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Design, Synthesis, and Biological Activities of Novel 2-Cyanoacrylates Containing Oxazole, Oxadiazole, or Quinoline Moieties

QIQI ZHAO, SHAOHUA LIU, YONGHONG LI, AND QINGMIN WANG*

State Key Laboratory of Elemento-Organic Chemistry, Research Institute of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, People's Republic of China

A series of novel 2-cyanoacrylates containing an oxazole, oxadiazole, or quinoline moiety were designed and synthesized, and their structures were characterized by ^{1}H NMR and elemental analysis (or high-resolution mass spectrometry). Their herbicidal activities against four weeds were evaluated, and the result indicated that some of the title compounds showed excellent herbicidal activities against rape and amaranth pigweed in postemergence treatment at a dose of 375 g/ha. Furthermore, most of these cyanoacrylates exhibited interesting plant growth regulatory activities.

KEYWORDS: Cyanoacrylates; oxazole; oxadiazole; quinoline; herbicidal activity; plant growth regulatory activity

INTRODUCTION

2-Cyanoacrylates **A** are inhibitors of photosystem II (PSII) electron transport that disrupt photosynthetic electron transport at the PSII reaction center so as to inhibit the growth of weeds. Among these cyanoacrylates, some compounds have been reported to exhibit high inhibitory activity of the Hill reaction and good herbicidal activities (*1*−*5*). Furthermore, 2-cyanoacrylates have also been reported to show fungicidal (*6, 7*) and antiviral (*8*−*11*) activities.

Bioisosterism is an effective way to optimize bioactive compounds, and there are many successful examples such as nitenpyram, acetamiprid, and thiacloprid (*12, 13*). In previous works, we have reported the syntheses of cyanoacrylates containing a heterocycle such as pyridine (**B**) and thiazole (**C**) groups, and some of these compounds exhibited notable activities (*14*−*16*).

The binding model of cyanoacrylate PSII electron transport inhibitor **B** with the D1 protein of PSII was built, and the structure−activity relationship research by comparative molecular field analysis (CoMFA) was reported in our previous work (*4, 17*). We have found that the N atom on the pyridine ring could form an H-bond with the backbone amide of Phe265 on the D1 protein. At the same time, a bulky and electronegative group around the para-position of the aromatic rings would have the potential for higher activity. Moreover, the structure−activity relationship also indicated that the activity of **A** could be enhanced by decreasing the size of R^2.

It is known that nitrogen-containing heterocycles such as oxazole, oxadiazole, or quinoline often appear as bioisosteric analogues of benzene, pyridine, and thiazole. Hence, we have designed a series of new 2-cyanoacrylates (**D**) bearing an oxazole, oxadiazole, or quinoline group, in which R^2 was chosen as methylthio, isopropyl, or ethyl and R^3 was fixed as an ethoxyethyl group according to the structure−activity relationship. Herein, we report the synthesis of these new 2-cyanoacrylates (**D**) bearing an oxazole, oxadiazole, or quinoline group. The target compounds were evaluated for herbicidal activity and plant growth regulatory activity.

MATERIALS AND METHODS

Instruments. ^{1}H NMR spectra were obtained at 300 MHz using a Bruker AV300 spectrometer or at 400 MHz using a Varian Mercury Plus400 spectrometer in $CDCl_3$ solution with tetramethylsilane as the internal standard. Chemical shift values (δ) were given in ppm. Elemental analyses were determined on a Yanaca CHN Corder MT-3 elemental analyzer. High-resolution mass spectrometry (HRMS) data were obtained on a FTICR-MS instrument (Ionspec 7.0T). The melting points were determined on an X-4 binocular microscope melting point apparatus (Beijing Tech Instruments Co., Beijing, China) and were uncorrected. Yields were not optimized.

General Synthesis. Different aminomethyl-substituted oxazoles, oxadizoles, and quinolines were synthesized via the corresponding halomethyl compounds by the Gabriel reaction, which involved alkylation of potassium phthalimide followed by cleavage of the phthaloyl protecting group (*5, 16, 18*).

Compounds **IVa**, **IVb**, and **IVc** were prepared according to our previous work (*14, 15*). All of the anhydrous solvents were dried and distilled by standard techniques. The heterocycles were listed in **Table 1**.

General Synthetic Procedures for I1 and I2. A mixture of **1** (12.4 mmol) and 1,3-dichloroacetone (3.15 g, 24.8 mmol) was heated at 130 °C for 1 h. After the mixture was cooled to room temperature, water (30 mL) was added, and the mixture was extracted with dichloromethane (3 × 15 mL). The organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo, and then, the crude product was recrystallized with petroleum ether (60−90 °C) and ethyl acetate to give a white solid.

* To whom correspondence should be addressed. Tel: +86(0)22-23499842. Fax: +86(0)22-23499842. E-mail: wang98h@263.net.

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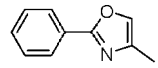
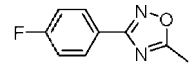
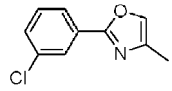
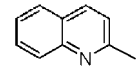
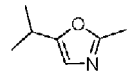
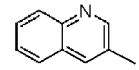
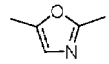
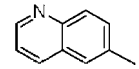
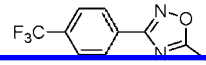
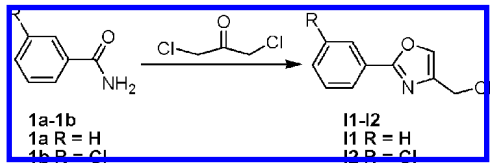
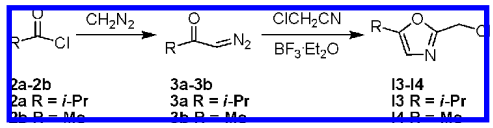
Table 1. Type of Heterocycle Ar

I, II, III	Ar	I, II, III	Ar
1		6	
2		7	
3		8	
4		9	
5			

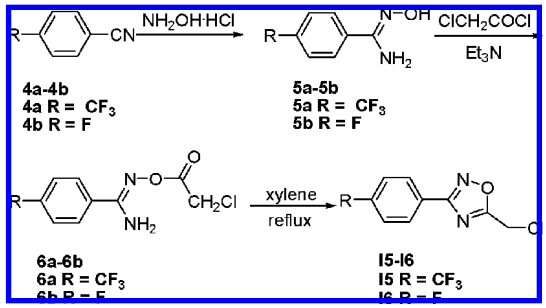
Scheme 1. General Synthetic Route for Phenyl-Substituted Oxazolmethylchloride **I1** and **I2**



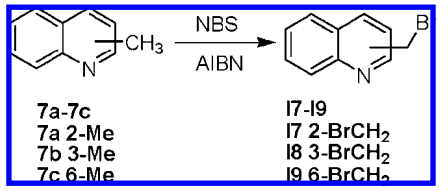
Scheme 2. General Synthetic Route for Alkyl-Substituted Oxazolmethylchloride **I3** and **I4**



Scheme 3. General Synthetic Route for 3-Phenyl-1,2,4-oxadiazole-5-methylchloride **I5** and **I6**



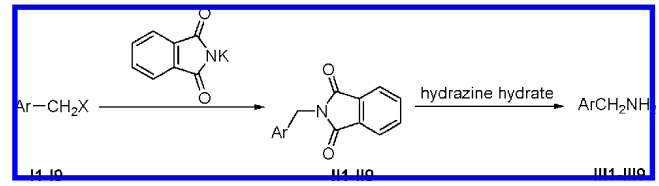
Scheme 4. General Synthetic Route for Quinolinylmethylbromide **I7**, **I8**, and **I9**



Data for **I1.** Yield, 70.1%; mp, 53−55 °C. ^{1}H NMR ($CDCl_3$): δ 4.56 (s, 2H, CH_2), 7.43−7.45 (m, 3H, Ar−H), 7.68 (s, 1H, Ar−H), 8.01−8.04 (m, 2H, Ar−H).

