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Synthesis and Herbicidal Activity of 12-(Aryloxyacyloxyimino)-1,15-pentadecanlactone Derivatives

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A series of novel 12-(aryloxyacyloxyimino)-1,15-pentadecanlactone derivatives (**3**) were synthesized, and their structures including configuration of C=N bond were confirmed by ^{1}H NMR, elemental analysis and X-ray diffraction analysis. The bioassay showed that some of them exhibited excellent herbicidal activity against *Amaranthus tricolor* L. The activity of compounds **3** except compounds **3A1−2** was much higher than the commercial herbicide 2,4-D and the activity of about half of compounds **3** was comparable to the commercial herbicide tribenuron-methyl. The further bioassay showed that the representative of compounds **3**, **3A1−12**, exhibited excellent herbicidal activity not only against dicotyledon, such as *Amaranthus tricolor* L., *Cucumis sativus* L., *Glycine max* L., and *Phaseolus radiatus* L., but also against monocotyledon, such as *Zea mays* L. and *Oryza sativa* L.

KEYWORDS: Macrolactone; synthesis; herbicidal activity; herbicide

1. INTRODUCTION

Mimicking the chemistry of biologically active natural products is an important approach for developing new pesticides with high efficacy and selectivity against target species. Naturally occurring macrolactams and macrolactones have a broad spectrum of biological activity. Some of them exhibited anthelmintic and insecticidal activity such as avermectins (*1*), fungicidal activity such as discodermide (*2*), maltophilin (*3*), and xanthobaccin A (*4*) and some others exhibited good herbicidal activity such as pyrenophorol, a macrodiolide compound, isolated from a *Drechslera avenae* pathotype, which was phytotoxic to *Avena sterilis* at a concentration of 320 μM (*5*). The discovery of fungicidal lead compounds with new chemotypes by mimicking the structure of naturally occurring macrolactams was succeeded in our laboratory and the bioassay showed that 12-alkoxyiminopentadecanlactam derivatives exhibited not only good fungicidal activity but also a broad spectrum of fungicidal activity (*6*). On the other hand, in our searching for potential pesticides, 2-acyloxyiminocyclododecanones (**1**) with some herbicidal activity was found (*7*). Thus, their pentadecanlactone analogous (**2**) (**Figure 1**) were synthesized and the bioassay showed that several compounds with aryloxy(iso-butyryloxy)imino side chain exhibited relatively better herbicidal activity (*8*), which stimulated our interest in the modification of phenoxyalkanoic acids used as herbicides.

The development of phenoxyalkanoic acid herbicides dates from 1940s. 2,4-D (2,4-dichlorophenoxy acetic acid) (**a**) is the successful representative, which is a readily systemic herbicide (*9*). Although 2,4-D constituted a real hazard for human and animal health as numerous accidents of poisoning deaths caused by this herbicide have been reported (*10*), it meets safety standards for all countries in which it is registered (*11*). Therefore, so far, it is still applied to weed control in the world. Since it was discovered, much research has been carried out on its molecules and many modified derivatives with improved herbicidal activity and broader herbicidal spectrum have been commercialized. Some examples are as follows: MCPA (**b**), 2,4-DB (**c**), 2,4-D butylate (**d**), diclofop-methyl (**e**), phenothiol (**f**), MCPCA (**g**), fluazifop-butyl (**h**), haloxyfop (**i**), fenoxaprop (**j**), fenoxaprop-P (**k**), and quizalofop-P (**l**) (**Figure 2**).

It can be seen from the examples mentioned above that structural modification of 2,4-D mainly focus on the modifica-

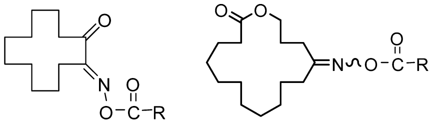

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Figure 1. Compounds **1** and **2**.

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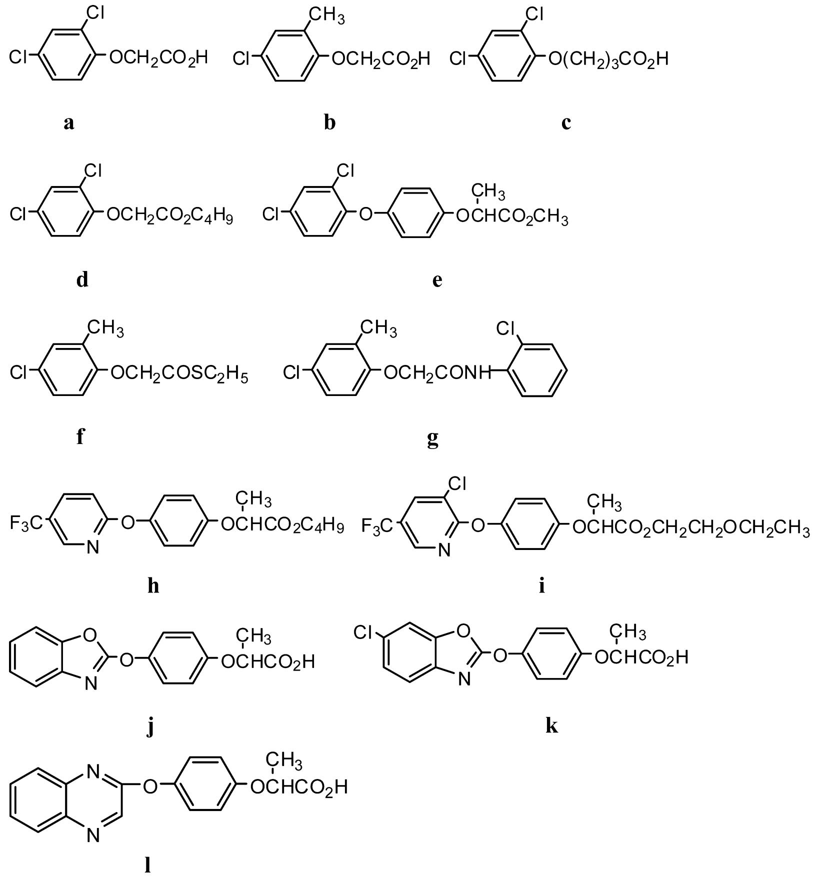
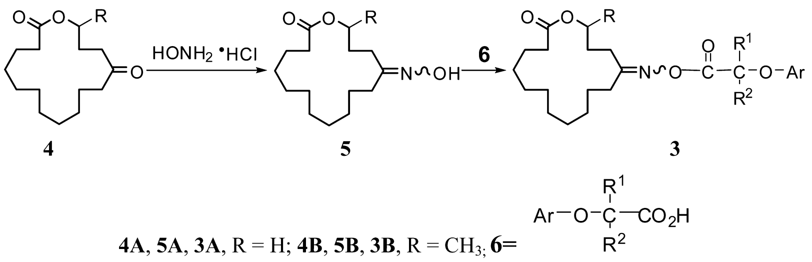


Figure 2. Commercial herbicides **a**−**l**.

Scheme 1. Synthetic Route of the Compounds **3**



4A, **5A**, **3A**, R = H; **4B**, **5B**, **3B**, R = CH_3; **6**=

tion of Ar and the formation of simple esters. In this paper, we decided to introduce aryloxyalkanoic acids as active groups into molecule **2** to improve their herbicidal activity. Namely, 1.15-pentadecanlactone ring is combined with phenoxyalkanoic acids and imino group as a link bridge. Thus a series of 12-(aryloxyacyloxyimino)-1,15-pentadecanloctone derivatives (**3**) were synthesized and their herbicidal activity was evaluated. The synthetic route of compounds **3** is shown in **Scheme 1**.

