−**22**



RESULTS AND DISCUSSION

Synthesis. The target compounds **1**−**17** were synthesized from (*E*)-4-nitrobenzaldehyde oxime (**m**) as shown in **Scheme 1**. *p*-Nitrobenzaldehyde was condensed with hydroxylamine hydrochloride to give intermediate **m** according to the reported procedure (*27*), and subsequent reaction with R−X or TsOR yielded

Table 4. Physical Properties and ^{1}H NMR Data of Intermediates **19a**−**22a** and **19b**−**22b**

compd.	R	yield	m.p. (°C)	^{1}H NMR δ (ppm)
19a		38.0%	pale yellow solid 86-88	^{1}H NMR (400 MHz, $CDCl_3$): 8.21 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 8.10 (s, 1H, CH=N), 7.73 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 4.08 (dt, 1H, J = 4.0, 10.6 Hz), 2.03-2.20 (m, 2H), 1.68-1.71 (m, 2H), 1.41-1.50 (m, 2H), 1.04-1.12 (m, 3H), 0.94 (d, 3H, $^3J_{HH}$ = 6.5 Hz), 0.91 (d, 3H, $^3J_{HH}$ = 7.0 Hz), 0.83 (d, 3H, $^3J_{HH}$ = 7.0 Hz).
19b		55.6%	orange yellow oil	^{1}H NMR (400 MHz, $CDCl_3$): 8.10 (s, 1H, CH=N), 7.38 (d, 2H, $^3J_{HH}$ = 8.3 Hz, Ar-H), 6.64 (d, 2H, $^3J_{HH}$ = 8.3 Hz, Ar-H), 3.95 (dt, J = 4.3, 10.9 Hz, 1H), 3.81 (brs, 2H, NH_2), 2.11-2.23 (m, 2H), 1.65-1.68 (m, 2H), 1.23-1.48 (m, 2H), 0.98-1.11 (m, 3H), 0.82-0.93 (m, 9H).
20a	CF_3CH_2	69.0%	pale yellow solid 76-78	^{1}H NMR (400 MHz, $CDCl_3$): 8.25 (d, 2H, $^3J_{HH}$ = 8.6 Hz, Ar-H), 8.24 (s, 1H, CH=N), 7.77 (d, 2H, $^3J_{HH}$ = 8.6 Hz, Ar-H), 4.29 (q, 2H, $^3J_{HF}$ = 8.2 Hz, OCH_2CF_3).
20b	CF_3CH_2	45.1%	orange yellow oil	^{1}H NMR (400 MHz, $CDCl_3$): 8.05 (s, 1H, CH=N), 7.38 (d, 2H, $^3J_{HH}$ = 8.1 Hz, Ar-H), 6.64 (d, 2H, $^3J_{HH}$ = 8.1 Hz, Ar-H), 4.46 (q, 2H, $^3J_{HF}$ = 8.2 Hz, OCH_2CF_3), 3.89 (brs, 2H, NH_2).
21a[a]		28.3%	pale yellow solid 47-49	^{1}H NMR (400 MHz, $CDCl_3$): 8.23 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 8.13 (s, 1H, CH=N), 7.74d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 4.12 (d, 2H, $^3J_{HH}$ = 7.2 Hz), 2.27-2.38 (m, 1H), 1.77-1.83 (m, 2H), 1.58-1.64 (m, 2H), 1.24-1.41 (m, 4H).
21b		67.3%	orange yellow oil	^{1}H NMR (400 MHz, $CDCl_3$): 7.98 (s, 1H, CH=N), 7.37 (d, 2H, $^3J_{HH}$ = 8.4 Hz, Ar-H), 6.64 (d, 2H, $^3J_{HH}$ = 8.4 Hz, Ar-H), 4.00 (d, 2H, $^3J_{HH}$ = 7.2 Hz), 3.83 (brs, 2H, NH_2), 2.55-2.33 (m, 1H), 1.73-1.80 (m, 2H), 1.54-1.63 (m, 4H), 1.22-1.34 (m, 2H).
22a[b]		40%	pale yellow solid 69-71	^{1}H NMR (400 MHz, $CDCl_3$): 8.22 (d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 8.15 (s, 1H, CH=N), 7.74d, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 4.04 (d, 2H, $^3J_{HH}$ = 7.2 Hz), 1.17-1.24 (m, 1H), 0.58-0.63 (m, 2H), 0.32-0.36 (m, 2H).
22b		67.6%	orange yellow oil	^{1}H NMR (400 MHz, $CDCl_3$): 8.01 (s, 1H, CH=N), 7.38 (d, 2H, $^3J_{HH}$ = 8.3 Hz, Ar-H), 6.64 (d, 2H, $^3J_{HH}$ = 8.3 Hz, Ar-H), 3.94 (d, 2H, $^3J_{HH}$ = 7.1 Hz), 3.83 (brs, 2H, NH_2), 1.14-1.28 (m, 1H), 0.55-0.59 (m, 2H), 0.29-0.33 (m, 2H).