Data for **I2.** Yield, 79.3%; mp, 93− 95 °C. ^{1}H NMR ($CDCl_3$): δ 4.57 (s, 2H, CH_2), 7.37−7.44 (m, 2H, Ar−H), 7.72 (s, 1H, Ar−H), 7.92 (d, $^3J_{HH}$ = 7.6 Hz, 1H, Ar−H), 8.04 (s, 1H, Ar−H).

Scheme 5. General Synthetic Route for Arylmethylamines **III1**−**III9**



Scheme 6. General Synthetic Route for the Title Compounds **Va**−**Vs**

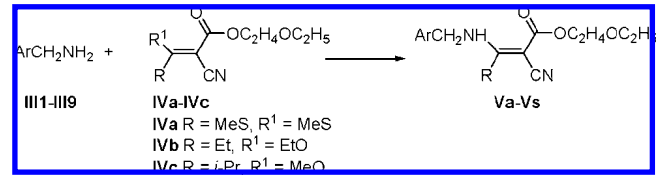


Table 2. Title Compounds **Va**−**Vs**[a]

compound	Ar	R	compound	Ar	R
Va	1	SMe	**Vk**	6	*i*-Pr
Vb	1	*i*-Pr	**Vl**	6	Et
Vc	2	SMe	**Vm**	7	SMe
Vd	2	*i*-Pr	**Vn**	7	Et
Ve	4	SMe	**Vo**	7	*i*-Pr
Vf	3	SMe	**Vp**	9	SMe
Vg	3	*i*-Pr	**Vq**	9	*i*-Pr
Vh	5	SMe	**Vr**	8	*i*-Pr
Vi	5	*i*-Pr	**Vs**	8	SMe
Vj	6	SMe			

[a] Note: The meanings of the number in the Ar column were identical with those of intermediates **I**, **II**, and **III** in **Table 1**.

General Synthetic Procedures for 3a and 3b. To a cooled solution (below 0 °C) of diazomethane in ethyl ether was added dropwise a solution of isoburyryl chloride or acetyl chloride (20 mmol) in ethyl ether (10 mL). The mixture was stirred below 0 °C for 24 h, and then, nitrogen gas was guided in to remove the remaining diazomethane. The solution was dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to give the crude product as a yellow oil (**3**), which was utilized in the next step without further purification.

Data for **3a.** Yield, 99.2%. ^{1}H NMR ($CDCl_3$): δ 1.08 [d, $^3J_{HH}$ = 6.8 Hz, 6H, $(CH_3)_2CH$], 2.27 [m, 1H, $(CH_3)_2CH$], 5.27 (s, 1H, CH=N).

Data for **3b.** Yield, 98.1%. ^{1}H NMR ($CDCl_3$): δ 2.01 (s, 3H, CH_3), 5.26 (s, 1H, CH).

General Synthetic Procedures for I3 and I4. To a cooled (−15 °C) flask containing chloroacetonitrile (15 mL) was added boron

Table 3. Herbicidal Activities of Compounds **Va**−**Vs** (1.5 kg/ha, Percent Inhibition)

	postemergence treatment				preemergence treatment			
compound	rape	amaranth pigweed	alfalfa	hairy crabgrass	rape	amaranth pigweed	alfalfa	hairy crabgrass
Va	34.7	0	0	0	5.0	5.0	5.0	0
Vb	87.3	71.4	0	87.0	0	10.0	0	5.0
Vc	25.4	0	0	6.5	0	0	10.0	0
Vd	80.5	84.1	0	0	15.0	0	5.0	0
Ve	10.0	**100**	0	10.0	0	43.9	0	0
Vf	5.0	26.8	0	0	10.0	5.0	0	0
Vg	**100**	80.5	15.0	10.0	52.7	0	0	0
Vh	**100**	0	0	37.5	0	0	0	0
Vi	**100**	**100**	43.2	57.5	48.4	50.3	0	10.0
Vj	15.0	0	0	10.0	10.0	0	0	0
Vk	**100**	**100**	10.0	82.5	**88.0**	0	0	0
Vl	0	0	0	0	15.0	0	0	0
Vm	35.6	0	15.0	0	0	0	0	0
Vn	8.5	0	0	0	0	20.0	0	0
Vo	72.0	77.8	0	50.6	0	0	0	0
Vp	**100**	**100**	0	66.2	10.0	0	0	10.0
Vq	73.7	0	10.0	0	0	0	0	0
Vr	**100**	**100**	0	45.5	18.2	41.9	0	0
Vs	**100**	**100**	67.8	48.1	**74.9**	35.5	10.0	0

Table 4. Herbicidal Activities of Compounds **V** (Postemergence Treatment, Percent Inhibition)

compound	dose (g/ha)	rape	amaranth pigweed
Vg	750	57.4	
	375	35.4	
Vp	750	100	100
	375	**99.5**	**96.0**
Vr	750	100	100
	375	87.2	57.6
Vs	750	100	100
	375	**100**	**91.9**

trifluoride-ethyl ether (5− 6 mL), and then, a solution of **3** (17 mmol) in chloroacetonitrile (10 mL) was added dropwise while the temperature was kept at −10 °C. After it was stirred at room temperature for 1 h, the solution was poured into a mixture of ice and ethyl ether and modulated to alkalescence, and the aqueous layer was extracted with ethyl ether (2 × 20 mL). The combined organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to afford yellow oil.

Data for **I3.** Yield, 67.6%. ^{1}H NMR ($CDCl_3$): δ 1.25 [d, $^3J_{HH}$ = 7.2 Hz, 6H, $(CH_3)_2CH$], 2.92−2.99 [m, 1H, $(CH_3)_2CH$], 4.55 (s, 2H, CH_2), 6.68 (s, 1H, Ar−H).

Data for **I4.** Yield, 43.4%. ^{1}H NMR ($CDCl_3$): δ 2.31 (s, 3H, CH_3), 4.54 (s, 2H, CH_2), 6.70 (s, 1H, Ar−H).

General Synthetic Procedure for 5. To a stirred mixture of hydroxylamine hydrochloride (0.69 g, 10 mmol), water (1 mL), and sodium hydroxide (0.4 g, 10 mmol) was added dropwise substituted benzonitrile (**4**, 8.54 mmol) in ethanol (7 mL). Then, the mixture was refluxed for 18 h and cooled to room temperature. After most ethanol was removed in vacuo, water was added and extracted with dichloromethane (3 × 10 mL). The organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to give a white solid (**5**).