2. MATERIALS AND METHODS

2.1. General. ^1H NMR spectra were recorded in CD_3COCD_3 with a Bruker DPX300 spectrometer, using TMS as internal standard; elemental analysis was performed by the analytical center in Institute of Chemistry (Beijing), Chinese Academy of Science; Melting points were measured on a Yanagimoto melting-point apparatus and are uncorrected. The solvents and reagents were used as received or were dried prior to use as needed.

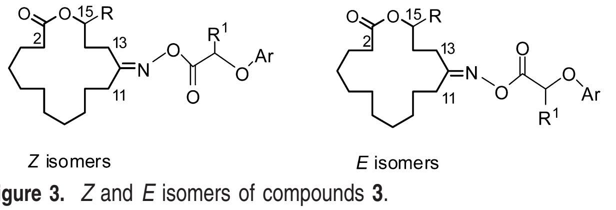


Figure 3. *Z* and *E* isomers of compounds **3**.

2.2. Chemical Synthesis. *2.2.1. Synthesis of Compounds **4**.* Compound **4A** was synthesized from 2-nitrocyclododecanone according to the method given in ref *8b*. Compound **4B** was synthesized in the same method for the synthesis of **4A** just using methyl vinyl ketone instead of acrolein. **4A**: Yield 91%; mp 29−31 ((*8*)b: 28.5−30). **4B**: Yield 92%; mp 28~29 °C; ^1H NMR δ1.20(d, 3H, J = 6.3 Hz, CH_3), 1.25~1.48(m, 12H), 1.54~1.92(m, 6H), 2.27~2.43(m, 4H), 2.52~2.61(m, 2H), 4.87~4.98(m, 1H, C15−H).

*2.2.2. Synthesis of Compounds **5**.* Compounds **5A** and **5B** were synthesized from **4A** and **4B**, respectively, according to the method given in ref *8*b. Compound **5A** (a mixture of *Z* and *E* isomers): Yield 93%; mp 57−62 (*8*b: 57−62 °C). **5B** (a mixture of *Z*- and *E*-isomers): Yield 90%; mp 72~78. ^1H NMR $\delta\delta$1.20(d, 3H, J = 1.9 Hz, CH_3)), 1.25~1.45(m, 12H), 1.54~1.79(m, 6H), 2.17~2.44(m, 6H), 4.88~4.98(m, 1H, C15−H), 9.41, 9.44 (1H, HO-*N* =).

*2.2.3. Preparation of Compounds **6**.* Compound **6** was prepared from phenols and chloroacetic acid or α-chloro propionic acid according to the methods given in ref *12* (for preparation of aryloxyacetic acids) and ref *13* (for preparation of α-aryloxypropionic acids).

Table 1. Experimental Data of Compounds **3**

compound no.	R^1	R^2	configuration	Ar	eluant for column chromatography[a]	R_f value	mp	yield %
3A1−1(1)	H	H	*Z*	C$_6$H$_4$	a	0.62	24∼25	90
3A1−1(2)			*E*			0.50	35∼35	
3A1−2(1)	H	H	*Z*	2-MeC$_6$H$_4$	a	0.60	39∼40	86
3A1−2(2)			*E*			0.53	40∼41	
3A1−3(1)	H	H	*Z*	4-MeC$_6$H$_4$	a	0.71	/	91
3A1−3(2)			*E*			0.64	44∼45	
3A1−4(1)	H	H	*Z*	4-MeOC$_6$H$_4$	a	0.71	/	87
3A1−4(2)			*E*			0.60	49∼50	
3A1−5(1)	H	H	*Z*	2-ClC$_6$H$_4$	a	0.57	80∼81	83
3A1−5(2)			*E*			0.48	66∼67	
3A1−6(1)	H	H	*Z*	3-ClC$_6$H$_4$	a	0.65	61∼62	81
3A1−6(2)			*E*			0.50	79∼80	
3A1−7(1)	H	H	*Z*	4-ClC$_6$H$_4$	a	0.70	68∼70	93
3A1−7(2)			*E*			0.55	70∼71	
3A1−8(1)	H	H	*Z*	3-O$_2$NC$_6$H$_4$	f	0.58	64∼65	85
3A1−8(2)			*E*			0.50	66∼67	
3A1−9(1)	H	H	*Z*	2,3-Me$_2$C$_6$H$_3$	a	0.67	50∼51	90
3A1−9(2)			*E*			0.58	52∼53	
3A1−10(1)	H	H	*Z*	3,4-Me$_2$C$_6$H$_3$	a	0.70	/	85
3A1−10(2)			*E*			0.67	47∼48	
3A1−11(1)	H	H	*Z*	4-Cl-2-MeC$_6$H$_3$	b	0.62	43∼44	91
3A1−11(2)			*E*			0.55	57∼58	
3A1−12(1)	H	H	*Z*	2,4-Cl$_2$C$_6$H$_3$	a	0.48	**/**	85
3A1−12(2)			*E*			0.36	**/**	
3A1−13(1)	H	H	*Z*	4-Br-2-ClC$_6$H$_3$	a	0.63	77∼78	89
3A1−13(2)			*E*			0.45	67∼68	
3A2−1(1)	Me	H	*Z*	C$_6$H$_4$	d	0.74	37∼38	90
3A2−1(2)			*E*			0.73	40∼41	
3A2−2(1)	Me	H	*Z*	4-MeC$_6$H$_4$	g	0.73	51∼52	89
3A2−2(2)			*E*			0.62	50∼51	
3A2−3(1)	Me	H	*Z*	2-ClC$_6$H$_4$	a	0.67	33∼34	85
3A2−3(2)			*E*			0.58	39∼40	
3A2−4(1)	Me	H	*Z*	3-ClC$_6$H$_4$	a	0.69	58∼59	80
3A2−4(2)			*E*			0.52	44∼45	
3A2−5(1)	Me	H	*Z*	4-ClC$_6$H$_4$	a	0.71	67∼68	92
3A2−5(2)			*E*			0.65	60∼61	
3A2−6(1)	Me	H	*Z*	2,3-Me$_2$C$_6$H$_3$	g	0.71	59∼60	79
3A2−6(2)			*E*			0.62	40∼41	
3A2−7(1)	Me	H	*Z*	4-Cl-3-MeC$_6$H$_3$	g	0.69	75∼76	86
3A2−7(2)			*E*			0.62	88∼89	
3A2−8(1)	Me	H	*Z*	2,4-Cl$_2$C$_6$H$_3$	a	0.74	48∼49	94
3A2−8(2)			*E*			0.72	76∼77	
3B−1(1)	H	H	*Z*	4-ClC$_6$H$_4$	a	0.63	60∼61	90
3B−1(2)			*E*			0.56	36∼37	
3B−2(1)	H	H	*Z*	4-Cl-2-MeC$_6$H$_3$	e	0.70	/	89
3B−2(2)			*E*			0.66	57∼58	
3B−3(1)	H	H	*Z*	4-Cl-3-MeC$_6$H$_3$	c	0.73		76
3B−3(2)			*E*			0.61	60∼61	
3B−4(1)	H	H	*Z*	2,4-Cl$_2$C$_6$H$_3$	a	0.65	−67∼68	85
3B−4(2)			*E*			0.56	/	
3B−5(1)	H	H	*Z*	4-Br-2-ClC$_6$H$_3$	c	0.68	/	79
3B−5(2)			*E*			0.59	48∼49	
3B−6(1)	Me	H	*Z*	4-ClC$_6$H$_4$	d	0.73	/	91
3B−6(2)			*E*			0.63	72∼73	

[a] Petroleum ether:dichloromethane:ethyl acetate = 30:20:2 (v/v) for a; 30:20:3 (v/v) for b; 30:20:1 (v/v) for c; 30:15:2 (v/v) for d; 30:15:1 (v/v) for e; 30:10:4 (v/v) for f; and 30:10:2 (v/v) for g.

