Synthesis and herbicidal activity of 1,3-substituted quinazolinedione derivatives

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Abstract

Quinazolinediones derivatives are a new family of diphenyl ether herbicides. Twenty four 1,3-substituted quinazolinediones derivatives were designed and synthesized. Their structures were confirmed by ^{1}H NMR and elemental analysis. The preliminary bioassay results show that most of these compounds have herbicidal activity in post-emergence treatment. The compounds 3c, 3d, 3e, 3f showed 90-100% herbicidal efficacy at 200 gha^{-1} against dicotyledonous weeds such as *Abutilon theophrasti*.

Keywords: Quinazolinediones, herbicidal activity, diphenyl ether

Introduction

Many herbicides have recently been phased out because of their potential toxicological or environmental impact. These side effects are often caused by high use-rates. Thus, products such as protoporphyinogen-IX oxidase (protox) inhibitors, which can control weeds at a low use-rate of a few gha^{-1}, are of top interest. Protox is the last enzyme in the porphin pathway that is common to both chlorophyll and heme synthesis. In treated tissues, these herbicides cause membrane leakage, pigment breakdown and eventually necrosis of the leaf.[1-3]

Research on protox inhibitors has been actively pursued since the 1970s, producing roughly two classes of product: diphenyl ethers (DPEs) and *N*-phenylnitrogen heterocycles.[4] DPEs were the first widely used family of herbicides. Several novel heterocyclic phenyl ethers have been reported by several groups (Fig. 1 and Fig. 2).[5-8] Heterocyclic phenyl ethers are highly active both pre- and postemergence on a wide variety of weeds.[9-17] A few recently reported examples include 6-aryloxy-1*H*-benzotriazoles,[18] aryloxyindolin-2-(3*H*)-ones, 5-aryloxybenzisoxazoles, 6-aryloxyquinoxalin-2,3-diones, benzoheterocycles,[19-21] and benzoxazines.[22]

Through studying the structure-activity relationships of heterocyclic phenyl ethers, we added an ester or an acylamide on N-3 of quinzaolinediones to improve the activity. In this paper, we

describe synthesis of 1,3-substituted quinazolinediones derivatives and their structure-activity relationships for herbicidal activity.

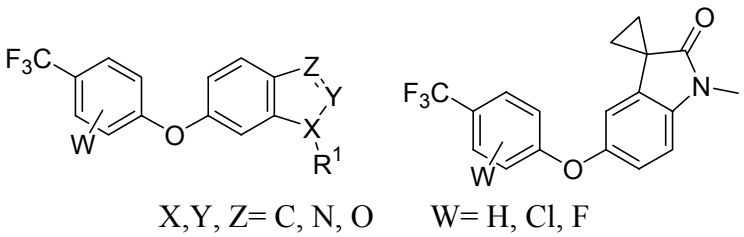


Figure 1. Structural characteristics of benzoheterocyclic analogs.

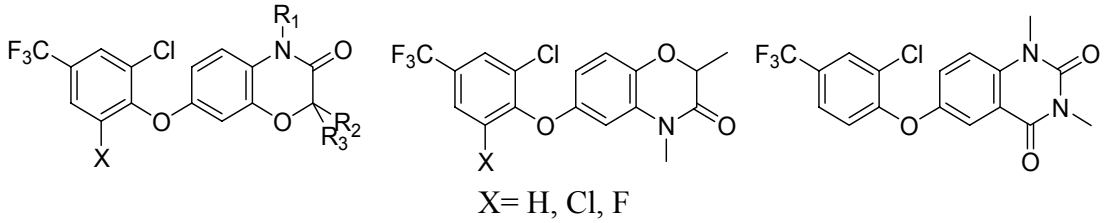


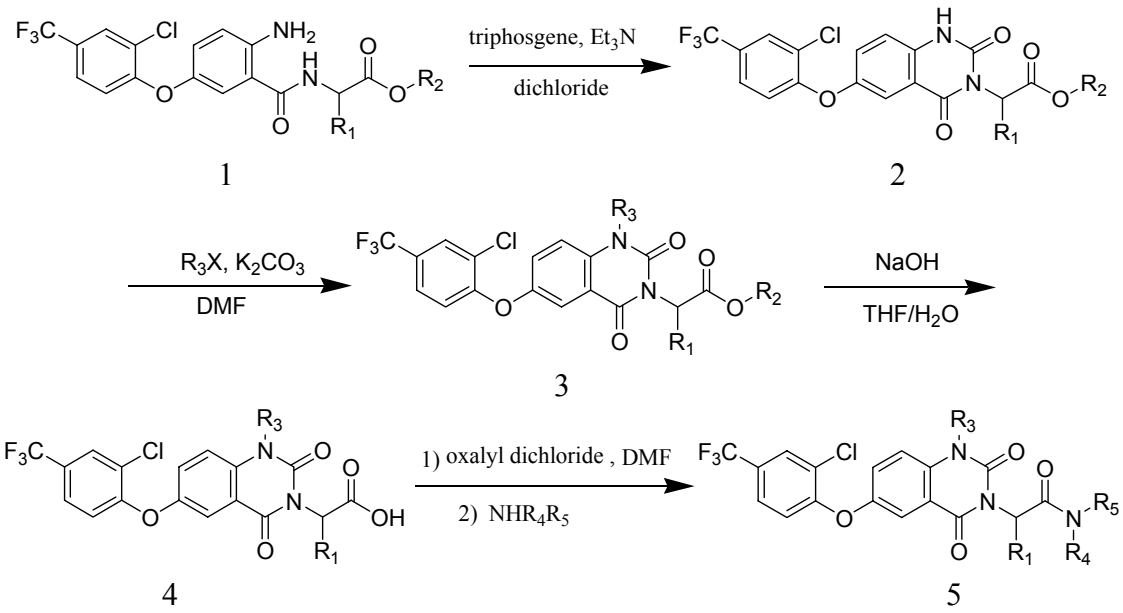
Figure 2. Structural characteristics of benzoxazines and quinazolinediones.