Table 5. Physical Properties and Elemental Analyses of the Target Compounds **19**−**22**

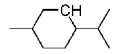
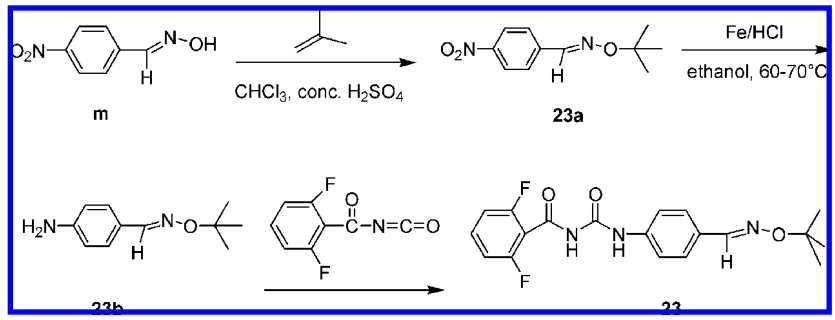
compd.	R	yield	m.p. (°C)	Element analysis (%,calc.) C H N
19		78.3%	white solid 174-175	65.33 (65.63) 6.40 (6.39) 9.27 (9.18)
20	CF_3CH_2	67.3%	white solid 189-190	50.51 (50.88) 3.27 (3.01) 10.65 (10.47)
21		81.1%	white solid 171-173	62.66 (62.84) 5.42 (5.27) 10.65 (10.47)
22		81.3%	white solid 185-187	60.91 (61.12) 4.70 (4.59) 11.49 (11.25)