Table 2. Elemental Data of Compounds **3**

	C%		H%		N%	
compound no.	calcd	found	calcd	found	calcd	found
3A1–1(1)	68.46	68.40	8.24	8.43	3.47	3.44
3A1–1(2)	68.46	68.36	8.24	8.22	3.47	3.36
3A1–2(1)	69.04	69.14	8.45	8.54	3.35	3.34
3A1–2(2)	69.04	68.99	8.45	8.43	3.35	3.38
3A1–3(1)	69.04	69.06	8.45	8.47	3.35	3.35
3A1–3(2)	69.04	69.36	8.45	8.49	3.35	3.41
3A1–4(1)	66.49	66.02	8.14	8.14	3.23	3.22
3A1–4(2)	66.49	66.56	8.14	8.17	3.23	3.27
3A1–5(1)	63.08	63.06	7.36	7.34	3.20	3.05
3A1–5(2)	63.08	63.48	7.36	7.42	3.20	2.84
3A1–6(1)	63.08	63.08	7.36	7.33	3.20	3.15
3A1–6(2)	63.08	63.04	7.36	7.36	3.20	3.28
3A1–7(1)	63.08	63.05	7.36	7.37	3.20	3.07
3A1–7(2)	63.08	63.55	7.36	7.52	3.20	3.41
3A1–8(1)	61.59	61.16	7.19	7.16	6.25	6.12
3A1–8(2)	61.59	61.67	7.19	7.14	6.25	6.31
3A1–9(1)	69.58	69.41	8.64	8.90	3.25	3.24
3A1–9(2)	69.58	69.25	8.64	8.64	3.25	3.25
3A1–10(1)	69.58	69.42	8.64	8.61	3.25	3.10
3A1–10(2)	69.58	69.48	8.64	8.62	3.25	3.27
3A1–11(1)	63.78	63.77	7.58	7.56	3.10	3.10
3A1–11(2)	63.78	63.81	7.58	7.60	3.10	3.06
3A1–12(1)	58.48	58.44	6.61	6.60	2.97	2.85
3A1–12(2)	58.48	58.65	6.61	6.57	2.97	2.75
3A1–13(1)	53.45	53.41	6.05	6.10	2.71	2.62
3A1–13(2)	53.45	53.44	6.05	6.06	2.71	2.61
3A2–1(1)	69.04	68.95	8.45	8.45	3.35	3.35
3A2–1(2)	69.04	69.11	8.45	8.43	3.35	3.37
3A2–2(1)	69.58	69.51	8.64	8.59	3.25	2.99
3A2–2(2)	69.58	69.50	8.64	8.64	3.25	3.35
3A2–3(1)	63.78	63.81	7.58	7.83	3.10	3.08
3A2–3(2)	63.78	63.88	7.58	7.58	3.10	3.10
3A2–4(1)	63.78	63.35	7.58	7.56	3.10	3.13
3A2–4(2)	63.78	63.36	7.58	7.52	3.10	3.03
3A2–5(1)	63.78	63.45	7.58	7.52	3.10	2.91
3A2–5(2)	63.78	63.75	7.58	7.58	3.10	3.10
3A2–6(1)	70.08	70.20	8.82	8.86	3.14	3.14
3A2–6(2)	70.08	69.99	8.82	8.79	3.14	3.12
3A2–7(1)	64.43	64.61	7.79	7.79	3.01	3.01
3A2–7(2)	64.43	64.38	7.79	7.78	3.01	2.92
3A2–8(1)	59.26	59.29	6.84	6.84	2.88	2.82
3A2–8(2)	59.26	59.28	6.84	6.84	2.88	2.88
3B–1(1)	63.78	63.59	7.58	7.55	3.10	3.01
3B–1(2)	63.78	63.88	7.58	7.57	3.10	3.03
3B–2(1)	64.43	64.54	7.79	7.90	3.01	3.08
3B–2(2)	64.43	64.00	7.79	7.80	3.01	3.09
3B–3(1)	64.43	64.97	7.79	7.93	3.01	2.79
3B–3(2)	64.43	64.55	7.79	7.80	3.01	2.93
3B–4(1)	59.26	59.45	6.64	6.93	2.88	3.12
3B–4(2)	59.26	59.63	6.64	6.88	2.88	2.90
3B–5(1)	54.30	54.56	6.27	6.46	2.64	2.71
3B–5(2)	54.30	54.27	6.27	6.28	2.64	2.64
3B–6(1)	64.43	64.29	7.79	7.76	3.01	2.85
3B–6(2)	64.43	64.31	7.79	7.78	3.01	2.97

2.2.4. General Procedure for Synthesis of Compounds ***3.*** To a solution of **5**(4 mmol) and **6** (5 mmol) in CH_2Cl_2 (30 mL) was added DCC (dicyclohexylcarbodiimide, 1.03 g, 5 mmol). The mixture was stirred at room temperature for 12 h. After filtration, the filtrate was washed with saturated $NaHCO_3$ solution, water and brine, dried over Na_2SO_4, and evaporated under reduced pressure to give a crude product. Further purification on silica gel chromatography gave three portions in the order of (a) *Z* isomer (**1**), (b) mixture and (c) *E* isomer (**2**) (**Figure 3**). The experimental data of the target compounds are summarized in **Table 1**, in which only the total yields of the *Z* and *E* isomers are given. Elemental data are given in **Table 2**. ^{1}H NMR data are listed in **Table 3**.

2.3. X-ray Diffraction Analysis of 3A1–7(1). The crystal of compounds **3A1–7(1)** was obtained by slow evaporation from a solution of *n*-hexane and ethyl ether (10:1). All measurements were made with a Siemens CCD area detector under graphite monochromatized Mo Kα ($\lambda = 0.071073$ nm) radiation at 293 K. The structure was solved by direct method using SHELX (*14*), and refined on F^2 using all data by full-matrix least-squares procedures with SHELXL-97 (*15*). The crystal structure is shown in **Figure 4**.