Data for **5a.** Yield, 70.2%; mp, 128−129 °C. ^{1}H NMR ($CDCl_3$): δ 4.92 (brs, 3H, NH_2 and OH), 7.67 (d, $^3J_{HH}$ = 8.4 Hz, 2H, Ar−H), 7.75 (d, $^3J_{HH}$ = 8.4 Hz, 2H, Ar−H).

Data for **5b.** Yield, 75.3%; mp, 79− 81 °C. ^{1}H NMR ($CDCl_3$): δ 4.92 (brs, 3H), 7.08 (t, $^3J_{HH}$ = 8.4 Hz, 2H, Ar−H), 7.60−7.63 (m, 2H, Ar−H).

General Synthetic Procedure for 6. To a cooled (below 0 °C) solution of **5** (4.9 mmol) in chloroform (20 mL) was added dropwise chloroacetyl chloride (0.55 g, 4.9 mmol) in chloroform (10 mL), and the mixture was stirred for 20 min. Then, triethylamine (0.65 g, 6.5 mmol) in chloroform (10 mL) was added dropwise, and the solution was stirred under room temperature for 5 h. The mixture was washed with water (2 × 10 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on a silica gel [eluent, ethyl acetate/petroleum ether (60− 90 °C), 1:2, v/v] to afford a white solid.

Data for **6a.** Yield, 54.7%; mp, 126− 128 °C. ^{1}H NMR ($CDCl_3$): δ 4.32 (s, 2H, CH_2), 5.31 (brs, 2H, NH_2), 7.69 (d, $^3J_{HH}$ = 8.4 Hz, 2H, Ar−H), 7.82 (d, $^3J_{HH}$ = 8.4 Hz, 2H, Ar−H).

Data for **6b.** Yield, 60.2%; mp, 134− 136 °C. ^{1}H NMR ($CDCl_3$): δ 4.32 (s, 2H, CH_2), 5.13 (brs, 2H, NH_2), 7.13 (t, $^3J_{HH}$ = 8.7 Hz, 2H, Ar−H), 7.67− 7.72 (m, 2H, Ar−H).

General Synthetic Procedures for I5 and I6. A solution of **6** in xylene (20 mL) was refluxed for 5 h and then concentrated. The residue was purified by flash chromatography on a silica gel [eluent, ethyl acetate/petroleum ether (60− 90 °C), 1:10, v/v] to give **I5** and **I6** as a light yellow oil.

Data for **I5.** Yield, 95.1%. ^{1}H NMR ($CDCl_3$): δ 4.77 (s, 2H, CH_2), 7.76 (d, $^3J_{HH}$ = 8.0 Hz, 2H, Ar−H), 8.21 (d, $^3J_{HH}$ = 8.0 Hz, 2H, Ar−H).

Data for **I6.** Yield, 87.0%. ^{1}H NMR ($CDCl_3$): δ 4.74 (s, 2H, CH_2), 7.18 (t, $^3J_{HH}$ = 8.8 Hz, 2H, Ar−H), 8.06−8.10 (m, 2H, Ar−H).

General Synthetic Procedures for I7, I8, and I9. A mixture of methylquinoline (3 g, 21 mmol), *N*-bromosuccinimide (NBS, 3.7 g, 21 mmol), azodiisobutyronitrile (AIBN, 0.05 g), and carbon tetrachloride (100 mL) was refluxed for 2 h. After the mixture was cooled, the precipitate was filtered off, and the filtrate was washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on a silica gel [eluent, ethyl acetate/petroleum ether (60− 90 °C), 1:9, v/v] to afford a yellow oil, which was sent to the next step as soon as possible to avoid polymerization.

Data for **I7.** Yield, 41.6%. ^{1}H NMR ($CDCl_3$): δ 4.71 (s, 2H, CH_2), 7.53−7.58 (m, 2H, Ar−H), 7.73 (t, $^3J_{HH}$ = 7.2 Hz, 1H, Ar−H), 7.81 (d, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 8.06 (d, $^3J_{HH}$ = 8 0.4 Hz, 1H, Ar−H), 8.17 (d, $^3J_{HH}$ = 8.4 Hz, 1H).

Data for **I8.** Yield, 73.4%. ^{1}H NMR ($CDCl_3$): δ 4.70 (s, 2H, CH_2), 7.55 (t, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 7.74 (t, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 7.80 (d, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 8.01 (s, 1H, Ar−H), 8.12 (d, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 8.82 (d, $^4J_{HH}$ = 2.4 Hz, 1H).

Data for **I9.** Yield, 72.6%. ^{1}H NMR ($CDCl_3$): δ 4.66 (s, 2H, CH_2), 7.41−7.45 (m, 1H, Ar−H), 7.57−7.61 (m, 1H, Ar−H), 7.66 (s, 1H, Ar−H), 8.15 (t, $^3J_{HH}$ = 7.5 Hz, 2H, Ar−H), 8.93−8.95 (m, 1H, Ar−H).

General Synthetic Procedures for II. To a solution of **I** (6 mmol) in *N*,*N*-dimethylformamide (10 mL) was added potassium phthalimide (6 mmol) in portions. After the mixture was stirred at room temperature for 5 h, water (50 mL) was added, and the precipitate was collected by filtration and washed with water. After recrystallization from ethanol, a white crystal was obtained.

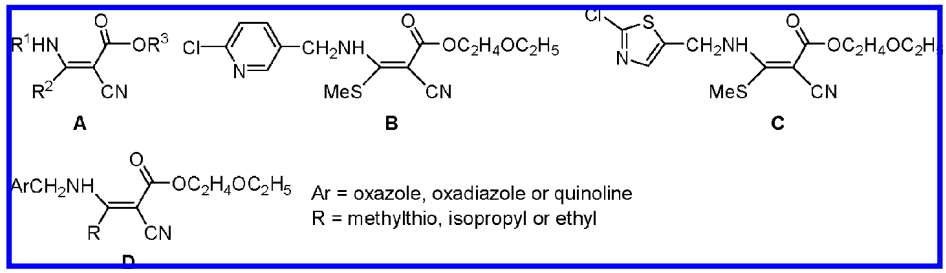


Figure 1. Chemical structures of compounds **A**−**D**.

Table 5. Plant Growth Regulatory Activities (10 mg/L) of Some of Compounds **V**

compound	Va	Vb	Vc	Vd	Ve	Vf	Vg
plant growth regulatory activities	50.0	60.0	80.0	−20.0	−20.6	63.7	98.2

compound	Vm	Vn	Vo	Vp	Vq	Vr	Vs
plant growth regulatory activities	60.0	95.4	115.0	**145.0**	85.0	85.0	**110.0**

Data for **II1.** Yield, 86.3%; mp, 133− 135 °C. ^{1}H NMR ($CDCl_3$): δ 4.87 (s, 2H, CH_2), 7.41 (s, 3H, Ar−H), 7.67 (s, 1H, Ar−H), 7.72 (m, 2H, Ar−H), 7.87 (m, 2H, Ar−H), 7.99 (s, 2H, Ar−H).