Table 6. ^{1}H NMR of the Target Compounds **19**−**22**

compd.	^{1}H NMR δ (ppm)
19	^{1}H NMR (400 MHz, $CDCl_3$): 10.49 (brs, 1H, CONHCO), 8.56 (brs, 1H, CONHAr), 8.03 (s, 1H, CH=N), 7.50-7.59 (m, 5H, Ar), 7.06 (t, 2H, $^3J_{HH}$ = 8.7 Hz, Ar-H), 4.01 (dt, 1H, J = 4.1, 11.1 Hz), 2.11-2.25 (m, 2H), 1.67-1.70 (m, 2H), 1.39-1.50 (m, 2H), 0.99-1.13 (m, 3H), 0.93 (t, 6H, $^3J_{HH}$ = 7.7 Hz), 0.84 (d, 3H, $^3J_{HH}$ = 6.9 Hz).
20	^{1}H NMR (400 MHz, $CDCl_3$): 10.57 (brs, 1H, CONHCO), 8.88 (brs, 1H, CONHAr), 8.14 (s, 1H, CH=N), 7.51-7.58 (m, 5H, Ar), 7.06 (t, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 4.52 (q, 2H, $^3J_{HF}$ = 8.5 Hz, OCH_2CF_3).
21	^{1}H NMR (400 MHz, $CDCl_3$): 10.51 (brs, 1H, CONHCO), 8.79 (brs, 1H, CONHAr), 8.06 (s, 1H, CH−N), 7.49-7.59 (m, 5H, Ar), 7.06 (t, 2H, $^3J_{HH}$ = 8.5 Hz, Ar-H), 4.06 (d, 2H, $^3J_{HH}$ = 7.2 Hz), 2.24-2.39 (m, 1H), 1.74-1.84 (m, 2H), 1.57-1.64 (m, 4H), 1.25-1.38 (m, 2H).
22	^{1}H NMR (400 MHz, $CDCl_3$): 10.51 (brs, 1H, CONHCO), 8.93 (brs, 1H, CONHAr), 8.08 (s, 1H, CH=N), 7.49-7.55 (m, 5H, Ar), 7.05 (t, 2H, $^3J_{HH}$ = 8.6 Hz, Ar-H), 3.99 (d, 2H, $^3J_{HH}$ = 7.1 Hz), 1.16-1.26 (m, 1H), 0.57-0.61 (m, 2H), 0.31-0.35 (m, 2H).

Scheme 4. Synthetic Route for the Target Compound **23**



compounds **1a**−**17a**; further reduction using iron powder as a reductant provided compounds **1b**−**17b** (*28*), which were combined with 2,6-difluorobenzoyl isocyanate to afford compounds **1**−**17**.

To obtain the target compound **22**, we attempted to synthesize intermediate (*E*)-*O*-(1,1,1-trifluoroethyl)-4-nitrobenzaldehyde oxime (**22a**) from 4-nitrobenzaldehyde oxime and 2,2,2-trifluoroethyl 4-methylbenzenesulfonate according to **Scheme 1**

Scheme 5. Synthetic Route for the Target Compound **24**

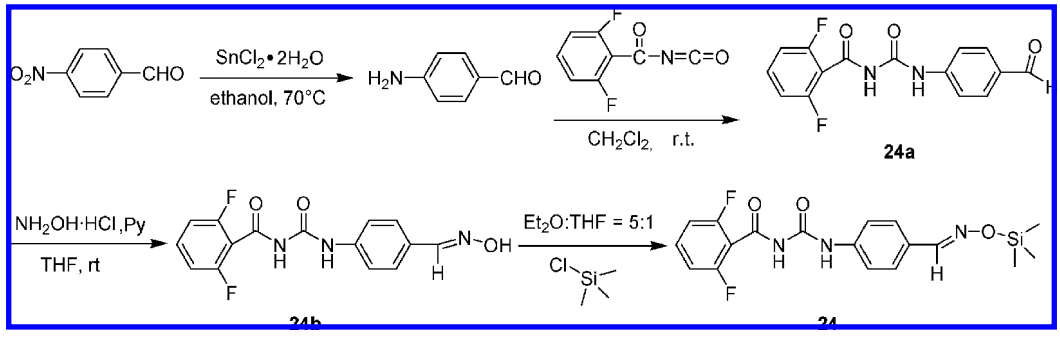


Table 7. Larvicidal Activities against Oriental Armyworm and Mosquito of Compounds **1**−**24** and Flucycloxuron