2.4. Herbicidal Activity. Compounds **3** (*Z* isomer, *E* isomer or a mixture of *Z* and *E* isomers) were formulated as 10 g/L emulsible concentrates (EC) using xylene as solvent and Nongru 0204 (25 g/L) and Nongru 2201 (25 g/L) as the emulsifying agents. Commercial herbicides 2,4-D and tribenuron-methyl were used as the standards of comparison for the activity of the compounds **3**. The blank test was made using xylene containing emulsifying agents Nongru 0204 (25 g/L) and Nongru 2201 (25 g/L). Each EC was diluted with water to give emulsions of five different concentrations (6.25, 12.5, 25, 50, 100 mg/L). The plastic cups (40 mm in diameter) were filled with soil and kept wet by watering. We placed 50–60 seeds of *Amaranthus tricolor* L. in the emergence state in the soil, covered them with fine soil, and

Table 3. ^{1}H NMR Data of Compounds **3**

compound no.	^{1}H NMR, δ
3A1−1(1)	1.36∼1.40(m, 12H), 1.54∼1.67(m, 4H), 1.75∼1.84(m, 2H), 2.30∼2.35(m, 4H), 2.41∼2.47(m, 2H), 4.04(t, 2H, *J* = 5.8 Hz), 4.93(s, 2H), 6.96∼7.00(m, 3H), 7.28∼7.35(m, 2H)
3A1−1(2)	1.27∼1.34(m, 12H), 1.34∼1.56(m, 2H), 1.62∼1.67(m, 2H), 1.90∼1.99(m, 2H), 2.30∼2.41(m, 4H), 2.45∼2.50(m, 2H), 4.16∼4.20(m, 2H), 4.94(s, 2H), 6.95∼7.00(m, 3H), 7.28∼7.33(m, 2H)
3A1−2(1)	1.36∼1.44(m, 12H), 1.56∼1.67(m, 4H), 1.75∼1.83(m, 2H), 2.26(s, 3H), 2.30∼2.35(m, 4H), 2.41∼2.46(m, 2H), 4.03(t, 2H, *J* = 5.8 Hz), 4.95(s, 2H), 6.85∼6.90(m, 2H), 7.12∼7.19(m, 2H)
3A1−2(2)	1.26∼1.33(m, 12H), 1.45∼1.55(m, 2H), 1.60∼1.69(m, 2H), 1.90∼1.99(m, 2H), 2.25(s, 3H), 2.30∼2.40(m, 4H), 2.45∼2.50(m, 2H), 4.16∼4.20(m, 2H), 4.96(s, 2H), 6.85∼6.89(m, 2H), 7.11∼7.18(m, 2H)
3A1−3(1)	1.36∼1.40(m, 12H), 1.54∼1.67(m, 4H), 1.74∼1.83(m, 2H), 2.26(s, 3H), 2.30∼2.35(m, 4H), 2.40∼2.46(m, 2H), 4.03(t, 2H, *J* = 5.8 Hz), 4.88(s, 2H), 6.86(dd, 2H, *J* = 6.6 Hz, *J* = 2.1 Hz), 7.11(dd, 2H, *J* = 8.8 Hz, *J* = 0.7 Hz)
3A1−3(2)	1.26∼1.33(m, 12H), 1.45∼1.55(m, 2H), 1.60∼1.69(m, 2H), 1.90∼1.96(m, 2H), 2.25(s, 3H), 2.30∼2.40(m, 4H), 2.44∼2.50(m, 2H), 4.16∼4.20(m, 2H), 4.89(s, 2H), 6.83−6.88(m, 2H), 7.08∼7.12(m, 2H)
3A1−4(1)	1.36∼1.39(m, 12H), 1.56∼1.67(m, 4H), 1.78∼1.83(m, 2H), 2.30∼2.35(m, 4H), 2.41∼2.48(m, 2H), 3.74(s, 3H), 4.05(t, 2H, *J* = 5.8 Hz), 4.86(s, 2H), 6.85∼6.94(m, 4H)
3A1−4(2)	1.29∼1.34(m,12H), 1.49∼1.54(t, 2H), 1.62∼1.67(m, 2H), 1.92∼1.96(m, 2H), 2.30∼2.41(m, 4H), 2.45∼2.50(m, 2H), 3.74(s, 3H),4.18(t,2H, *J* = 5.6 Hz),4.86(s, 2H), 6.84∼6.93(m, 4H)
3A1−5(1)	1.30∼1.45(m, 12H), 1.54∼1.67(m, 4H), 1.77∼1.86(m, 2H), 2.30∼2.36(m, 4H), 2.43∼2.49(m, 2H), 4.06(t, 2H, *J* = 5.8 Hz), 5.06(s, 1H), 6.97∼7.03(m, 1H), 7.09−7.12(m,1H), 7.27−7.33(m, 1H), 7.42−7.45(m, 1H)
3A1−5(2)	1.25∼1.35(m, 12H), 1.48∼1.53(m, 2H), 1.62∼1.67(m, 2H), 1.90∼1.99 (m, 2H), 2.30∼2.41(m, 4H), 2.45∼2.50(m, 2H), 4.16∼4.20(m, 2H), 5.07(s, 2H), 6.97∼7.02(m, 1H), 7.08∼7.12(m, 1H), 7.26∼7.31(m, 1H), 7.41∼7.44(m, 1H)
3A1−6(1)	1.36∼1.44(m, 12H), 1.57∼1.67(m, 4H), 1.80∼1.86(m, 2H), 2.30∼2.36(m, 4H), 2.44∼2.50(m, 2H), 4.08(t, 2H, *J* = 5.8 Hz), 5.00(s, 2H), 6.94∼7.05(m, 3H), 7.30∼7.36(m, 1H)
3A1−6(2)	1.28∼1.34(m, 12H), 1.50∼1.54(m, 2H), 1.63∼1.67(m, 2H), 1.92∼1.99(m, 2H), 2.31∼2.82(m, 6H), 4.18(t, 2H, *J* = 5.6 Hz), 5.02(s, 2H), 6.94∼7.05(m, 3H), 7.30∼7.36(m, 1H)
3A1−7(1)	1.35∼1.50(m, 12H), 1.54∼1.67(m, 4H), 1.18∼1.87(m, 2H), 2.30∼2.36(m, 4H), 2.44∼2.49(m, 2H), 4.07(t, 2H, *J* = 5.8 Hz), 4.97(s, 2H), 6.98∼7.04(m, 2H), 7.30∼7.36(m, 2H)
3A1−7(2)	1.25∼1.35(m, 12H), 1.48∼1.53(m, 2H), 1.64∼1.67(m, 2H), 1.90∼1.99(m, 2H), 2.30∼2.41(m, 4H), 2.45∼2.50(m, 2H), 4.18(t, H, *J* = 5.6 Hz), 4.98(s, 2H), 6.99∼7.03(m, 2H), 7.29∼7.34(m, 2H)
3A1−8(1)	1.36∼1.41(m, 12H), 1.57∼1.67(m, 4H), 1.83∼1.87(m,2 H), 2.30∼2.37(m, 4H), 2.47∼2.52(m, 2H), 4.09(t, 2H, *J* = 5.8 Hz), 5.16(s, 2H), 7.45∼7.49(m, 1H), 7.60∼7.65(m, 1H), 7.79−7.81(m, 1H), 7.87∼7.91(m, 1H)
3A1−8(2)	1.30−1.34(m, 12H), 1.50−1.55(m, 2H), 1.62∼1.67(m, 2H), 1.92∼1.97(m, 2H), 2.30∼2.35(m, 2H), 2.39∼2.51(m, 4H), 4.18(t, 2H, *J* = 5.6 Hz), 5.19(s, 2H), 7.44∼7.48(m, 1H), 7.62−7.65(m, 1H), 7.79−7.81(m, 1H), 7.87∼7.91(m, 1H)