Data for **II2.** Yield, 92.6%; mp, 135− 137 °C. ^{1}H NMR ($CDCl_3$): δ 4.86 (s, 2H, CH_2), 7.35 (s, 2H, Ar−H), 7.69−7.73 (m, 3H, Ar−H), 7.86−7.92 (m, 3H, Ar−H), 7.98 (s, 1H, Ar−H).

Data for **II3.** Yield, 91.1%; mp, 140−142 °C. ^{1}H NMR ($CDCl_3$): δ 1.21 [d, $^3J_{HH}$ = 6.8 Hz, 6H, $(CH_3)_2$CH], 2.88−2.95 [m, 1H, $(CH_3)_2CH$], 4.94 (s, 2H, CH_2), 6.60 (s, 1H, Ar−H), 7.74−7.76 (m, 2H, Ar−H), 7.86−7.89 (m, 2H, Ar−H).

Data for **II4.** Yield, 71.9%; mp, 138− 140 °C. ^{1}H NMR ($CDCl_3$): δ 2.27 (s, 3H, CH_3), 4.94 (s, 2H, CH_2), 6.64 (s, 1H, Ar−H), 7.74−7.77 (m, 2H, Ar−H), 7.89−7.92 (m, 2H, Ar−H).

Data for **II5.** Yield, 95.2%; mp, 146− 147 °C. ^{1}H NMR ($CDCl_3$): δ 5.19 (s, 2H, CH_2), 7.70 (d, $^3J_{HH}$ = 8.0 Hz, 2H, Ar−H), 7.81−7.83 (m, 2H, Ar−H), 7.95−7.97 (m, 2H, Ar−H), 8.15 (d, $^3J_{HH}$ = 8.0 Hz, 2H, Ar−H).

Data for **II6.** Yield, 96.7%; mp, 144−146 °C. ^{1}H NMR ($CDCl_3$): δ 5.17 (s, 2H, CH_2), 7.12 (t, $^3J_{HH}$ = 8.4 Hz, 2H, Ar−H), 7.80−7.82 (m, 2H, Ar−H), 7.94−7.96 (m, 2H, Ar−H), 8.00−8.04 (d, $^3J_{HH}$ = 8.0 Hz, 2H, Ar−H).

Data for **II7.** Yield, 90.0%; mp, 171−173 °C. ^{1}H NMR ($CDCl_3$): δ 5.20 (s, 2H, CH_2), 7.36 (d, $^3J_{HH}$ = 8.8 Hz, 1H, Ar−H), 7.49 (t, $^3J_{HH}$ = 7.6 Hz, 1H, Ar−H), 7.65 (t, $^3J_{HH}$ = 7.6 Hz, 1H, Ar−H), 7.75−7.78 (m, 3H, Ar−H), 7.90−7.92 (m, 2H, Ar−H), 7.97 (d, $^3J_{HH}$ = 8.4 Hz, 1H, Ar−H), 8.10 (d,$^3J_{HH}$ = 8.4 Hz, 1H, Ar−H).

Data for **II8.** Yield, 92.1%; mp, 154−156 °C. ^{1}H NMR ($CDCl_3$): δ 5.05 (s, 2H, CH_2), 7.54 (t, $^3J_{HH}$ = 6.9 Hz, 1H, Ar−H), 7.67−7.74 (m, 3H), 7.80 (d, $^3J_{HH}$ = 8.1 Hz, 1H, Ar−H), 7.85−7.88 (m, 2H, Ar−H), 8.09 (d, $^3J_{HH}$ = 8.1 Hz, 1H, Ar−H), 8.22 (s, 1H, Ar−H), 9.03 (s, 1H, Ar−H).

Data for **II9.** Yield, 91.5%; mp, 163−165 °C. ^{1}H NMR ($CDCl_3$): δ 5.03 (s, 2H, CH_2), 7.37−7.40 (m, 1H, Ar−H), 7.71−7.80 (m, 7H, Ar−H), 7.66 (s, 1H, Ar−H), 8.17 (t, $^3J_{HH}$ = 7.5 Hz, 2H, Ar−H), 8.91−8.94 (m, 1H, Ar−H).

General Synthetic Procedures for III. To a suspension of N-substituted phthalimide **II** (4 mmol) in ethanol (20 mL) was added hydrazine hydrate (50%, 0.48 g, 4.8 mmol). The reaction mixture was refluxed for 5 h and then cooled. The precipitated phthalylhydrazide was filtered off and washed with ethanol, and then, the filtrate was concentrated under reduced pressure to give crude **III**, which was utilized in the next reaction without further purification.

Data for **III1.** Yield, 73.3%. ^{1}H NMR ($CDCl_3$): δ 1.75 (brs, 2H, NH_2), 3.83 (s, 2H, CH_2), 7.42−7.43 (m, 3H, Ar−H), 7.53 (s, 1H, Ar−H), 7.99−8.01 (s, 2H, Ar−H).

Data for **III2.** Yield, 78.8%. ^{1}H NMR ($CDCl_3$): δ 3.83 (s, 2H, NH_2), 7.35−7.41 (m, 2H, Ar−H), 7.56 (s, 1H, Ar−H), 7.89 (d, $^3J_{HH}$ = 7.6 Hz, 1H, Ar−H), 8.01 (s, 1H, Ar−H).

Data for **III3.** Yield, 72.7%. ^{1}H NMR ($CDCl_3$): δ 1.19 [d, $^3J_{HH}$ = 6.8 Hz, 6H, $(CH_3)_2$CH], 1.70 (brs, 2H, NH_2), 2.85−2.92 [m, 1H, $(CH_3)_2CH$], 3.85 (s, 2H, CH_2), 6.56 (s, 1H, Ar−H).

Data for **III4.** Yield, 70.5%. ^{1}H NMR ($CDCl_3$): δ 1.74 (s, 2H, NH_2), 2.27 (s, 3H, CH_3), 3.87 (s, 2H, CH_2), 6.62 (s, 1H, Ar−H).

Data for **III5.** Yield, 84.7%. ^{1}H NMR ($CDCl_3$): δ 4.32 (brs, 2H, CH_2), 5.31 (s, 2H, NH_2), 7.69 (d, $^3J_{HH}$ = 8.4 Hz, 2H, Ar−H), 7.82 (d, $^3J_{HH}$ = 8.4 Hz, 2H, Ar−H).

Data for **III6.** Yield, 92.9%. ^{1}H NMR ($CDCl_3$): δ 1.72 (s, 2H, NH_2), 4.15 (s, 2H, CH_2), 7.16 (t, $^3J_{HH}$ = 8.4 Hz, 2H, Ar−H), 8.05−8.09 (m, 2H, Ar−H).

Data for **III7.** Yield, 87.2%. ^{1}H NMR ($CDCl_3$): δ 3.02 (brs, 2H, NH_2), 4.23 (s, 2H, CH_2), 7.37 (d, $^3J_{HH}$ = 8.4 Hz, 1H, Ar−H), 7.51 (t, $^3J_{HH}$ = 6.8 Hz, 1H, Ar−H), 7.69 (t, $^3J_{HH}$ = 6.8 Hz, 1H, Ar−H), 7.79 (d, $^3J_{HH}$ = 8.8 Hz, 1H, Ar−H), 8.04 (d, $^3J_{HH}$ = 6.8 Hz, 1H, Ar−H), 8.10 (d, $^3J_{HH}$ = 8.8 Hz, 1H, Ar−H).