Results and Discussion

2-(2-Amino-5-(2-chloro-4-4(trifluoromethyl)phenoxy)benzamido) acetate (1, R^1 was H or methyl, R^2 was methyl or ethyl), obtained via multistep synthesis,[23,24] were treated triphosgene with at 0 °C and Et_3N as the base, to produce 2-(6-(2-chloro-4-4(trifluoromethyl)phenoxy)-2,4-dioxo-1,2-dihydroquinzaolin-3(4*H*)-yl) acetate (2)[25]. The hydrogen atom was substituted by methyl, allyl or propargyl to give (3). The ester was hydrolyzed to afforded (4), which was converted to various amide groups using standard amidation methods to provide the 2-(1-substituted-2,4-dioxoquinazolin-3(4*H*)-yl)-*N*-substituted acetamides (5) (Scheme 1).

Through the herbicidal activity testing, we found that the benzoquinazoline derivatives were more active on dicotyledonous than monocotyledonous species (Table 1). Some compounds showed excellent herbicidal activity at the rate of 200 gha^{-1} such as, compound 3c, 3d, 3e, 3f, Which have a better herbicidal activity compare to the related compound 1,3-substituted quinazolinedione reported in the literature (the reported compounds show low herbicidal activity at the same rate). The order of herbicidal activity of benzoquinazoline compounds was as follows: (3)>(2)>(4)>(5). The activity of the ester was greater than acid and acylamide. Some of the compounds exist in enantiomeric forms, their herbicidal activity were similar. While R^3 was substituted with propynyl, allyl, the compounds showed good herbicidal activity. Activities may

be characterized with propynyl or allyl group because the higher hydrophobicity, which affecting the uptake, translocation or metabolism in the plant.



Scheme 1. Synthesis route for 1,3-substituted quinazolinediones derivatives.

Experimental Section

General Procedures. Melting points were measured by using a RY-1 melting point apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian-300 spectrometer using TMS as an internal reference. Mass spectra (GC-MS) were obtained on an Agilest 6890-5973 instrument. Elemental analysis was performed on a Yananca CDRDER MT-3A elemental analyzer (The analysis was carried out by state key laboratory of Elemeto-Organic chemistry, Nankai University, Tianjin 30071, P.R.China). The structures of new compounds were confirmed by ^{1}H NMR and elemental analysis (Table 2 and Table 3). Some compound structures were further confirmed by ^{13}C NMR and mass spectra (Table 4).

Table 1. Herbicidal activity

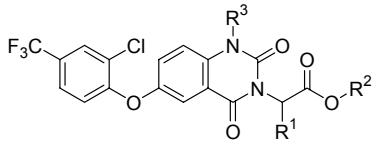
Comd	Dose (g/ha)	BYG	CRB	VEL	Comd	Dose (g/ha)	BYG	CRB	VEL
2a	1000	0	0	10	2b	1000	0	10	95
	200	0	0	0		200	0	0	0
2c	1000	0	0	0	2d	1000	0	0	10
	200	0	0	0		200	0	0	0
3a	1000	10	35	70	3b	1000	10	50	98
	200	0	15	20		200	0	0	0
3c	1000	50	70	100	3d	1000	50	70	100
	200	0	10	95		200	10	40	90
3e	1000	70	70	100	3f	1000	5	15	95
	200	20	20	100		200	5	10	90
3g	1000	0	0	45	3h	1000	0	0	85
	200	0	0	30		200	0	0	75
3i	1000	0	0	30	3j	1000	5	5	30
	200	0	0	10		200	5	5	25
4a	1000	0	10	95	4b	1000	5	5	10
	200	0	0	0		200	0	0	0
4c	1000	5	10	25	4d	1000	40	35	80
	200	0	0	0		200	30	20	55
5a	1000	50	70	75	5b	1000	0	0	0
5c	1000	0	0	0	5d	1000	5	0	20
5e	1000	10	5	10	5f	1000	0	30	60

0 equals no activity; 100 equals total control. BYG: Barnyard (*Echinochloa crusgalli*); CRB: crabgrass (Digitaria sanguinalis). VEL: Velvetleaf (*Abutilon thophrasti*).