3A1−9(1)	1.36∼1.44(m, 12H), 1.53∼1.66(m, 4H), 1.72∼1.79(m, 2H), 2.19(s, 3H), 2.26(s, 3H), 2.30∼2.35(m, 4H), 2.39∼2.45(m, 2H), 4.01(t, 2H, *J* = 5.7 Hz), 4.92(s, 2H), 6.72∼6.81(m, 2H), 7.00−7.05(m, 1H)
3A1−9(2)	1.26∼1.33(m, 12H), 1.47∼1.52(m, 2H), 1.62∼1.67(m, 2H), 1.91∼1.98(m, 2H), 2.18(s, 3H), 2.25(s, 3H), 2.30∼2.40(m, 4H), 2.44∼2.49(m, 2H), 4.16∼4.20(m, 2H), 4.92(s, 2H), 6.72∼6.80(m, 2H), 7.00−7.05(m, 1H)
3A1−10(1)	1.26∼1.40(m, 12H), 1.59∼1.65(m, 4H), 1.78∼1.88(m, 2H), 2.17(s, 3H), 2.22(s, 3H), 2.28∼2.34(m, 4H), 2.38∼2.44(m, 2H), 4.00(t, 2H, *J* = 5.8 Hz), 4.86(s, 2H), 6.66−6.0(m, 1H), 6.77−6.79(m, 1H), 7.02−7.05(m, 1H)
3A1−10(2)	1.25∼1.33(m, 12H), 1.45∼1.54(m, 2H), 1.62∼1.67(m, 2H), 1.89∼1.98(m, 2H), 2.16(s, 3H), 2.21(s, 3H), 2.30∼2.40 (m, 4H), 2.44∼2.49(m, 2H), 4.18(t, 2H, *J* = 5.6 Hz), 4.87(s, 2H), 6.66∼6.69(m, 1H), 6.77∼6.78(m, 1H), 7.02∼7.04(m, 1H)
3A1−11(1)	1.36∼1.44(m, 12H), 1.55∼1.67(m, 4H), 1.77∼1.87(m, 2H), 2.26 (s, 3H), 2.30∼2.36(m, 4H), 2.44∼2.49(m, 2H), 4.07(t, 2H, *J* = 5.8 Hz), 4.99(s, 2H), 6.92(d, 1H, *J* = 8.7 Hz), 7.15∼7.22 (m, 2H)
3A1−11(2)	1.26∼1.33(m, 12H), 1.47∼1.52(m, 2H), 1.62∼1.66(m, 2H), 1.91∼1.98(m, 2H), 2.25(s, 3H), 2.30∼2.40(m, 4H), 2.45∼2.50(m, 2H), 4.18(t, 2H, *J* = 5.6 Hz), 4.99(s, 2H), 6.91(d, 1H, *J* = 8.7 Hz), 7.13−7.21(m, 2H)
3A1−12(1)	1.25−1.44(m, 14H), 1.57−1.97(m, 6H), 2.28−2.47(m, 4H), 4.07(t, 2H, *J*═5.6 Hz), 4.87(s, 2H), 6.80−6.87(m, 1H), 7.15−7.21(m, 1H), 7.37−7.42(m, 1H)
3A1−12(2)	1.27−1.44(m, 14H), 1.63−1.97(m, 6H), 2.31−2.37(m, 2H), 2.42−2.47(m, 2H), 4.18(t, 2H, *J*═5.6 Hz), 4.87(s, 2H), 6.81−6.85(m, 1H), 7.16−7.20(m, 1H), 7.37−7.40(m, 1H)
3A1−13(1)	1.36∼1.44(m,12H), 1.57∼1.67(m, 4H), 1.81∼1.88(m, 2H), 2.31∼2.36(m, 4H), 2.45∼2.51(m, 2H), 4.09(t, 2H, *J* = 5.8 Hz), 5.10(s, 2H), 7.10(d, 1H, *J* = 8.9 Hz), 7.47(dd, 1H, *J*═8.9 Hz, *J* = 2.4 Hz), 7.62(d, 1H, *J* = 2.4 Hz)
3A1−13(2)	1.27∼1.34(m, 12H), 1.45∼1.55(m, 2H), 1.62∼1.67(m, 2H), 1.90∼1.99(m, 2H), 2.30∼2.41(m, 4H), 2.45∼2.50(m, 2H), 4.18(t, 2H, *J* = 5.6 Hz), 5.11(s, 2H), 7.10(d, 1H, *J* = 8.9 Hz), 7.45(dd, 1H, *J* = 8.9 Hz, *J* = 2.4 Hz), 7.61(d, 1H, *J* = 2.4 Hz)
3A2−1(1)	1.35(s, 12H),1.51∼1.77(m, 9H),2.28∼2.39(m, 6H), 3.99(t, 2H, *J* = 5.6 Hz), 5.06(q, 1H, *J* = 6.7 Hz), 6.94∼7.00(m, 3H, 7.27∼7.33(m, 2H))
3A2−1(2)	1.22∼1.46(m, 14H), 1.62∼1.66(m, 5H), 1.89∼1.94 (m, 2H), 2.28∼2.35(m, 4H), 2.42∼2.47(m, 2H), 4.16(t, 2H, *J* = 5.6 Hz), 5.06(q, 1H, *J* = 6.8 Hz), 6.92∼6.99(m, 3H), 7.27∼7.32(m, 2H)
3A2−2(1)	1.26−1.90(m, 12H), 1.53∼1.76(m, 9H), 2.25∼2.38(m, 9H), 3.98 (t, 2H, *J* = 5.7 Hz), 5.00(q, 1H, *J* = 6.7 Hz), 6.83∼6.85(m, 2H), 7.09∼7.12(m, 2H)
3A2−2(2)	1.21∼1.46(m, 14H), 1.60∼1.66(m, 5H), 1.89∼1.94(m, 2H), 2.24∼2.35(m, 7H), 2.42∼2.47(m, 2H), 4.14∼4.18(m, 2H), 4.99(q, 1H, *J* = 6.7 Hz), 6.80∼6.84(m, 2H), 7.06∼7.11(m, 2H)
3A2−3(1)	1.35∼1.39(m, 12H), 1.53∼1.80(m, 9H), 2.28∼2.44(m, 6H), 3.99∼4.03(m, 2H), 5.17(q, 1H, *J* = 6.7 Hz), 6.97∼7.08(m, 2H), 7.26∼7.32(m, 1H), 7.43∼7.46(m, 1H)
3A2−3(2)	1.22∼1.47(m, 14H), 1.61∼1.71(m, 5H), 1.87∼1.95(m, 2H), 2.25∼2.38(m, 4H), 2.44∼2.47(m, 2H), 4.16(t, 2H, *J* = 5.6 Hz), 5.17(q, 1H, *J* = 6.8 Hz), 6.96∼7.07(m, 2H), 7.25∼7.30(m, 1H), 7.41∼7.45(m, 1H)
3A2−4(1)	1.35∼1.39(m, 12H), 1.54∼1.81(m, 9H), 2.29∼2.44(m, 6H), 4.03(t, 3H, *J* = 5.6 Hz), 5.16(q, 1H, *J* = 6.7 Hz), 6.91∼6.95 (m, 1H), 7.01∼7.04(m, 2H), 7.30∼7.36(m, 1H)
3A2−4(2)	1.23∼1.32(m, 12H), 1.40∼1.49(m, 2H), 1.55−1.72(m, 5H), 1.87∼1.96(m, 2H), 2.27∼2.39(m, 4H), 2.43∼2.48 (m, 2H), 4.16(t, 2H, *J* = 5.6 Hz), 5.15(t, 1H, *J* = 6.8 Hz), 6.90∼6.94(m, 1H), 6.99∼7.03(m, 2H), 7.29∼7.34(m, 1H)
3A2−5(1)	1.35∼1.39(m, 12H), 1.54∼1.80(m, 9H), 2.29∼2.43(m, 6H), 4.03(t, 2H, *J* = 5.7 Hz), 5.09(q, 1H, *J* = 6.8 Hz), 6.96∼7.01(m, 2H), 7.30∼7.35(m, 2H)
3A2−5(2)	1.21∼1.47(m, 14H), 1.60−1.65(m, 5H), 1.86−1.96(m, 2H), 2.23∼2.48(m, 6H), 4.16(t, 2H, *J* = 5.6 Hz), 5.09(q, 1H, *J* = 6.7 Hz), 6.95∼7.00 (m, 2H), 7.29∼7.34(m, 2H)
3A2−6(1)	1.34∼1.38(m, 12H), 1.50∼1.72(m, 9H), 2.18(s, 3H), 2.23∼2.36(m, 9H), 3.91∼3.96(m, 2H), 4.97∼5.04(m, 1H), 6.70(d, 1H, *J* = 8.2 Hz), 6.79(d, 1H, *J* = 7.6 Hz), 6.98−7.03(m, 1H)