Data for **III8.** Yield, 78.3%. ^{1}H NMR ($CDCl_3$): δ 1.80 (s, 2H, NH_2), 3.87 (s, 2H, CH_2), 7.38 (t, $^3J_{HH}$ = 6.8 Hz, 1H, Ar−H), 7.53 (t, $^3J_{HH}$ = 6.8 Hz, 1H, Ar−H), 7.62 (d, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 7.86 (s, 1H, Ar−H), 7.97 (d, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 8.70 (d, $^4J_{HH}$ = 2.4 Hz, 1H).

Data for **III9.** Yield, 73.5%. ^{1}H NMR ($CDCl_3$): δ 1.70 (s, 2H, NH_2), 4.05 (s, 2H, CH_2), 7.35−7.39 (m, 1H, Ar−H), 7.64−7.66 (m, 1H, Ar−H), 7.73 (s, 1H, Ar−H), 8.05 (d, $^3J_{HH}$ = 8.8 Hz, 1H, Ar−H), 8.11 (d, $^3J_{HH}$ = 8.8 Hz, 1H, Ar−H), 8.85−8.87 (m, 1H, Ar−H).

General Synthetic Procedures for the Title Compounds V. A mixture of **IVa** (or **IVb** or **IVc**, prepared according to our previous work; *14, 15*) (1.35 mmol), crude **III** (1.45 mmol), and ethanol (20 mL) was refluxed for 1.5−2 h [monitored by thin-layer chromatography (ethyl acetate/petroleum ether (60−90 °C), 1:2, v/v)] and then evaporated under reduced pressure to give crude product. The residue was purified by vacuum column chromatography on a silica gel [eluent, ethyl acetate/petroleum ether (60−90 °C), 1:2, v/v] to afford the title compounds.

Data for **Va.** Yield, 96.8%; mp, 51−52 °C. ^{1}H NMR ($CDCl_3$): δ 1.18 (t, $^3J_{HH}$ = 7.2 Hz, 3H, CH_2CH_3), 2.72 (s, 3H, SCH_3), 3.55 (q, $^3J_{HH}$ = 7.2 Hz, 2H, CH_2CH_3), 3.67 (t, $^3J_{HH}$ = 5.2 Hz, 2H, OCH_2), 4.28 (t, $^3J_{HH}$ = 5.2 Hz, 2H, OCH_2), 4.75 (d, $^3J_{HH}$ = 5.6 Hz, 2H, NCH_2), 7.44−7.46 (m, 3H, Ar−H), 7.62 (s, 1H, Ar−H), 7.99−8.01 (m, 2H, Ar−H), 10.30 (brs, 1H, NH). Anal. calcd for $C_{19}H_{21}N_3O_4S$ (%): C, 58.90; H, 5.46; N, 10.85. Found: C, 59.09; H, 5.79; N, 11.49.

Data for **Vb.** Yield, 85.3%; oil. 1.19 (t, $^3J_{HH}$ = 7.2 Hz, 3H, CH_2CH_3), 1.46 [d, $^3J_{HH}$ = 7.2 Hz, 6H, $CH(CH_3)_2$], 3.29−3.36 [m, 1H, $CH(CH_3)_2$], 3.56 (q, $^3J_{HH}$ = 7.2 Hz, 2H, CH_2CH_3), 3.68 (t,$^3J_{HH}$ = 5.2 Hz, 2H, OCH_2), 4.27 (t, $^3J_{HH}$ = 5.2 Hz, 2H, OCH_2), 4.57 (d, $^3J_{HH}$ = 5.6 Hz, 2H, NCH_2), 7.45−7.47 (m, 3H, Ar−H), 7.62 (s, 1H, Ar−H), 8.00−8.02 (m, 2H, Ar−H), 10.56 (brs, 1H, NH). HRMS, *m/z* 382.1772. Calcd for $C_{21}H_{25}N_3O_4$ − H, 382.1767.

Data for **Vc.** Yield, 88.1%; mp, 83−84 °C. 1.19 (t, $^3J_{HH}$ = 7.2 Hz, 3H, CH_2CH_3), 2.72 (s, 3H, SCH_3), 3.55 (q, $^3J_{HH}$ = 7.2 Hz, 2H, CH_2CH_3), 3.68 (t, $^3J_{HH}$ = 5.2 Hz, 2H, OCH_2), 4.28 (t, $^3J_{HH}$ = 5.2 Hz, 2H, OCH_2), 4.75 (d, $^3J_{HH}$ = 5.6 Hz, 2H, NCH_2), 7.36−7.42 (m, 2H, Ar−H), 7.63 (s, 1H, Ar−H), 7.88 (d, $^3J_{HH}$ = 7.6 Hz, 1H, Ar−H), 7.99 (s, 1H, Ar−H), 10.30 (brs, 1H, NH). Anal. calcd for $C_{19}H_{20}ClN_3O_4S$ (%): C, 54.09; H, 4.78; N, 9.96; Found: C, 54.11; H, 4.79; N, 9.70.

Data for **Vd.** Yield, 90.9%; oil. 1.20 (t, $^3J_{HH}$ = 7.2 Hz, 3H, CH_2CH_3), 1.46 [d, $^3J_{HH}$ = 7.2 Hz, 6H, $CH(CH_3)_2$], 3.27−3.34 [m, 1H, $CH(CH_3)_2$], 3.56 (q, $^3J_{HH}$ = 7.2 Hz, 2H, CH_2CH_3), 3.69 (t, $^3J_{HH}$ = 5.2 Hz, 2H, OCH_2), 4.27 (t, $^3J_{HH}$ = 5.2 Hz, 2H, OCH_2), 4.57 (d, $^3J_{HH}$ = 5.6 Hz, 2H, OCH_2), 7.38−7.45 (m, 2H, Ar−H), 7.64 (s, 1H, Ar−H), 7.89 (d, $^3J_{HH}$ = 7.6 Hz, 1H, Ar−H), 8.00 (s, 1H, Ar−H), 10.56 (brs, 1H, NH). HRMS, *m*/*z* 416.1383. Calcd for $C_{21}H_{24}ClN_3O_4$ − H, 416.1377.

Data for **Ve.** Yield, 63.8%; mp, 73−74 °C. 1.21 (t, $^3J_{HH}$ = 6.9 Hz, 3H, CH_2CH_3), 2.32 (s, 3H, Ar−CH_3), 2.70 (s, 3H, SCH_3), 3.57 (q, $^3J_{HH}$ = 6.9 Hz, 2H, CH_2CH_3), 3.70 (t, $^3J_{HH}$ = 5.1 Hz, 2H, OCH_2), 4.32 (t, $^3J_{HH}$ = 5.1 Hz, 2H, OCH_2), 4.84 (d, $^3J_{HH}$ = 5.7 Hz, 2H, NCH_2), 6.72 (s, 1H, Ar−H), 10.43 (brs, 1H, NH). Anal. calcd for $C_{14}H_{19}N_3O_4S$ (%): C, 51.68; H, 5.89; N, 12.91. Found: C, 51.65; H, 5.93; N, 12.70.