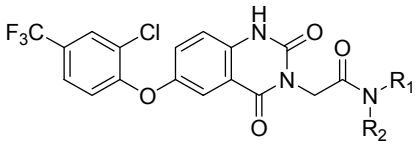
2-(6-(2-Chloro-4-trifluoromethyl)phenoxy)-2,4-dioxo-1,2-dihydroquinazolin-3(4*H*)-yl) acetates (2). A mixture of 1 (1mmol), triphosgene (1.2mmol), Et_3N (2.4mmol) was stirred in CH_2Cl_2 on an ice-water bath for 2h. The reaction mixture was extracted with CH_2Cl_2 (2×100mL), washed with the solution of $NaHCO_3$, NaCl, dried over anhydrous magnesium sulfate and the solvent evaporated. The residue was purified by column chromatography (20% EtOAc in hexanes as eluent) to give the target compound.

Ethyl 2-(6-(2-chloro-4-(trifluoromethyl)phenoxy)-1,2-dihydro-2,4-dioxoquinazolin-3(4*H*)-yl) acetate (2b). Yield 75%, white solid, mp 199-201 °C. ^{1}H NMR (300MHz, $CDCl_3$) δ(ppm) 1.30 (t, *J* 6.9 Hz, 3H), 4.26 (q, *J* 6.9 Hz, 2H), 4.83 (s, 2H), 7.01 (d, *J* 8.7 Hz, 1H, Ar-H), 7.21 (d, *J* 8.7 Hz, 1H, Ar-H), 7.39 (dd, *J* 3.0 and 3.0 Hz, 1H, Ar-H), 7.48 (dd, *J* 2.1 and 3.0 Hz, 1H, Ar-H), 7.64 (d, 1H, *J* 3.0 Hz, Ar-H), 7.75 (d, 1H, *J* 2.1 Hz, Ar-H), 10.79 (s, 1H, H-NCO). Anal. Calcd. for $C_{19}H_{14}ClF_3N_2O_5$: C, 51.54; H, 3.19; N, 6.33; Found: C, 51.6; H, 3.44; N, 6.19.

Table 2. Physical constants and elemental analysis



Cpd	R^1	R^2	R^3	Yield, (%)	M.p.(ºC)	Analysis (%), (calc./found) C H N
2a	H	Me	H	71	202-204	50.42 2.82 6.53 50.31 3.01 6.41
2b	H	ethyl	H	75	199-201	51.54 3.19 6.33 51.66 3.34 6.19
2c (*R*)	Me	Me	H	67	32-134	51.54 3.19 6.33 51.40 3.01 6.03
2d (*S*)	Me	Me	H	70	119-121	51.54 3.19 6.33 51.78 3.09 6.08
3a	H	Me	Me	65	190-192	51.54 3.19 6.33 51.31 3.22 6.60
3b	H	ethyl	Me	63	201-202	52.59 3.53 6.13 52.78 3.66 6.58
3c	H	Me	allyl	65	yellow oil	53.80 3.44 5.98 53.63 3.24 5.80
3d	H	ethyl	allyl	63	120-122	54.03 3.76 5.80 54.68 3.78 5.62
3e	H	Me	propynyl	66	yellow oil	54.03 3.02 6.00 53.89 2.98 6.13
3f	H	ethyl	propynyl	64	118-120	54.96 3.35 5.83 54.87 3.37 5.80
3g (*R*)	Me	Me	allyl	61	130-131	54.73 3.76 5.80 54.99 3.85 5.49
3h (*S*)	Me	Me	allyl	64	yellow oil	54.73 3.76 5.80 54.60 3.81 5.88
3I (*R*)	Me	Me	propynyl	62	118-119	54.96 3.35 5.83 54.76 3.76 5.80
3j (*S*)	Me	Me	propynyl	60	yellow oil	54.96 3.35 5.83 55.20 3.69 6.00
4a	H	H	H	55	190-192	49.23 2.43 6.75 49.02 2..78 6.45
4b	H	H	Me	58	190-196	50.42 2.82 6.53 50.39 2.89 6.40
4c	H	H	allyl	60	172-174	52.82 3.10 6.16 52.48 3.26 6.59
4d	H	H	propynyl	60	200-202	53.05 2.67 6.19 53.44 2.88 6.09



Cpd	R^1	R^2	Yield (%)	mp (ºC)	Analysis (%) (calc./found) C H N
5a	H	Me	54	238-241	50.54 3.06 9.82 50.66 3.25 9.99
5b	H	isopropyl	56	252-254	52.70 3.76 9.22 52.52 4.00 9.12
5c	H	phenyl	51	270-272	56.40 3.09 8.58 56.81 3.39 8.79
5d	H	p-tolyl	52	280-281	57.21 3.40 8.34 57.11 3.33 8.31
5e	H	4-nitrophenyl	52	247-248	51.65 2.64 10.68 51.70 2.45 10.99
5f		morpholin	50	239-241	52.13 3.54 8.68 52.09 3.13 8.45