compd.	R	Toxicities against Oriental armyworm		Toxicities against Mosquito	
		concentration (mg L^{-1})	larvicidal activity (%)	concentration (mg L^{-1})	larvicidal activity (%)
1	$CH(CH_3)_2$	2.5	100	1	100
		1.0	100	0.5	100
		0.5	50	0.25	100
		0.25	0	0.1	100
				0.05	100
				0.025	100
				0.01	100
				0.005	75
				0.0025	15
				0.001	0
2	$PhCH_2$	200	40	1	100
		100	30	0.5	100
		50	10	0.25	20
		25	0	0.1	10
3	CH_3	100	90	1	100
		50	40	0.5	100
		25	0	0.25	100
				0.1	100
				0.05	100
				0.025	10
				0.01	0
4	CH_3CH_2	100	100	1	100
		50	100	0.5	100
		25	75	0.25	100
		10	10	0.1	100
		5	0	0.05	10
				0.025	10
				0.01	0
5	$CH_3CH_2CH_2$	100	80	1	100
		50	70	0.5	100
		25	20	0.25	100
		2.5	0	0.1	100
				0.05	50
				0.025	0
6	CH_2CH_2Cl	50	100	1	100
		10	100	0.5	100
		5	75	0.25	100
		2.5	55	0.1	90
		1.0	0	0.05	90
				0.025	20
				0.01	0
7	CH_2CH_2F	50	90	1	100
		25	90	0.5	100
		10	20	0.25	100
		2.5	0	0.1	60
				0.05	10
				0.025	0
8	$CH_2CH{=}CH_2$	100	90	1	100
		50	66.7	0.5	100
		25	10	0.25	100
		10	0	0.1	90
				0.05	10
				0.025	0

Table 7. Continued

compd.	R	Toxicities against Oriental armyworm		Toxicities against Mosquito	
		concentration (mg L^{-1})	larvicidal activity (%)	concentration (mg L^{-1})	larvicidal activity (%)
9	$H_2C{-}{\equiv}{-}H$	50	100	1	100
		25	75	0.5	100
		10	55	0.25	100
		2.5	10	0.1	100
		1.0	0	0.05	40
				0.025	10
				0.01	0
10	$CH_2CO_2CH_3$	200	90	1	100
		100	80	0.5	100
		50	56.7	0.25	80
		25	30	0.1	0
		10	10		
		2.5	0		
11	$CH_2CH_2OCH_3$	200	40	1	100
		100	10	0.5	0
		50	0		
12	$CH_2CH_2CH_2CH_3$	200	50	1	100
		100	40	0.5	100
		50	0	0.25	100
				0.1	100
				0.05	10
				0.025	0
13	$CH(CH_3)CH_2CH_3$	25	100	0.1	100
		10	80	0.05	100
		5	50	0.025	100
		2.5	30	0.01	40
		1.0	0	0.005	20
				0.0025	10
14	$CH(CH_3)(CH_2)_2CH_3$	50	80	0.1	100
		25	70	0.05	100
		10	20	0.025	100
		2.5	0	0.01	40
				0.005	20
				0.0025	10
15	$CH_2CH(CH_3)_2$	100	100	1	100
		50	80	0.5	100
		25	30	0.25	100
		2.5	0	0.1	100
				0.05	10
				0.025	10
				0.01	0
16	$CH_2(CH_2)_3CH_3$	50	90	2	100
		25	20	1	100
		10	0	0.5	90
				0.25	80
				0.1	15
				0.05	0
17	cyclopentyl	200	70	1	100
		100	20	0.5	100
		50	0	0.25	100
				0.1	100
				0.05	10
				0.025	0