Table 3. Continued

compound no.	^{1}H NMR, δ
3A2−6(2)	1.19∼1.47(m, 14H), 1.61∼1.67(m, 5H),1.86∼1.95(m, 2H), 2.18(s, 3H), 2.24−2.36(m, 7H), 2.41−2.46(m, 2H), 4.16(t, 2H, $J = 5.6$ Hz), 5.14(q, 1H, $J = 6.6$ Hz), 6.71(d, 1H, $J = 8.2$ Hz), 6.78(d, 1H, $J = 7.6$ Hz), 6.99(t, 1H, $J = 7.9$ Hz)
3A2−7(1)	1.35(s, 12H),1.54∼1.79(m, 9H), 2.28∼2.41(m, 9H), 3.99∼4.03 (m, 2H), 5.07(q, 1H, $J = 6.7$ Hz), 6.80(dd, 1H, $J = 8.6$ Hz, $J = 2.7$ Hz), 6.95(d, 1H, $J = 2.7$ Hz), 7.29(d, 1H, $J = 8.8$ Hz)
3A2−7(2)	1.97∼1.46(m, 14H), 1.61∼1.66(m, 5H), 1.89∼1.95(m, 2H), 2.26∼2.35(m, 7H), 2.42∼2.47(m, 2H), 4.16(t, 2H, $J = 5.6$ Hz), 5.07(q, 1H, $J = 6.8$ Hz), 6.79(dd, 1H, $J = 8.6$ Hz, $J = 2.9$ Hz), 6.94(d, 1H, $J = 2.8$ Hz), 7.27(d, 1H, $J = 8.7$ Hz)
3A2−8(1)	1.35∼1.54(m, 12H), 1.59∼1.81(m, 9H), 2.29∼2.37(m, 4H), 2.39∼2.44(m, 2H), 4.03∼4.07(m, 2H), 5.20(q, 1H, $J = 6.8$ Hz), 7.11(d, 1H, $J = 8.9$ Hz), 7.31−7.35(m, 1H), 7.51 (d, 1H, $J = 2.6$ Hz)
3A2−8(2)	1.24−1.46(m, 14H), 1.61−1.71(m, 5H), 1.89−1.96(m, 2H), 2.26−2.37(m, 4H), 2.43−2.48(m, 2H), 4.14−4.18(m, 2H), 5.20(q, 1H, J=6.5 Hz), 7.10(d, 1H, J=8.9 Hz), 7.30−7.34 (m, 1H), 7.50(d, 1H, J=2.5 Hz)
3B−1(1)	1.21(d, 3H, $J = 6.3$ Hz), 1.35∼1.39(m, 12H), 1.59∼1.79(m, 6H), 2.27∼2.49(m, 6H), 4.81∼4.91(m, 1H), 4.96(s, 2H), 6.98∼7.03(m, 2H), 7.30∼7.35(m, 2H)
3B−1(2)	1.22∼2.06(m, 21H, 1.23(d, 3H, $J = 6.3$ Hz), 2.28∼2.49(m, 6H), 4.94∼5.00(m, 3H, 5.00(s, 2H)), 6.96∼7.03(m, 2H), 7.29∼7.34(m, 2H)
3B−2(1)	1.20(d, 3H, $J = 6.3$ Hz), 1.25∼1.50(m, 12H), 1.56∼1.77(m, 6H), 2.26∼2.55(m, 9H, 2.27(s, 3H)), 4.81∼4.97(m, 3H), 6.91 (d, 1H, $J = 8.7$ Hz), 7.13∼7.20(m, 2H)
3B−2(2)	1.23(d, 3H, $J = 6.3$ Hz), 1.24∼1.44(m, 12H), 1.46∼1.61(m, 4H), 1.83∼1.91(m, 2H), 2.25(s, 3H), 2.28∼2.46(m, 6H), 4.91∼4.99(m, 3H), 6.91(d, 1H, $J = 8.7$ Hz), 7.13∼7.21(m, 2H)
3B−3(1)	1.19∼1.78(m, 21H), 2.27∼2.45(m, 9H), 4.81∼5.00(m, 3H), 6.83(dd, 1H, $J = 8.8$ Hz, $J = 3.1$ Hz), 6.97(s, 1H), 7.29(dd, 1H, $J = 8.8$ Hz, $J = 2.4$ Hz)
3B−3(2)	1.23(d, 3H, $J = 6.3$ Hz), 1.25∼1.50(m, 12H), 1.46∼1.50(m, 2H), 1.59∼1.69(m, 2H), 1.80∼1.92(m, 2H), 2.25∼2.46(m, 9H), 4.95−5.05(m, 3H), 6.78∼6.85(m, 1H), 6.94∼6.97(m, 1H), 7.26∼7.30(m, 1H)
3B−4(1)	1.21(d, 3H, $J = 6.3$ Hz), 1.35∼1.39(m, 12H), 1.57∼1.80(m, 6H), 2.27∼2.55(m, 6H), 4.83∼4.92(m, 1H), 5.09(s, 2H), 7.13∼7.17(m, 1H), 7.31∼7.35(m, 1H), 7.49∼7.51(m, 1H)
3B−4(2)	1.24(d, 3H, $J = 6.3$ Hz), 1.25∼1.45(m, 12H), 1.47∼1.61(m, 4H), 1.80∼1.92(m, 2H), 2.28∼2.46(m, 6H), 4.94∼5.00(m, 1H), 5.10(s, 2H), 7.14(d, 1H, $J = 8.9$ Hz), 7.32(dd, 1H, $J = 8.9$ Hz, J=2.6 Hz), 7.49(d, 1H, $J = 2.5$ Hz)
3B−5(1)	1.21(d, 3H, $J = 6.3$ Hz), 1.25∼1.50(m, 12H), 1.59∼1.79(m, 6H), 2.27∼2.55(m, 6H), 4.84∼4.90(m, 1H), 5.09(s, 2H), 7.10(d, 1H, $J = 8.9$ Hz), 7.46(dd, 1H, $J = 8.8$ Hz, $J = 2.4$ Hz), 7.61(d, 1H, $J = 2.4$ Hz)
3B−5(2)	1.22∼1.92(m, 21H, 1.23(d, 3H, $J = 6.3$ Hz), 2.28 ∼2.46(m, 6H), 4.94∼5.00(m, 1H), 5.11(s, 2H), 7.10(d, 1H, $J = 8.9$ Hz), 7.45(dd, 1H, $J = 8.8$ Hz, $J = 2.4$ Hz), 7.61(d, 1H, $J = 2.4$ Hz)
3B−6(1)	1.17∼1.20(m, 3H), 1.20∼1.45(m, 12H), 1.54∼1.75(m, 9H), 2.26∼2.45(m, 6H), 4.79∼4.86(m, 1H), 5.09(q, 1H, J=6.7 Hz), 6.95∼7.01(m, 2H), 7.29∼7.35(m, 2H)
3B−6(2)	1.21∼1.44(m, 17H, 1.22(d, 3H, $J = 6.3$ Hz), 1.60∼1.65(m, 5H), 1.80∼1.86(m, 2H), 2.25∼2.44(m, 6H), 4.92∼4.97(m, 1H), 5.09(q, 1H, $J = 6.7$ Hz), 6.95∼7.00(m, 2H), 7.29∼7.34(m, 2H)