Table 3. ^{1}H NMR

Cpd	^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm)
2a	3.80 (s, 3H), 4.85 (s, 2H), 7.02(d, *J* 9.0 Hz, 1H, Ar-H), 7.22 (d, *J* 9.0 Hz, 1H, Ar-H), 7.41 (dd, *J* 3.0 and 3.0 Hz, 1H, Ar-H), 7.49 (dd, *J* 2.1 and 3.0 Hz, 1H, Ar-H), 7.65 (d, 1H, *J* 3.0 Hz, Ar-H), 7.77 (d, 1H, *J* 2.1 Hz, Ar-H), 10.66 (s, 1H, H-NCO)
2b	1.30 (t, *J* 6.9 Hz, 3H), 4.26 (q, *J* 6.9 Hz, 2H), 4.83 (s, 2H), 7.01 (d, *J* 8.7 Hz, 1H, Ar-H), 7.21 (d, *J* 8.7 Hz, 1H, Ar-H), 7.39 (dd, *J* 3.0 and 3.0 Hz, 1H, Ar-H), 7.48 (dd, *J* 2.1 and 3.0 Hz, 1H, Ar-H), 7.64 (d, 1H, *J* 3.0 Hz, Ar-H), 7.75 (d, 1H, *J* 2.1 Hz, Ar-H), 10.79 (s, 1H, H-NCO)
2c (R)	1.67 (d, 3H, *J* 6.9 Hz, CH_3), 3.75 (s, 3H, OCH_3), 5.64 (q, 1H, *J* 6.9 Hz, CH), 7.03 (d, 1H, *J* 8.4 Hz, Ar-H), 7.17 (d, 1H, *J* 8.4 Hz, Ar-H), 7.42 (dd, 1H, *J* 2.7 and 8.7 Hz, Ar-H), 7.50 (dd, 1H, *J* 2.4 and 6.0 Hz, Ar-H), 7.64 (d, 1H, *J* 2.7 Hz, Ar-H), 7.77 (d, 1H, *J* 1.5Hz, Ar-H)
2d (S)	1.68 (d, 3H, *J* 6.9 Hz, CH_3), 3.75 (s, 3H, OCH_3), 5.65 (q, 1H, *J* 6.9 Hz,CH), 7.03 (d, 1H, *J* 8.4 Hz, Ar-H), 7.19 (d, 1H, *J* 9.0 Hz, Ar-H), 7.42 (dd, 1H, *J* 3.0 and 8.7 Hz, Ar-H), 7.50 (dd, 1H, *J* 2.4 and 6.0 Hz, Ar-H), 7.64 (d, 1H, *J* 2.7 Hz, Ar-H), 7.77 (d, 1H, *J* 1.8 Hz, Ar-H)
3a	3.64 (s, 3H), 3.78 (s, 3H), 4.85 (s, 2H), 7.17 (d, *J* 9 Hz, 1H, Ar-H), 7.61-7.69 (m, 3H, Ar-H), 7.70 (d, *J* 9 Hz, 1H, Ar-H), 7.98 (s, 1H, Ar-H)