Data for **Vf.** Yield, 88.1%; oil. 1.21 (t, $^3J_{HH}$ = 7.2 Hz, 3H, CH_2CH_3), 1.25 [d, $^3J_{HH}$ = 6.9 Hz, 6H, $CH(CH_3)_2$], 2.70 (s, 3H, SCH_3), 2.92−3.00 [m, 1H, $CH(CH_3)_2$], 3.57 (q,$^3J_{HH}$ = 7.2 Hz, 2H, CH_2CH_3), 3.70 (t, $^3J_{HH}$ = 5.1 Hz, 2H, OCH_2), 4.32 (t, $^3J_{HH}$ = 5.1 Hz, 2H, OCH_2), 4.85 (d, $^3J_{HH}$ = 5.7 Hz, 2H, NCH_2), 6.68 (s, 1H, Ar−H), 10.44 (brs, 1H, NH). HRMS, *m*/*z* 376.1301. Calcd for $C_{16}H_{23}N_3O_4S$ + Na, 376.1307.

Data for **Vg.** Yield, 70.4%; oil. 1.21 (t, $^3J_{HH}$ = 7.2 Hz, 3H, CH_2CH_3), 1.25 [d, $^3J_{HH}$ = 6.9 Hz, 6H, Ar-$CH(CH_3)_2$], 1.41 [d, $^3J_{HH}$ = 6.9 Hz, 6H, vinyl-$CH(CH_3)_2$], 2.92−3.01 [m, 1H, CH, Ar−$CH(CH_3)_2$], 3.20−3.29 [m, 1H, CH, vinyl-$CH(CH_3)_2$], 3.58 (q, $^3J_{HH}$ = 7.2 Hz, 2H, CH_2CH_3), 3.70 (t,$^3J_{HH}$ = 5.1 Hz, 2H, OCH_2), 4.31 (t, $^3J_{HH}$ = 5.1 Hz, 2H, OCH_2), 4.65 (d, $^3J_{HH}$ = 5.7 Hz, 2H, NCH_2), 6.70 (s, 1H, Ar−H), 10.71 (brs, 1H, NH). HRMS, *m*/*z* 372.1894. Calcd for $C_{18}H_{27}N_3O_4$ + Na, 372.1899.

Data for **Vh.** Yield, 79.4%; mp, 79−81 °C. 1.22 (t, $^3J_{HH}$ = 7.2 Hz, 3H, CH_2CH_3), 2.72 (s, 3H, SCH_3), 3.58 (q, $^3J_{HH}$ = 6.8 Hz, 2H, CH_2CH_3), 3.72 (t, $^3J_{HH}$ = 4.8 Hz, 2H, OCH_2), 4.35 (t, $^3J_{HH}$ = 4.8 Hz, 2H, OCH_2), 5.11 (d, $^3J_{HH}$ = 6.4 Hz, 2H, NCH_2), 7.76 (d, $^3J_{HH}$ = 8.4 Hz, 2H, Ar−H), 8.21 (d,$^3J_{HH}$ = 8.4 Hz, 2H, Ar−H), 10.53 (brs, 1H, NH). Anal. calcd for $C_{19}H_{19}F_3N_4O_4S$: C, 50.00; H, 4.20; N, 12.27. Found: C, 50.27; H, 4.28; N, 12.13.

Data for **Vi.** Yield, 47.1%; oil. 1.21 (t, $^3J_{HH}$ = 7.2 Hz, 3H, CH_2CH_3), 1.46 [d, $^3J_{HH}$ = 7.2 Hz, 6H, $CH(CH_3)_2$], 3.17 [m, 1H, $CH(CH_3)_2$], 3.58 (q, $^3J_{HH}$ = 7.2 Hz, 2H, CH_2CH_3), 3.71 (t, $^3J_{HH}$ = 4.8 Hz, 2H, OCH_2), 4.33 (t, $^3J_{HH}$ = 4.8 Hz, 2H, OCH_2), 4.91 (d, $^3J_{HH}$ = 6.4 Hz, 2H, NCH_2), 7.76 (d, $^3J_{HH}$ = 8.4 Hz, 2H, Ar−H), 8.21 (d, $^3J_{HH}$ = 8.4 Hz, 2H, Ar−H), 10.83 (brs, 1H, NH). HRMS, *m*/*z* 453.1750. Calcd for $C_{21}H_{23}F_3N_4O_4$ + H, 453.1744.

Data for **Vj.** Yield, 89.5%; mp, 116−117 °C. 1.22 (t, $^3J_{HH}$ = 7.2 Hz, 3H, CH_2CH_3), 2.71 (s, 3H, SCH_3), 3.58 (q, $^3J_{HH}$ = 6.8 Hz, 2H, CH_2CH_3), 3.72 (t, $^3J_{HH}$ = 4.8 Hz, 2H, OCH_2), 4.36 (t, $^3J_{HH}$ = 4.8 Hz, 2H, OCH_2), 5.08 (d, $^3J_{HH}$ = 6.4 Hz, 2H, NCH_2), 7.16−7.20 (m, 2H, Ar−H), 8.06−8.09 (m, 2H, Ar−H), 10.51 (brs, 1H, NH). Anal. calcd for $C_{18}H_{19}FN_4O_4S$: C, 53.19; H, 4.71; N, 13.79. Found: C, 53.18; H, 4.90; N, 13.70.

Data for **Vk.** Yield, 87.2%; oil. 1.20 (t, $^3J_{HH}$ = 7.2 Hz, 3H, CH_2CH_3), 1.44 [d, $^3J_{HH}$ = 7.2 Hz, 6H, $CH(CH_3)_2$], 3.15 [m, 1H, $CH(CH_3)_2$], 3.56 (q, $^3J_{HH}$ = 7.2 Hz, 2H, CH_2CH_3), 3.70 (t, $^3J_{HH}$ = 4.8 Hz, 2H, OCH_2), 4.31 (t, $^3J_{HH}$ = 4.8 Hz, 2H, OCH_2), 4.87 (d, $^3J_{HH}$ = 6.4 Hz, 2H, NCH_2), 7.17−7.20 (m, 2H, Ar−H), 8.05−8.08 (m, 2H, Ar−H), 10.79 (brs, 1H, NH). HRMS, *m*/*z* 425.1601. Calcd for $C_{20}H_{23}FN_4O_4$ + Na, 425.1596.

Data for **Vl.** Yield, 76.0%; mp, 109−110 °C. 1.21 (t, $^3J_{HH}$ = 7.2 Hz, 3H, OCH_2CH_3), 1.31 (t, $^3J_{HH}$ = 7.6 Hz, 3H, vinyl-CH_2CH_3), 2.72 (q, $^3J_{HH}$ = 7.6 Hz, 2H, vinyl-CH_2CH_3), 3.57 (q, $^3J_{HH}$ = 7.2 Hz, 2H, OCH_2CH_3), 3.71 (t, $^3J_{HH}$ = 4.8 Hz, 2H, OCH_2), 4.33 (t, $^3J_{HH}$ = 4.8 Hz, 2H, OCH_2), 4.83 (d, $^3J_{HH}$ = 6.4 Hz, 2H, NCH_2), 7.17−7.21 (m, 2H, Ar−H), 8.06−8.10 (m, 2H, Ar−H), 10.40 (brs, 1H, NH). Anal. calcd for $C_{19}H_{21}FN_4O_4$: C, 58.76; H, 5.45; N, 14.43. Found: C, 58.53; H, 5.62; N, 14.25.