Table 7. Continued

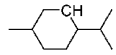
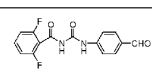
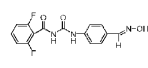
compd.	R	Toxicities against Oriental armyworm		Toxicities against Mosquito	
		concentration (mg L^{-1})	larvicidal activity (%)	concentration (mg L^{-1})	larvicidal activity (%)
18	$CH(CF_3)_2$	25	100	0.1	100
		10	100	0.05	100
		5	100	0.025	100
		2.5	100	0.01	100
		1	90	0.005	100
		0.5	40	0.0025	100
		0.25	0	0.001	90
				0.0005	60
				0.00025	30
19		25	100	0.01	100
		10	100	0.005	100
		5	100	0.0025	100
		2.5	100	0.001	80
		1	80	0.0005	10
		0.5	40		
		0.25	10		
		0.125	0		
20	CH_2CHF_3	25	100	0.1	100
		10	100	0.05	100
		5	100	0.025	100
		2.5	100	0.01	100
		1.0	90	0.005	100
		0.5	60	0.0025	70
		0.25	0	0.001	10
21		200	80	2	100
		100	40	1	100
		50	10	0.5	10
		25	10	0.25	10
		10	0	0.1	10
22		25	100	0.01	100
		10	100	0.005	100
		5	100	0.0025	60
		2.5	90	0.001	0
		1.0	0		
23	$C(CH_3)_3$	25	100	0.1	100
		10	100	0.05	100
		5	100	0.025	100
		2.5	100	0.01	100
		1.0	100	0.005	100
		0.5	85	0.0025	90
		0.25	0	0.001	70
				0.0005	20
24	$Si(CH_3)_3$	200	100	2	100
		100	60	1	100
		50	0	0.5	100
				0.25	0
24a		200	0	2	100
		100	0	1	80
				0.5	0
24b		200	80	2	100
				1	100
				0.5	60
				0.25	40
				0.1	10
Flucycloxuron		10	95	0.1	100
		5	90	0.05	100
		2.5	50	0.025	15
		1.0	10	0.01	0
		0.5	0		

Table 8. Plant Growth Regulatory Activities of Compounds **1**−**4**, **6**−**8**, **11**, **12**, and **14**−**17**

compd.	plant growth regulatory activities on the radicle growth of cucumber at concentration of 10 mg L^{-1} (%)	rank*
1	55.0	+
2	60.0	+
3	30.0	-
4	0	-
6	110	++
7	110	++
8	120	++
11	30.0	-
12	50.0	+
14	45.0	-
15	45.0	-
16	50.0	-
17	85.0	+

*Symbols: +++, ≥150%; ++, ≥100%; +, ≥50%; −, <50%.

Table 9. Selected Bond Lengths and Torsion Angles of Compound **1a**

selected bond	bond length (Å)	selected torsion angles	torsion angles (°)
C(4)-C(7)	1.470(3)	C(5)-C(4)-C(7)-N(2)	-178.28(14)
N(1)-C(1)	1.470(3)	C(3)-C(4)-C(7)-N(2)	2.0(2)
N(1)-O(1)	1.229(2)	C(7)-N(2)-O(3)-C(8)	-173.07(12)
N(2)-C(7)	1.276(2)	O(1)-N(1)-C(1)-C(6)	11.6(2)
N(2)-O(3)	1.408(2)	O(2)-N(1)-C(1)-C(2)	12.4(2)
O(3)-C(8)	1.460(2)	N(2)-O(3)-C(8)-C(9)	62.85(17)
C(8)-C(9)	1.514(3)	O(3)-N(2)-C(7)-C(4)	-179.81(12)

(*29*). Unfortunately, we did not get the desired compound **22a**. Then the solvent was changed to DMF and the reaction was stirred at 70−80 °C for 12 h. Surprisingly, compound **22a** was obtained as byproduct, whereas the product was 4-hydroxybenzonitrile, which was confirmed by ^{1}H NMR ((400 MHz, $CDCl_3$), δ 6.92 (d, J = 8.8 Hz, 2 H), 7.56 (d, J = 8.8 Hz, 2 H), 6.17 (br s, 1H)) and GC-MS (m/z M^+ = 119) (*30*). The possible mechanism, which was reported by Knudsen et al. in 1975, is shown in **Scheme 2** (*31*).

The target compounds **18**−**22** were synthesized from *O*-(mesitylsulfonyl)hydroxylamine (**n**) as shown in **Scheme 3**. The powerful aminating reagent **n** was prepared according to the method of the literature and preserved at −20 °C (*32, 33*). The reagent **n** was treated with RONa to provide *O*-alkylhydroxylamines, which were used without further purification and reacted with *p*-nitrobenzaldehyde to afford compounds **18a**−**22a** (*34*). Then reduction of compounds **18a**−**22a** using iron powder as a reductant provided compounds **18b**−**22b**, which were combined with 2,6-difluorobenzoyl isocyanate to afford compounds **18**−**22**.