3b	1.23 (t, *J* 6.9 Hz, 3H), 3.57 (s, 3H), 4.15 (q, *J* 6.9 Hz, 2H), 4.67 (s, 2H), 7.17 (d, *J* 9.0 Hz, 1H, Ar-H), 7.61-7.69 (m, 3H, Ar-H), 7.70(d, *J* 9.0 Hz, 1H, Ar-H), 7.98 (s, 1H, Ar-H)
3c	3.78 (s, 3H), 4.79 (d, *J* 2.1 Hz, 2H), 4.83 (s, 2H), 5.29-5.31 (m, 2H), 5.88-5.92 (m, 1H), 7.02 (d, *J* 8.1 Hz, 1H, Ar-H), 7.23 (s, 1H, Ar-H), 7.41(d, *J* 8.1 Hz, 1H, Ar-H), 7.49 (d, *J* 8.1 Hz, 1H, Ar-H), 7.76 (d, 2H, Ar-H)
3d	1.29 (t, *J* 6.9 Hz, 3H), 4.23 (q, *J* 6.9 Hz, 2H), 4.82 (s, 2H), 5.26-5.31 (m, 2H), 5.89-5.98 (m, 1H), 7.03 (d, *J* 9.0 Hz, 1H, Ar-H), 7.26 (d, *J* 9.0 Hz, 1H, Ar-H), 7.39-7.51 (m, 2H, Ar-H), 7.760 (s, 2H, Ar-H)
3e	2.35 (t, *J* 2.4 Hz, 1H), 3.78 (s, 3H), 4.84 (s, 2H), 4.94 (d, *J* 2.4 Hz, 2H), 7.03 (d, *J* 8.4 Hz, 1H, Ar-H), 7.47-7.51 (m, 3H, Ar-H), 7.75-7.77 (m, 2H, Ar-H)
3f	1.29 (t, *J* 6.9 Hz, 3H), 2.35 (q, *J* 3.1 Hz, 1H), 4.25 (q, *J* 6.9 Hz, 2H), 4.78 (s, 2H), 4.95 (s, 2H), 7.03 (d, *J* 9.0 Hz, 1H, Ar-H), 7.64-7.78 (m, 4H, Ar-H), 7.77 (s, 1H, Ar-H)
3g (*R*)	1.64 (d, 3H, *J* 6.9 Hz, CH_3), 3.75 (s, 3H, OCH_3), 4.77 (t, 2H, *J* 6.9 Hz, CH_2), 5.29-5.33 (m, 2H, C CH), 5.64 (q, *J* 6.9 Hz, 1H, CH), 5.89-5.98 (m, 1H, -CH), 7.03 (d, 1H, *J* 8.7 Hz, Ar-H), 7.25 (d, 1H, *J* 9.0 Hz, Ar-H), 7.44 (dd, 1H, *J* 3.0 and 6.0 Hz, Ar-H), 7.49 (dd, 1H, *J* 2.4 and 8.7 Hz, Ar-H), 7.74 (d, 1H, *J* 3.0 Hz, Ar-H), 7.77 (d, 1H, *J* 2.1 Hz, Ar-H)
3h (*S*)	1.65 (d, 3H, *J* 6.9 Hz, CH_3), 3.73 (s, 3H, OCH_3), 4.78 (t, 2H, *J* 6.9 Hz, CH_2), 5.29-5.32 (m, 2H, C CH), 5.64 (q, 1H, *J* 6.3 Hz, CH), 5.93-5.99 (m, 1H, -CH), 7.04 (d, 1H, *J* 8.7 Hz, Ar-H), 7.23 (d, 1H, *J* 9.0 Hz, Ar-H), 7.42 (dd, 1H, *J* 3.0 and 6.0 Hz, Ar-H), 7.48 (dd, 1H, *J* 2.4 and 8.7 Hz, Ar-H), 7.74 (d, 1H, *J* 3.0 Hz, Ar-H), 7.76 (d, 1H, *J* 2.1Hz, Ar-H)
3i (*R*)	1.64 (d, 3H, *J* 6.9 Hz, CH_3), 2.37 (t, 1H, *J* 3.1 Hz, C≡H), 3.74 (s, 3H, OCH_3), 4.94 (d, 2H, *J* 3.1 Hz, CH_2), 5.63 (q, 1H, *J* 6.9 Hz, CH), 7.05 (d, 1H, *J* 8.4 Hz, Ar-H), 7.49 (m, 3H, Ar-H), 7.74 (d, 1H, *J* 1. 8Hz, Ar-H), 7.77 (d, 1H, *J* 1.8 Hz, Ar-H)
3j (*S*)	1.64 (d, 3H, *J* 6.9 Hz, CH_3), 2.36 (t, 1H, *J* 3.0 Hz, C≡CH), 3.74 (s, 3H, OCH_3), 4.95 (t, 2H, *J* 3.0 Hz, CH_2), 5.62 (q, 1H, *J* 6.9 Hz, CH), 7.06 (d, 1H, *J* 8.4 Hz, Ar-H), 7.51 (m, 3H, Ar-H), 7.76 (d, 1H, *J* 8.4 Hz, Ar-H), 7.78 (d, 1H, *J* 1.8 Hz, Ar-H)
4a	4.54 (s, 2H), 7.04 (d, *J* 9.0 Hz, 1H, Ar-H), 7.31 (d, *J* 9.0 Hz, 1H, Ar-H), 7.40 (dd, *J* 3.0 and 9.0 Hz, 1H, Ar-H), 7.43 (dd, *J* 2.1 and 3.0 Hz, 1H, Ar-H), 7.59 (d, 1H, *J* 3.0 Hz, Ar-H), 7.81 (d, 1H, *J* 2.1 Hz, Ar-H), 11.69 (s, 1H, COOH)
4b	3.58 (s, 3H), 4.60 (s, 2H), 7.15 (d, 1H, *J* 8.1 Hz Ar-H), 7.60-7.67 (m, 4H, Ar-H), 7.93 (s, 1H)
4c	4.61 (s, 2H), 4.80 (d, *J* 3.1 Hz, 2H), 5.22 (t, *J* 3.1 Hz, 2H), 5.93 (m, 1H), 7.15 (d, *J* 8.4 Hz, 1H, Ar-H),7.51 (m, 2H, Ar-H), 7.65 (m, 2H, Ar-H), 7.88 (d, *J* 8.4 Hz, 1H, Ar-H)
4d	2.25 (t, *J* 2.4 Hz, 1H), 4.82 (s, 2H), 4.96 (d, *J* 2.4 Hz, 2H), 7.13 (d, *J* 8.4 Hz, 1H, Ar-H), 7.56-7.62 (m, 3H, Ar-H), 7.77-7.88 (m, 2H, Ar-H)
5a	2.63 (s, 3H), 4.47 (s, 2H), 7.06 (d, *J* 8.7 Hz, 1H, Ar-H), 7.19-7.59 (m, 4H, Ar-H), 7.86 (s, 1H, Ar-H)