Data for **Vm.** Yield, 80.0%; mp, 83−84 °C. 1.22 (t, $^3J_{HH}$ = 6.8 Hz, 3H, CH_2CH_3), 2.71 (s, 3H, SCH_3), 3.59 (q, $^3J_{HH}$ = 6.8 Hz, 2H, CH_2CH_3), 3.73 (t, $^3J_{HH}$ = 5.2 Hz, 2H, OCH_2), 4.36 (t, $^3J_{HH}$ = 5.2 Hz, 2H, OCH_2), 5.06 (d, $^3J_{HH}$ = 4.8 Hz, 2H, NCH_2), 7.31 (d, $^3J_{HH}$ = 8.8 Hz, 1H, Ar−H), 7.57 (t, $^3J_{HH}$ = 7.6 Hz, 1H, Ar−H), 7.75 (t, $^3J_{HH}$ = 7.6 Hz, 1H, Ar−H), 7.83 (d, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 8.13 (d, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 8.18 (d, $^3J_{HH}$ = 8.8 Hz, 1H, Ar−H), 11.03 (brs, 1H, NH). Anal. calcd for $C_{19}H_{21}N_3O_3S$: C, 61.44; H, 5.70; N, 11.31. Found: C, 61.41; H, 5.79; N, 11.49.

Data for **Vn.** Yield, 84.0%; mp, 117−118 °C. 1.22 (t, $^3J_{HH}$ = 6.8 Hz, 3H, OCH_2CH_3), 1.30 (t, $^3J_{HH}$ = 7.6 Hz, 3H, vinyl-CH_2CH_3), 2.72 (q, $^3J_{HH}$ = 7.6 Hz, 2H, vinyl-CH_2CH_3), 3.59 (q, $^3J_{HH}$ = 6.8 Hz, 2H, OCH_2CH_3), 3.72 (t, $^3J_{HH}$ = 5.2 Hz, 2H, OCH_2), 4.35 (t, $^3J_{HH}$ = 5.2 Hz, 2H, OCH_2), 4.86 (d, $^3J_{HH}$ = 5.6 Hz, 2H, NCH_2), 7.32 (d, $^3J_{HH}$ = 8.8 Hz, 1H, Ar−H), 7.57 (t, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 7.76 (t, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 7.83 (d, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 8.13 (d, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 8.19 (d, $^3J_{HH}$ = 8.8 Hz, 1H, Ar−H), 10.87 (brs, 1H, NH). Anal. calcd for $C_{20}H_{23}N_3O_3$: C, 67.97; H, 6.56; N, 11.89. Found: C, 67.72; H, 6.53; N, 12.00.

Data for **Vo.** Yield, 75.0%; mp, 74−75 °C. 1.22 (t, $^3J_{HH}$ = 6.9 Hz, 3H, CH_2CH_3), 1.43 [d, $^3J_{HH}$ = 7.2 Hz, 6H, $CH(CH_3)_2$], 3.22−3.33 [m, 1H, $CH(CH_3)_2$], 3.60 (q, $^3J_{HH}$ = 7.2 Hz, 2H, CH_2CH_3), 3.73 (t, $^3J_{HH}$ = 5.4 Hz, 2H, OCH_2), 4.35 (t, $^3J_{HH}$ = 5.4 Hz, 2H, OCH_2), 4.91 (d, $^3J_{HH}$ = 5.7 Hz, 2H, NCH_2), 7.33 (d, $^3J_{HH}$ = 8.7 Hz, 1H, Ar−H), 7.57 (t, $^3J_{HH}$ = 7.8 Hz, 1H, Ar−H), 7.76 (t, $^3J_{HH}$ = 7.8 Hz, 1H, Ar−H), 7.83 (d, $^3J_{HH}$ = 7.5 Hz, 1H, Ar−H), 8.13 (d, $^3J_{HH}$ = 7.5 Hz, 1H, Ar−H), 8.20 (d,$^3J_{HH}$ = 8.7 Hz, 1H, Ar−H), 11.21 (brs, 1H, NH). Anal. calcd for $C_{21}H_{25}N_3O_3$: C, 68.64; H, 6.86; N, 11.44. Found: C, 68.54; H, 6.76; N, 11.45.

Data for **Vp.** Yield, 96.8%; oil. 1.21 (t, $^3J_{HH}$ = 6.9 Hz, 3H, CH_2CH_3), 2.68 (s, 3H, SCH_3), 3.57 (q, $^3J_{HH}$ = 6.9 Hz, 2H, CH_2CH_3), 3.70 (t, $^3J_{HH}$ = 5.1 Hz, 2H, OCH_2), 4.31 (t, $^3J_{HH}$ = 5.1 Hz, 2H, OCH_2), 4.99 (d,$^3J_{HH}$ = 6.0 Hz, 2H, NCH_2), 7.43−7.47 (m, 1H, Ar−H), 7.57−7.61 (m, 1H, Ar−H), 7.66 (s, 1H, Ar−H), 8.14−8.16 (m, 2H, Ar−H), 8.93−8.95 (m, 1H, Ar−H), 10.48 (brs, 1H, NH). Anal. calcd for $C_{19}H_{21}N_3O_3S$: C, 61.44; H, 5.70; N, 11.31. Found: C, 61.27; H, 5.52; N, 11.29.

Data for **Vq.** Yield, 90.6%; oil. 1.20 (t, $^3J_{HH}$ = 7.2 Hz, 3H, CH_2CH_3), 1.35 [d,$^3J_{HH}$ = 7.2 Hz, 6H, $CH(CH_3)_2$], 3.17 [s, 1H, $CH(CH_3)_2$], 3.56 (q, $^3J_{HH}$ = 6.8 Hz, 2H, CH_2CH_3), 3.69 (t, $^3J_{HH}$ = 5.2 Hz, 2H, OCH_2), 4.28 (t, $^3J_{HH}$ = 5.2 Hz, 2H, OCH_2), 4.78 (d, $^3J_{HH}$ = 6.0 Hz, 2H, NCH_2), 7.42−7.45 (m, 1H, Ar−H), 7.56−7.58 (m, 1H, Ar−H), 7.65 (s, 1H, Ar−H), 8.14−8.16 (m, 2H, Ar−H), 8.91−8.93 (m, 1H, Ar−H), 10.71(brs, 1H, NH). Anal. calcd for $C_{21}H_{25}N_3O_3$: C, 68.64; H, 6.86; N, 11.44. Found: C, 68.44; H, 6.80; N, 11.32.