The target compound **23** was synthesized from (*E*)-4-nitrobenzaldehyde oxime (**m**) as shown in **Scheme 4**. Compound **m** was reacted with newly prepared isobutylene (*35*) using concentrated H_2SO_4 as a catalyst to afford **23a**, and subsequent reduction using iron powder as a reductant provided compound **23b**, which was combined with 2,6-difluorobenzoyl isocyanate to afford compound **23**.

The target compound **24** was synthesized from *p*-nitrobenzaldehyde as shown in **Scheme 5**. The reduction of *p*-nitrobenzaldehyde provided *p*-aminobenzaldehyde according to reported procedure (*36*), and subsequent combination with 2,6-difluorobenzoyl isocyanate afforded compound **24a**; further reaction with hydroxylamine hydrochloride gave compound **24b**. However, compound **24** was not obtained in dry tetrahydrofuran from **24b** and chlorotrimethylsilane. Interestingly, the mixture of diethyl ether and tetrahydrofuran (v/v = 1:5) was used as solvent to give compound **24** in good yield.

Structure. (*E*)-*O*-Isopropyl-4-nitrobenzaldehyde oxime (**1a**) was confirmed by ^{1}H NMR and melting point (*37*). Pejković-Tadić et al. reported that oximyl hydrogen chemical shifts of various substituted benzaldoximes were dramatically different for the *E* and *Z* isomers, with all *E* isomers having protons with $\delta_H > 8$, whereas the *Z* isomers had $\delta_H < 7.5$ (*38*). This distinction enabled us to assign the configuration of compound **1a** as the *E* configuration. Fortunately, compound **1a** was recrystallized from a mixture of ethyl acetate and petroleum ether (60−90 °C) to give a colorless crystal suitable for X-ray single-crystal diffraction. The crystal belongs to triclinic, space group $P\bar{1}$ with the following crystallographic parameters: a = 11.344(10) Å, b = 13.010(8) Å, c = 13.154(4) Å, α = 60.79(10)°, β = 70.08(10)°, γ = 76.65(10)°, μ = 0.098, V = 1588.1(18) Å^3, z = 4, Dx = 1.304 mg/m^3, F(000) = 658, T = 113(2) K, 1.80° ≤ θ ≤ 24.87°, and the final R factor R_1 = 0.0496, ωR_2 = 0.1233. It could be seen from the X-ray single-crystal figures (**Figures 1** and **2**) that *p*-nitrophenyl and *O*-isopropyl are of the opposite of the C═N double bond. Hence, compound **1a** was of the *E* configuration. Its subsequent reaction gave the *E* isomer of compound **1**. Selected bond lengths and torsion angles are listed in **Table 9**. The bond length of N(2)—O(3) (1.408 Å) is shorter than normal N—O (1.46 Å), the bond length of N(2)—C(7) is shorter than normal C═N (1.34 Å), the bond length of C(4)—C(7) (1.470 Å) and N(1)—C(1) (1.470 Å) is shorter than

typical C—O (1.51 Å), which suggest that the electron density is localized among the nitro group, phenyl, and C=N—O. We can conclude that the nitro group, phenyl, and C=N double bond are close to planar from the selected torsion angles of O(3)—N(2)—C(7)—C(4), C(5)—C(4)—C(7)—N(2), and O(1)—N(1)—C(1)—C(6) in **Table 9**.