5b	1.08 (t, *J* 6 Hz, 6H), 4.01 (m, 1H), 4.41 (s, 2H), 7.33 (d, *J* 8.4 Hz, 1H, Ar-H), 7.33-7.80 (m, 4H, Ar-H), 7.96 (s, 1H, Ar-H)
5c	4.69 (s, 2H), 7.20 (m, 1H, Ar-H), 7.11 (d, *J* 9.0 Hz, 1H, Ar-H), 7.27 (t, *J* 9.0 Hz, 2H, Ar-H), 7.35 (s, 1H, Ar-H), 7.48-7.65 (m, 5H, Ar-H), 7.90 (s, 1H, Ar-H), 10.20 (s, 1H), 11.69 (s, 1H)
5d	2.27 (s, 3H), 4.69 (s, 2H), 7.14 (d, *J* 8.7 Hz, 1H, Ar-H), 7.30-7.54 (m, 3H, Ar-H), 7.56-7.64 (m, 4H, Ar-H), 7.67 (d, *J* 8.7 Hz, 1H, Ar-H), 7.84 (s, 1H, Ar-H), 10.40 (s, 1H)
5e	4.75 (s, 2H), 7.11 (d, *J* 8.4 Hz, 1H, Ar-H), 7.36 (d, *J* 8.4 Hz, 1H, Ar-H), 7.45 (t, *J* 2.1 Hz, 1H, Ar-H), 7.56 (d, *J* 2.1 Hz, 1H, Ar-H), 7.59 (dd, *J* 2.4 Hz, 1H, Ar-H), 7.81-7.84 (m, 3H, Ar-H), 8.16 (d, *J* 8.4 Hz, 1H, Ar-H), 8.19 (s, 1H, Ar-H), 10.87 (s, 1H)
5f	3.19-3.66 (m, 8H), 7.09 (d, *J* 8.7 Hz, 1H, Ar-H), 7.32 (d, *J* 8.7 Hz, 1H, Ar-H), 7.46 (dd, *J* 3.0 and 3.0 Hz, 1H, Ar-H), 7.52 (dd, *J* 2 and 3 Hz, 1H, Ar-H), 7.62 (d, 1H, *J* 3 Hz, Ar-H), 7.88 (d, 1H, *J* 2.1 Hz, Ar-H), 11.65 (s, 1H)

Table 4. ^{13}C NMR and MS data

Cpd	13C NMR (100MHz, CDCl3) δ(ppm) GC–MS (EI), m/z (%)
3c	168.1, 160.5, 155.0, 154.9, 151.4, 149.0, 136.4, 130.7, 128.3, 128.2, 126.5, 125.8, 125.3, 125.2, 117.7, 117.3, 116.5, 116.4, 52.3, 46.2, 42.4 468 (M+, 100%), 437 (19%), 408 (32%), 380 (21%), 352 (86%), 340 (98%), 213 (45%), 129 (18%), 41 (23%)
3d	167.6, 160.6, 155.0, 151.4, 150.0, 136.5, 130.7, 128.5, 127.3, 126.8, 126.5, 125.8, 124.9, 121.3, 119.7, 117.7, 117.3, 116.5, 61.6, 46.2, 42.6, 14.0 482 (M+, 82%), 437 (19%), 408 (38%), 380 (19%), 352 (69%), 340 (100%), 213 (38%), 129 (13%), 41 (21%)
3e	168.1, 160.3, 154.8, 151.8, 149.6, 128.4, 128.3, 128.2, 126.5, 125.4, 125.3, 125.2, 119.8, 117.4, 116.7, 116.4, 76.6, 73.8, 57.5, 42.6, 33.6 466 (M+, 100%), 435 (7%), 406 (53%), 378 (8%), 364 (7%), 350(67%), 323 (20%), 288 (17%), 179 (10%), 156 (24%), 128 (12%), 56 (10%)
3f	167.6, 160.4, 151.8, 149.7, 135.6, 128.4, 128.3, 126.5, 126.0, 125.4, 125.3, 119.8, 117.4, 116.7, 116.5, 116.4, 76.7, 73.7, 67.0, 42.8, 33.6, 14.0 480 (M+, 100%), 435 (15%), 406 (85%), 378 (15%), 364 (15%), 350(70%), 323 (15%), 288 (14%), 179 (14%), 156 (25%), 128 (15%), 56 (13%).

2-(6-(2-Chloro-4-trifluoromethyl)phenoxy)-1,2-dihydro-1-alkyl-2,4-dioxoquinazolin-3(4*H*)-yl)acetates (3). A mixture of 2 (1mmol), K_2CO_3 (1.2mmol) and alkyl halide (1.1mmol) was stirred in *N,N*-dimethylformamide at 40 °C . The reaction mixture was extracted with EtOAc (2×100mL), washed with a solution of $NaHCO_3$, NaCl, dried over anhydrous magnesium sulfate

and the solvent evaporated. The residue was purified by column chromatography (20% EtOAc in hexanes as eluent) to give the target compound.