Data for **Vr.** Yield, 88.1%; mp, 95−96 °C. 1.18 (t, $^3J_{HH}$ = 6.8 Hz, 3H, CH_2CH_3), 1.37 [d, $^3J_{HH}$ = 7.2 Hz, 6H, $CH(CH_3)_2$], 3.12 [s, 1H, $CH(CH_3)_2$], 3.55 (q, $^3J_{HH}$ = 7.2 Hz, 2H, CH_2CH_3), 3.67 (t, $^3J_{HH}$ = 5.2 Hz, 2H, OCH_2), 4.27 (t, $^3J_{HH}$ = 5.2 Hz, 2H, OCH_2), 4.79 (d, $^3J_{HH}$ = 6.0 Hz, 2H, NCH_2), 7.56 (t, $^3J_{HH}$ =8.0 Hz, 1H, Ar−H), 7.73 (t, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 7.81 (d, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 8.00 (s, 1H, Ar−H), 8.11 (d, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 8.80 (d, $^4J_{HH}$ = 2.4 Hz, 1H, Ar−H), 10.68 (brs, 1H, NH). Anal. calcd for $C_{21}H_{25}N_3O_3$: C, 68.64; H, 6.86; N, 11.44. Found: C, 68.89; H, 6.82; N, 11.57.

Data for **Vs.** Yield, 96.8%; mp, 83−84 °C. 1.18 (t, $^3J_{HH}$ = 6.8 Hz, 3H, CH_2CH_3), 2.66 (s, 3H, SCH_3), 3.54 (q, $^3J_{HH}$ = 6.8 Hz, 2H, CH_2CH_3), 3.67 (t, $^3J_{HH}$ = 5.2 Hz, 2H, OCH_2), 4.28 (t, $^3J_{HH}$ = 5.2 Hz, 2H, OCH_2), 4.96 (d, $^3J_{HH}$ = 6.0 Hz, 2H, NCH_2), 7.56 (t, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 7.72 (t, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 7.80 (d, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 7.98 (s, 1H, Ar−H), 8.10 (d, $^3J_{HH}$ = 8.0 Hz, 1H, Ar−H), 8.80 (d, $^4J_{HH}$ = 2.4 Hz, 1H, Ar−H), 10.45 (brs, 1H, NH). Anal. calcd for $C_{19}H_{21}N_3O_3S$: C, 61.44; H, 5.70; N, 11.31. Found: C, 61.30; H, 5.51; N, 11.20.

Herbicidal Activity. Two dicotyledon crops, rape (*Brassica napus* L.) and amaranth pigweed (*Amaranthus retroflexus*), and two monocotyledon crops, alfalfa (*Medicago sativa* L.) and hairy crabgrass (*Digitaria sanguinalis* L. Scop.), were used to test the herbicidal activities of compounds **Va**−**s** using a previously reported procedure (*14*).

Plant Growth Regulatory Activities. The plant growth regulatory activities of the title compounds were evaluated using seeds of cucumber, and the procedures were previously reported in literature (*19, 20*).

RESULTS AND DISCUSSION

Synthesis. The synthesis of target compounds **Va**−**Vs** was started from preparation of halomethyl-substituted heterocycles **I1**−**I9**, which were the key intermediates in the whole routes. The synthetic routes of phenyl-substituted oxazolmethylchloride **I1**−**I2** were different from that of alkyl-substituted oxazolmethylchloride **I3**−**I4**. In detail, 2-phenyl-4-oxazolmethylchloride **I1** and **I2** were prepared by 2-chloroacetyl chloride and different benzamides (**Scheme 1**), whereas 2-(chloromethyl)-5-alkyloxazole **I3** and **I4** were synthesized via diazo compounds **3a**,**b** starting from corresponding acyl chloride **2a**,**b** (**Scheme 2**).

4-Trifluoromethyl- or 4-fluoro-benzonitrile **4** and hydroxylamine hydrochloride were refluxed in ethanol in the presence of sodium hydroxide to give compounds **5**, which was reacted with chloroacetyl chloride to afford intermediates **6a** and **6b**, respectively. Compounds **6** were refluxed in xylene to give 3-phenyl-1,2,4-oxadiazole-5-methylchloride **I5** and **I6** (**Scheme 3**).

Different methyl-substituted quinoline was reacted with NBS or NCS in the presence of AIBN to give quinolinylmethylbromide **I7**, **I8**, or **I9**, which was allowed to proceed the next step as soon as possible to avoid polymerization (**Scheme 4**).

Alkyoxy- or methylthio-substituted cyanoacrylate **IV** was prepared according to our previous work (*14, 15*). Arylmethylamines **III1**−**III9** were synthesized from the corresponding halomethyl compounds **I1**−**I9** by Gabriel reaction (**Scheme 5**). The title compounds **Va**−**Vs** were synthesized from **IV** and **III** with good yields (**Scheme 6** and **Tables 1** and **2**).

Herbicidal Activity Bioassay. Herbicidal activities of the title compounds **Va**−**Vs** are listed in **Table 3**. In postemergence treatment, most of the title compounds showed higher herbicidal activities as compared to preemergence treatment, and these compounds exhibited higher herbicidal activities against dicotyledon weeds (rape and amaranth pigweed) than against monocotyledon weeds (alfalfa and hairy crabgrass). For instance, the herbicidal activities of **Vi**, **Vk**, **Vp**, **Vr**, and **Vs** against rape and amaranth pigweed were 100% at 1.5 kg/ha in postemergence treatment, while **Vd** and **Vg** showed activities above 80% at the same dose. Interestingly, the herbicidal activities of **Vb** and **Vk** against hairy crabgrass were 87.2 and 82.5%, respectively. Furthermore, in preemergence treatment, **Vk** and **Vs** exhibited good herbicidal activities, 88.0 and 74.9% in detail, which were different from most of the 2-cyanoacrylates reported in our previous work (*13*−*16*).

Compound **Vr** exhibited excellent herbicidal activity at 750 g/ha; however, its activity decreased remarkably when the dose was reduced to 375 g/ha. At the rate of 375 g/ha, compounds **Vp** and **Vs** still showed excellent herbicidal activities; the results indicate that introduction of quinoline was effective for the herbicidal activities (**Table 4**).

Plant Growth Regulatory Activities. The plant growth regulatory activities of compounds **Va**−**Vg** and **Vm**−**Vs** were evaluated, and their effects on the radicle growth of cucumber are listed in **Table 5**. Interestingly, most of these compounds, such as **Vg**, **Vn**, **Vo**, **Vp**, and **Vs**, stimulated radicle growth of cucumber and showed nearly or more than 100% promotion, whereas other compounds, such as **Vd** and **Ve**, had an inhibitory effect, 20.0 and 18.6% inhibition, respectively.

In conclusion, a series of novel 2-cyanoacrylates containing an oxazole, oxadiazole, or quinoline moiety were synthesized from corresponding arylmethylamine and alkyoxy- or methylthio-substituted cyanoacrylate, and their structures were characterized by ^{1}H NMR and elemental analysis (or HRMS). Their herbicidal activities against four weeds and plant growth regulatory activities were evaluated. Some compounds exhibited excellent herbicidal activities at a dose of 375 g/ha, while most of these cyanoacrylates presented interesting plant growth regulatory activities.

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