Structure−Activity Relationship (SAR). *Larvicidal Activities against Oriental Armyworm (Mythimna separata).* **Table 7** shows the larvicidal activities of the target compounds **1**−**24** and Flucycloxuron against oriental armyworm and mosquito. The results indicate that most compounds have excellent larvicidal activities against oriental armyworm and that some compounds exhibit higher larvicidal activities than Flucycloxuron. For example, the larvicidal activities of compounds **1**, **18**, **19**, **20**, and **23** against oriental armyworm at 1.0 mg L^{-1} were 100, 90, 80, 90, and 100%, respectively, as compared with 10% mortality of Flucycloxuron at the same concentration. However, intermediates **24a** and **24b** showed no or poor larvicidal activities against oriental armyworm and mosquito, which suggest that the *O*-alkyl oxime ether group would have great influence on the activities. The result in **Table 7** shows that there exist steric effects and electric effects on the larvicidal activities. The activity becomes higher with the size of *O*-alkyl of compounds increasing, for example, compounds **23** and **1** exhibit higher larvicidal activities against oriental armyworm than compounds **5**, **12**, **13**, and **15**. The larvicidal activities of compounds **11**, **10**, **9**, **8**, **7**, and **23** against oriental armyworm increase subsequently with the electron density of the C atom connecting to the O atom in the *O*-alkyl chain decreasing. Although the electron density of the C atom connecting to the O atom in the *O*-alkyl chain of compound **18** is higher than that of compound **1**, compounds **18** and **1** displayed similar larvicidal activities against oriental armyworm. Compound **23** displayed excellent larvicidal activity against oriental armyworm, whereas compound **24** exibited poor larvicidal activity against oriental armyworm when the C atom connecting to the O atom in the *O*-alkyl chain was replaced by a Si atom. The larvicidal activities of several commercial benzoylphenylureas against oriental armyworm were tested under the same condition, and the results have been reported (*39*). The LC_{50} values of Chlorfluazuron, Teflubenzuron, Dichlorbenzuron, Chlorbenzuron, Flucycloxuron, and Hexaflumuron were 1.03, 1.14, 1.82, 2.29, 2.44, and 4.70 mg L^{-1}, respectively. From **Table 7**, it can be seen that the LC_{50} of compound **1** is 0.5 mg L^{-1}; therefore, the index of relative toxicity is 940-fold compared with that of Hexaflumuron.

Larvicidal Activities against Mosquito (Culex pipiens pallens). It is seen from **Table 7** that the target compounds **1**−**24** displayed similar structure−activity relationships (SAR) against mosquito. In particular, the larvicidal activities of compounds **18**, **19**, **20**, and **23** against mosquito were 10 times better than that of Flucycloxuron. Compound **18** exhibited the best larvicidal activity against mosquito, which had 90% mortality even at 0.001 mg L^{-1}.

Plant Growth Regulatory Activity. The plant growth regulatory activities of the target compounds **1**−**4**, **6**−**8**, **11**, **12**, and **14**−**17** were evaluated, and their effects on the radicle growth of cucumber are shown in **Table 89**. Interestingly, some compounds showed good stimulation of radicle growth of cucumber, for example, compounds **6**, **7**, and **8** gave 110, 110, and 120% promotion, respectively.

In summary, a series of novel benzoylphenylureas containing an oxime ether group were designed and synthesized and their structures characterized by ^{1}H NMR, elemental analysis (or HRMS), and single-crystal X-ray diffraction analysis. The larvicidal activities against oriental armyworm and mosquito and plant growth regulatory activities of these benzoylphenylureas were evaluated. The results of larvicidal activities showed that most compounds exhibited excellent larvicidal activities against oriental armyworm and mosquito. The structure−activity relationship indicated that a bigger size of *O*-alkyl of the target compounds increases the larvicidal activities. In particular, the larvicidal activities against oriental armyworm of compounds **1** and **23** were 5−10 times better than that of Flucycloxuron. Compound **18** exhibited excellent larvicidal activity against mosquito, which had 90% mortality even at 0.001 mg L^{-1}. Surprisingly, some of these benzoylphenylureas exhibited good plant growth regulatory activities.

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