Ethyl 2-(6-(2-chloro-4-(trifluoromethyl)phenoxy)-1,2-dihydro-1-propynyl-2,4-dioxo-quinazolin-3-(4*H*)-yl) acetate (3f). Yield 64%, white solid, mp 118-120 °C. ^{1}H NMR (300MHz, $CDCl_3$) δ(ppm) 1.29 (t, *J* 6.9 Hz, 3H), 2.35 (q, *J* 3.1 Hz, 1H), 4.25 (q, *J* 6.9 Hz, 2H), 4.78 (s, 2H), 4.95 (s, 2H), 7.03 (d, *J* 9.0 Hz, 1H, Ar-H), 7.64-7.78 (m, 4H, Ar-H), 7.77 (s, 1H, Ar-H). ^{13}C NMR (100MHz, $CDCl_3$) δ(ppm) 167.6, 160.4, 151.8, 149.7, 135.6, 128.4, 128.3, 126.5, 126.0, 125.4, 125.3, 119.8, 117.4, 116.7, 116.5, 116.4, 76.7, 73.7, 67.0, 42.8, 33.6, 14.0. GC–MS (EI), m/z (%) 480 (M^+, 100%), 435 (15%), 406 (85%), 378 (15%), 364 (15%), 350 (70%), 323 (15%), 288 (14%), 179 (14%), 156 (25%), 128 (15%), 56 (13%). Anal. Calcd. for $C_{22}H_{16}ClF_3N_2O_5$: C, 54.96; H, 3.35; N, 5.83; Found: C, 54.87; H, 3.37; N, 5.80.

2-(6-(2-Chloro-4-(trifluoromethyl)phenoxy)-1,2-dihydro-2,4-dioxoquinazolin-3(4*H*)-yl) acetic acids (4). A mixture of 3 (1mmol) and aqueous 10% NaOH (5mL) was refluxed in THF (5mL) for 4h. After evaporation of the THF, 10% HCl was added slowly to the residue under ice-water cooling. The resulting precipitates were collected by filtration, washed with water and recrystallized from EtOH to afford compounds 4.

2-(6-(2-Chloro-4-(trifluoromethyl)phenoxy)-1,2-dihydro-2,4-dioxoquinazolin-3(4*H*)-yl) acetic acid (4a). Yield 55%, white solid, mp 190-192 °C. ^{1}H NMR (300MHz, $CDCl_3$) δ(ppm) 4.54 (s, 2H), 7.04 (d, *J* 9 Hz, 1H, Ar-H), 7.31 (d, *J* 9 Hz, 1H, Ar-H), 7.405 (dd, *J* 3.0 and 3.0 Hz, 1H, Ar-H), 7.43 (dd, *J* 2.1 and 3.0 Hz, 1H, Ar-H), 7.59 (d, 1H, *J* 3.0 Hz, Ar-H), 7.81 (d, 1H, *J* 2 Hz, Ar-H), 11.69 (s, 1H, COOH). Anal. Calcd. for $C_{19}H_{14}ClF_3N_2O_5$: C, 49.23; H, 2.43; N, 6.75; Found: C, 49.02; H, 2.78; N, 6.45.

2-(6-(2-Chloro-4-trifluoromethyl)phenoxy)-2-(1-substituted-2,4dioxoquinazolin-3-(4*H*)-yl)-*N*-substituted acetamides (5). A mixture of 4 (1mmol) and oxalyl dichloride (2.0mmol) was stirred in CH_2Cl_2 at ice-water bath for 2h. Then the solvent was evaporated, afforded the yellow oil. The acyl chloride was added dropwise, the mixture of amide (1 mmol), and Et_3N (1.1 mmol) was stirred in CH_2Cl_2 at room temperature for 2h. The reaction mixture was extracted with CH_2Cl_2 (2×100mL), washed with a solution of $NaHCO_3$, NaCl, dried over anhydrous magnesium sulfate and the solvent evaporated. The residue was purified by column chromatography (50% EtOAc in hexanes as eluent) to give the target compound.

2-(6-(2-Chloro-4-(trifluoromethyl)phenoxy)-1,2-dihydro-2,4-dioxoquinazolin-3(4*H*)-yl)-*N*-(4-methylphenyl) acetamide (5d). Yield, 52%, white solid, mp 280-281 °C. ^{1}H NMR (300MHz, $CDCl_3$) δ(ppm) 2.27 (s, 3H), 4.69 (s, 2H), 7.14 (d, *J* 8.7 Hz, 1H, Ar-H), 7.30-7.54 (m, 3H, Ar-H), 7.56-7.64 (m, 4H, Ar-H), 7.67 (d, *J* 8.7 Hz, 1H, Ar-H), 7.84 (s, 1H, Ar-H), 10.40 (s, 1H). Anal. Calcd. for $C_{24}H_{17}ClF_3N_3O_4$: C, 57.21; H, 3.40; N, 8.34; Found: C, 57.11; H, 3.33; N, 8.31.

Biological Testing. Three plant species: Barnyard (*Echinochloa crusgalli*), crabgrass (*Digitaria sanguinalis*), and velvetleaf (*Abutilon theophrasti*) were used for the test. The seeds were allowed to germinate and grow for 14 days. Test plants were selected for uniformity, size and stage of development and then treated with the test compound, returned to the greenhouse and

watered. The plants not treated with the compound under evaluation were used as a comparison. The compound to be evaluated was dissolved in acetone and sprayed using a carrier volume equivalent to 187 liters per hectare at 1000 and 200 gha^{-1}. Two weeks after application of the test compounds, the state of the plants was observed. Each species was evaluated on a scale of 0-100 in which 0 equals no activity and 100 equals total control. The average control of the three plant species was calculated.