Table 4. Herbicidal Activity of *Z* and *E* Isomers of Some Compounds **3** to *Amaranthus tricolor* L.

compound no.	regression eq	EC$_{50}$ (95%CI)/mgL^{-1}
3A1−7(1)	$Y = 2.43 + 2.11x$	16.3 (12.6−21.3)
3A1−7(2)	$Y = 2.38 + 2.19x$	15.7 (12.0−20.5)
3A1−11(1)	$Y = 1.63 + 2.68x$	18.2 (14.3−23.0)
3A1−11(2)	$Y = 1.37 + 2.88x$	18.3 (14.9−22.5)
3A1−13(1)	$Y = 2.95 + 1.76x$	14.7 (10.9−19.9)
3A1−13(2)	$Y = 2.38 + 2.27x$	14.4 (11.6−17.9)

grew them at 25−32 °C for about 7 days. Thirty plants at the two-leaf stage were retained by thinning out the seedlings and the emulsions (1 mL of emulsion for each cup with plants) were applied by Potter spray tower. Then the plants were grown at 25−32 °C. Three replicates were performed for each concentration. The number of dead or withered plants was recorded after 7 days and the inhibition rate was calculated according to the formula

$$I = \frac{\bar{D}_1 - \bar{D}_0}{30 - \bar{D}_0} \times 100\% \qquad (1)$$

in which I is inhibition rate, $\bar{D}_1$ is the average number of dead or withered plants in the presence of test compounds, and $\bar{D}_0$ is the average number of dead or withered plants in the blank test. EC$_{50}$ values of compounds **3** against *Amaranthus tricolor* L. were estimated using logistic analysis (*16*). The EC$_{50}$ values of three pairs of *Z* and *E* isomers of compounds **3** (**3A1−7**, **3A1−11**, **3A1−13**) with 95% confidence interval are shown in **Table 4** and The EC$_{50}$ values of all of compounds **3** (a mixture of *Z* and *E* isomers) with 95% confidence interval are listed in **Table 5**. The herbicidal activity of **3A1−12** against dicotyledon *Amaranthus tricolor* L. (three colored amaranth), *Cucumis sativus* L. (cucumber), *Glycine max* L. (soybean), and *Phaseolus radiatus* L. (mung bean); and monocotyledon *Triticum aestivum* L. (wheat), *Zea mays* L. (maize), *Oryza sativa* L. (rice), and *Festuca arundinacea* L. (tall fescue) was determined using the same method. The results are listed in **Table 6**.

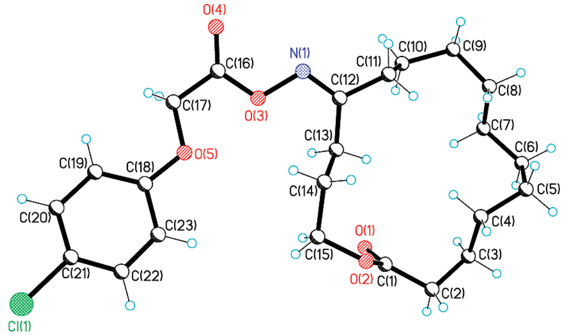


Figure 4. Crystal structure of compound **3A1−7(1)**.

3. RESULTS AND DISCUSSION

3.1. Synthesis of Compounds 3. As shown in **Scheme 1**, (15-methyl)-12- pentadecanolides (**4**), prepared from 2-nitrocyclododecanone, were allowed to react with hydroxylamine hydrochloride to give (15-methyl)-12-hydroxyimino-1,15- pentadecanolodes (**5**), which were then acylated using aryloxyalkanoic acids (**6**) to afford the title compounds (**3**). The experimental data of compounds **3** are given in **Table 1**. **Table 1** showed the yields of compounds **3** from **5** are good (76−94%). The structures of compounds **3** were confirmed by elemental analysis (**Table 2**) and ^{1}H NMR (**Table 3**).

3.2. Geometric Isomers of Compounds 3. The *Z* and *E* isomers of compounds **3** (**Figure 3**) were obtained by silica gel column chromatography and were distinguished based on the ^{1}H NMR features of the compounds.

Table 5. Herbicidal Activity of Compounds **3** to *Amaranthus tricolor* L.

compound no.[a]	regression eq	EC_{50} (95%CI)/mgL^{-1}
3A1−1	$Y = 2.98 + 1.08x$	73.2 (35.0−153.1)
3A1−2	$Y = 4.28 + 0.35x$	117.4 (80.1−1705.6)
3A1−3	$Y = 3.52 + 0.85x$	55.4 (25.5−120.5)
3A1−4	$Y = 3.11 + 1.12x$	48.8 (28.5−83.6)
3−5	$Y = 4.29 + 0.48x$	30.6 (9.8−95.9)
3A1−6	$Y = 3.96 + 0.76x$	23.8 (11.7−48.7)
3A1−7	$Y = 2.41 + 2.05x$	18.2 (12.3−27.0)
3A1−8	$Y = 1.76 + 1.70x$	80.9 (46.1−141.9)
3A1−9	$Y = 2.95 + 1.19x$	52.4 (27.4−100.3)
3A1−10	$Y = 2.61 + 1.37x$	55.4 (36.3−84.4)
3A1−11	$Y = 3.20 + 1.39x$	19.6 (11.2−34.6)
3A1−12	$Y = 4.56 + 0.50x$	7.7 (3.0−19.7)
3A1−13	$Y = 2.24 + 2.25x$	16.9 (11.7−24.4)
3A2−1	$Y = 2.85 + 1.60x$	22.4 (16.2−31.0)
3A2−2	$Y = 1.73 + 2.10x$	35.9 (26.7−48.3)
3A2−3	$Y = 2.85 + 1.71x$	18.0 (13.4−24.3)
3A2−4	$Y = 1.58 + 2.45x$	25.1 (20.2−31.1)
3A2−5	$Y = 2.72 + 1.82x$	17.8 (13.2−23.8)
3A2−6	$Y = 2.29 + 1.60x$	49.6 (34.7−70.8)
3A2−7	$Y = 3.44 + 1.60x$	9.5 (6.0−15.3)
3A2−8	$Y = 3.41 + 1.41x$	13.5 (9.0−20.4)
3A3−1	$Y = 3.07 + 1.25x$	34.6 (22.0−54.4)
3A3−2	$Y = 2.06 + 1.69x$	55.4 (36.0−85.2)
3A3−3	$Y = 1.31 + 2.21x$	46.5 (34.1−63.4)
3A3−4	$Y = 2.22 + 1.64x$	50.1 (34.4−72.9)
3B−1	$Y = 3.21 + 1.64x$	12.4 (9.1−16.9)
3B−2	$Y = 3.55 + 1.61x$	8.0 (5.9−10.9)
3B−3	$Y = 4.31 + 1.32x$	3.4 (2.3−5.0)
3B−4	$Y = 3.54 + 1.60x$	8.2 (6.1−11.2)
3B−5	$Y = 2.94 + 1.78x$	14.4 (10.6−19.4)
3B−6	$Y = 4.04 + 1.41x$	4.8 (3.4−6.7)
2,4-D	$Y = 2.07 + 1.42x$	117.3 (83.4−587.6)
tribenuron-methyl	$Y = 3.29 + 1.26x$	22.4 (14.6−34.3)