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References

1. Duke, S O; Lydon, J; Becerril, J M; Sherman, T D; Lehner, L P; Mastumoto, H. *Weed Science* **1991**, *39*, 465.
2. Duke, S O; Becerril, M J; Sherman, T D; Lydon, J; Matsumoto, H. *Pestic. Sci.* **1990**, *30*, 367.
3. Koch, M; Breithaupt, C; Kiefersauer, R; Freigang, J; Huber, R; Messerschmidt, A. *The EMBO Journal* **2004**, *23*, 1720.
4. Dyan, F E; Reddy, K N; Duke, S. O. In: *Peroxidizing Herbicides*; Boger, P., Wakabayashi, K. EDs; Springer, Berlin, 1999; pp141.
5. Duke, S. O.; Nandihalli, U. B.; Lee, H. J.; Duke, M. V. *ACS Symp. Ser.* **1994**, *559*, 191.
6. Wepplo, P. J.; Birk, J. H.; Lavanish, J. M.; Manfredi, M. C.; Nielsen, D. R. *ACS Symp. Ser.* **1995**, *584*, 136.
7. Ohki, A; Ohki, S; Koizumi, K; Kohno, H; Boger, P; Wakabayashi, K. *J. Pestic. Sci.* **1997**, *22*, 309.
8. Sakagami, K.; Fukami, J.; Kawaguchi, N.; Niwada, S.;Sago, R.; Igai, K. JP. Pat. 05339239, 1993: *Chem*. *Abstr*. **1994**, *120*, 292147.
9. Sumida, M.; Niwata, S.; Fukami, H.; Tanaka, T.; Wakabayashi, K.; Boger, P. *J. Agric. Food Chem.* **1995**, *43*, 1929.
10. Lee, H. j.; Duke, M. V.; Brik, J. H.; Yamamoto, M.; Duke, S. O. *J. Agric. Food Chem.* **1995**, *43*, 2722.
11. Cordon, M. E.; Karp, G. M; Birk, Jeffrey, H. Eur. Pat. Appl. 459,133, 1991: *Chem*. *Abstr*. **1992**, *117*, 48332.
12. Barton, J. E.; Cartwright, D.; McCormack, D. Eur. Pat. Appl. 448,206, 1991: *Chem*. *Abstr*. **1992**, *116*, 21047.

13. Chrystal, E. J.; Barton, J. E.; Cartwright, D.; Mathews, C. J. Eur. Pat. Appl. 442,655, 1991: *Chem*. *Abstr*. **1991**, *115*, 207984.
14. Cartwright, D; Mathews, C. J. Brit. UK. Pat. Appl. 225,3847, 1992: *Chem*. *Abstr*. **1993**, *118*, 59578.
15. Karp, G. M.; Agric. R. D. *J. Org. Chem.* **1992**, *57*, 4765.
16. Dayan, F. E.; Allen, S. N. *Pestic. Sci.* **2000**, *56*, 717.
17. Condon, M.E.; Alvarado, S. I.; Arthen, F. J.; Birk, J. H.; Brady, T. E.; Crews, A.D; Marc, P. A.; Karp, G. M.; Lavanish, J. M.; Nielsen, D.R.; Lies, T. A. In: *Synthesis and Chemistry of Agrochemicals IV*. Baker, D. R.; Fenyes, J. G.; Basarab, G. S. Eds; *ACS Symp. Ser.* **1995**, *584*, 122.
18. Wepplo, P.; Birk, J. H.; Lavanish, J. M.; Manfredi, M. Nielsen, D. R. In: *Synthesis and Chemistry of Agrochemicals IV*. Baker, D. R; Fenyes, J. G.; Basarab, G. S. EDs; *ACS Symp. Ser.* **1995**, *584*, 149.
19. Naoko, K.; Jiichi, F; Shinjiro, N.; Ryuichi, S.; Fumio, F. JP. Pat. 06,316,568, 1994: *Chem*. *Abstr*. **1995**, *122*, 160660.
20. Fukami, J.; Hashimoto,M.; Sago, R.; Ikai, K. JP. Pat. 06,227,918, 1994: *Chem*. *Abstr*. **1995**, *122*, 25875.
21. Barton, J. E.; Cartwright, D.; Mathews, C. J. Brit. UK. Pat. Appl. 2,253,848, 1992: *Chem*. *Abstr*. **1993**, *118*, 124391.
22. Hunt, D. A.; Schwindeman, J. A. Eur. Pat. Appl. 299,446, 1989: *Chem*. *Abstr*. **1989**, *110*, 231433.
23. Theissen, R. J. Eur. Pat. Appl. 34,883, 1981: *Chem*. *Abstr*. **1982**, *96*, 122433.
24. Johnson, W. O. Eur. Pat. Appl. 20,052, 1980: *Chem*. *Abstr*. **1981**, *94*, 191921.
25. Li, F.; Feng, Y. Q.; Meng, Q. Q.; Li, W. H.; Li, Z. M.; Wang, Q. R. *ARKIVOC* **2006**, *(i),* 40.