[a] Compounds **3A3−1**∼**3A3−4** were reported in ref *8*a. **3A3−1**: R = H, R (*1*) = Me, R^2 = Me, Ar = C_6H_5; **3A3−2**: R = H, R^1 = Me, R^2 = Me, Ar = 4-MeC_6H_4; **3A3−3**: R = H, R^1 = Me, R^2 = Me, Ar = 4-ClC_6H_4; **3A3−4**: R = H, R^1 = Me, R^2 = Me, Ar = 4-Cl-3-MeC_6H_4.

Table 6. Herbicidal Activity of **3A1−12** (a Mixture of *Z* and *E* Isomers) Against Eight Plants

plant	regression eq	EC_{50} (95%CI)/mgL^{-1}
dicotyledon		
Amaranthus tricolor L.	$Y = 3.10 + 1.72x$	7.7 (3.0−19.7)
Cucumis sativus L.	$Y = 4.88 + 0.73x$	1.5 (0.4−5.4)
Glycine max L.	$Y = 4.36 + 0.55x$	14.4 (8.3−25.0)
Phaseolus radiatus L.	$Y = 4.85 + 0.35x$	2.8(0.5−15.1)
monocotyledon		
Triticum aestivum L.	$Y = 4.32 + 0.43x$	38.4 (14.1−104.6)
Zea mays L.	$Y = 5.12 + 0.25x$	0.3 (0.02−51.9)
Oryza sativa L.	$Y = 4.80 + 0.51x$	2.5 (1.25−5.0)
Festuca arundinacea L.	$Y = 3.11 + 1.11x$	50.2 (32.6- 77.2)

In the case of *Z* isomers, the benzene ring on the side chain is closer to 15-C than that of *E* isomer, therefore the resonance lines of 15-CH_2 (**3A** series) or 15-CH (**3B** series) would be expected to shift upfield from the corresponding 15-CH_2 or 15-CH of *E* isomers due to the diamagnetic effect of the benzene ring (*17*). It can be seen from **Table 3** that the ^{1}H NMR signals of protons on the 15-C of (**1**)-isomers appeared upfield (δ 3.91−4.09 for **3A** series and δ 4.79−5.00 for **3B** series) relative to those of the (**2**)-isomers (δ 4.14−4.20 for **3A** series and δ 4.91−5.05 for 3B series). Therefore (**1**) is the *Z* isomer and (**2**) is the *E* isomer. The results also were confirmed by the X-ray diffraction analysis that **3A1−7(1)** is the *Z* isomer (**Figure 4**). Usually *Z* and *E* isomers of compounds **3** can not be separated completely; therefore, only total yields were given in this paper.

3.2. Herbicidal Activity. It can be seen from **Table 4** that the herbicidal activity against *Amaranthus tricolor* L was almost no difference between the *Z* isomer and *E* isomer of compounds **3**. May be it is easy to interconvert between *Z* an *E* isomers of imine systems (*18*). The ^{1}H NMR spectra of a mixture of *Z* and *E* isomers have been observed in several hours for a solution of single isomer of compounds **3** in chloroform containing trace hydrochloride in our experiment. Therefore the herbicidal activity of all compounds **3** was determined in the form of the mixture of *Z* and *E* isomers.

As shown in **Table 5**, some of compounds **3** displayed excellent herbicidal activity against *Amaranthus tricolor* L: the herbicidal activity of compounds **3** except compounds **3A1−2** was much higher than that of commercial herbicide 2,4-D and the herbicidal activity of about half of compounds **3**, the LC_{50} values of which are less than 20 mg/L, may be comparable to commercial herbicide tribenuron-methyl, which illustrated that herbicidal activity of compounds **3** is displayed by aryloxyalkanoic acid in coordination with macrolactone ring. Namely, herbicidal activity of phenoxyalkanoic acid herbicides such as 2,4-D, is significantly improved by combining with macrolactone ring. The structure−activity relationship is as follows: Compounds **3B** exhibited higher herbicidal activity than compounds **3A**, and the structural difference between series **3B** and series **3A** is only the existence of a methyl group on the C-15 of macrolactone ring in 3B instead of H in that of **3A**, which indicated that small structural modification of macrolactone ring will lead to obviously change the herbicidal activity. Above facts illustrated that the macrolactone ring plays an important role in the herbicidal activity of compounds **3**. The structures of alkanoic acid moiety also have an important effect on the herbicidal activity of compounds **3**. In general, compounds **3A** have a gradual increase of herbicidal activity in the order of **3A3** (alkanoic acid moiety is isobutanoic acid), **3A1** (alkanoic acid moiety is acetic acid) and **3A2** (alkanoic acid moiety is isopropanoic acid), which indicated that the existence of suitable substituent (here is methyl group) on the α-carbon of alkanoic acid will benefit the improvement of herbicidal activity for compounds **3**. However, more substituents (two methyl groups) on the α-carbon of alkanoic acid are unfavorable to the improvement of herbicidal activity. The herbicidal activity of the compounds **3** is also closely associated with Ar. The compounds **3** in which Ar is a phenyl bearing two chlorine atoms or one chlorine with one methyl group showed better activity than those in which Ar is a phenyl bearing only one chlorine, and the activity of latter is better than those in which Ar is a phenyl bearing 1−2 methyl groups or one another groups such as nitro group or methoxy group.

It can be seen from **Table 6** that compound **3A1−12** exhibited excellent herbicidal activity against *Amaranthus tricolor* L., *Cucumis sativus* L.), *Glycine max* L. *Phaseolus radiatus* L., *Zea mays* L. and *Oryza sativa* L. (The EC_{50} values were 7.7, 1.5, 14.4, 2.8, 0.3, and 2.5 mgL^{-1}, respectively); and good herbicidal activity against *Triticum aestivum* L. and *Festuca arundinacea* L. (The EC_{50} values were 38.4 and 50.2 mgL^{-1}, respectively.)

In conclusion, a series of novel 12-(aryloxyacyloxyimino)-1,15-pentadecanlactone derivatives were synthesized by introducing macrolide ring into aryloxyalkanoic acids. The bioassay showed that some of them exhibited excellent herbicidal activity against the model weed *Amaranthus tricolor* L. The further bioassay showed that compound **3A1−12** exhibited good to excellent herbicidal activity against both dicotyledon and monocotyledon. It could be developed to practicable herbicide in prospects and further research confirmation is needed.

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