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Construction and characterization of 3,7-dichloro-*N*-(2,6-diethylphenyl)-*N*-(2-propoxyethyl)quinolone-8-carboxamide: a potential novel pesticide compound

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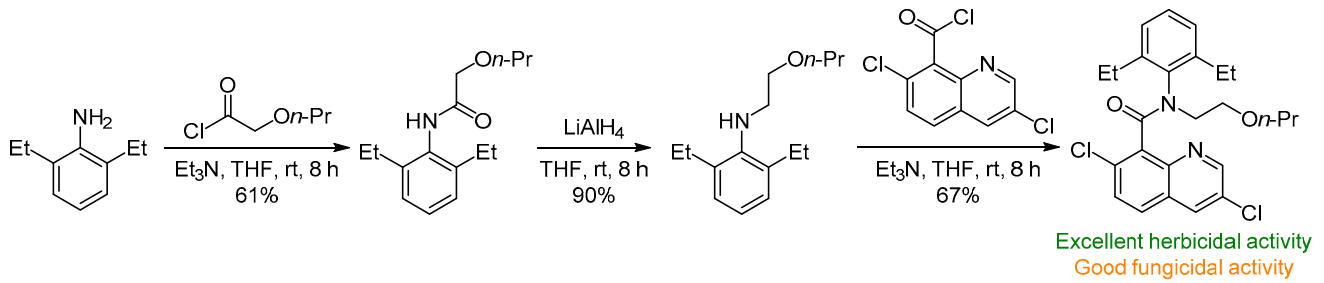


A novel compound, 3,7-dichloro-*N*-(2,6-diethylphenyl)-*N*-(2-propoxyethyl)quinoline-8-carboxamide was synthesized by splicing together a chloro-substituted quinoline moiety found in quinclorac (a selective herbicide) and a substituted amide moiety found in pretilachlor (another selective herbicide) using the active substructure splicing method. The chemical structure of this compound was characterized by ^{1}H, ^{13}C NMR, FTIR, high-resolution mass spectra and X-ray diffraction analysis. Pesticide potency (herbicidal and fungicidal activity) of this compound was evaluated. This compound displayed excellent control efficiency against *Echinochloa crus-galli* and also showed good fungicidal *in vitro* activity against *Phytophthora capsici*, *Phytophthora sojae*, and *Phytophthora infestans*.

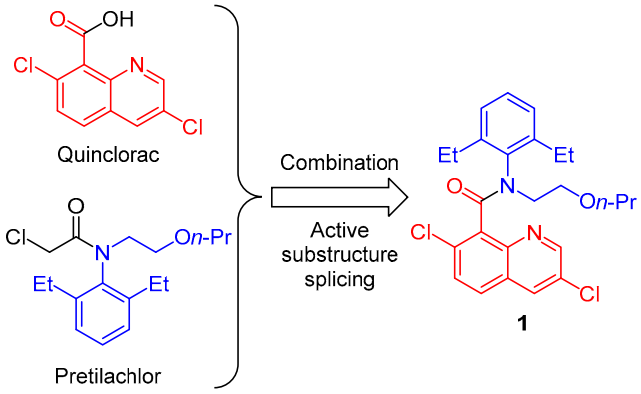
Keywords: pretilachlor, quinclorac, active substructure splicing, fungicidal activity, herbicide activity.

Infesting weeds are a major global challenge, because crop–weed competition can adversely impact production of globally important agricultural crops (e.g., rice (*Oryza sativa*), soybean (*Glycine max*), and wheat (*Triticum aestivum*)).[1–3] Currently, weeds are commonly controlled *via* herbicide application, which often presents an efficient and efficacious method to reduce unwanted crop weed populations.[4–8] However, due to the overuse of herbicidal products, weed resistance has emerged, leading to a gradual decrease in product efficacy and subsequent need to increase herbicide usage.[9–13] Therefore, it is important to identify and try new herbicides with high biological activity.

Quinclorac (3,4-dichloro-8-quinolinecarboxylic acid, CAS no. 84087-01-4) (Scheme 1) is a persistent quinoline herbicide first discovered in the 1980s by BASF.[14] Quinclorac acts a lipase inhibitor and contains a core chemical structure made up of a chloro-substituted quinoline group and a carboxyl moiety.[15] As a highly efficient and selective auxin-type herbicide, quinclorac is typically applied to control *Echinochloa crus-galli* and other common weeds (e.g., *Monochoria vaginalis*, *Digitaria sanguinalis*, *Setaria viridis*, *Sesbania exaltata*, and *Oenanthe javanica*),[16–20] although prolonged overuse of this product has led to the emergence of resistance in *Echinochloa crus-galli*.[21] Quinclorac still represents the primary herbicide product recommended for use on *Echinochloa crus-galli* around rice paddies, due to its highly efficient weed control and low phototoxicity to rice plants.[22,23]

Pretilachlor (Scheme 1) (2-chloro-*N*-(2,6-diethylphenyl)-*N*-(2-propoxyethyl)acetamide, CAS no. 51218-49-6) is a chloroacetanilide herbicide, first identified in 1970s by Ciba-Geigy A.-G.[24] The core chemical structure of this product is primarily made up of diethyl-substituted phenyl and chloroacetanilide moieties. Pretilachlor is a broad-spectrum herbicide commonly applied to control various plant pests, such as *Echinochloa crus-galli* and *Mono-*

Scheme 1



choria vaginalis.[25,26] Pretilachlor is often used as a selective pre- and post-emergence herbicide in rice crop protection, inhibiting the influx of weeds throughout plant growth.[27,28] To date, the primary mechanisms of the herbicide action of pretilachlor are still not absolutely clear. However, it was found that interferences in protein and carbohydrate synthesis were observed in rice and broad bean (*Vicia faba*) treated by pretilachlor.[29,30] Although this herbicide can decrease biomass production in treated rice and interfere with the abilities of rice plants to assimilate nutrients, it can be safely used on paddy fields if used alongside a herbicide safener (fenclorim) to reduce the phytotoxicity.[31–33]

Active substructure splicing is one of the most common methods used for pesticide design.[34–37] Hence, the compound of interest in this study, 3,7-dichloro-*N*-(2,6-diethylphenyl)-*N*-(2-propoxyethyl)quinoline-8-carboxamide (**1**), was synthesized using this technique (Scheme 1). We aimed to create a highly efficient pesticide compound by combining chemical moieties from the herbicides quinclorac and pretilachlor: a chloro-substituted quinoline group and *N*-alkylarylamine, respectively, joined by an amide bond.

The herbicidal activity of compound **1** was evaluated under greenhouse conditions. In addition, as this compound contained both a quinoline moiety and an amide group, which were also found in commercial fungicides, such as ethoxyquin and fluopicolide, and might possess fungicidal activity,[38,39] this latter activity of compound **1** was tested as well. This research provides an in depth characterization of a potentially novel herbicide, emphasizes how moieties from separate pesticide products can be used in novel pesticide designs, and also highlights how herbicide structures can be applied to develop and screen potential novel fungicide products.

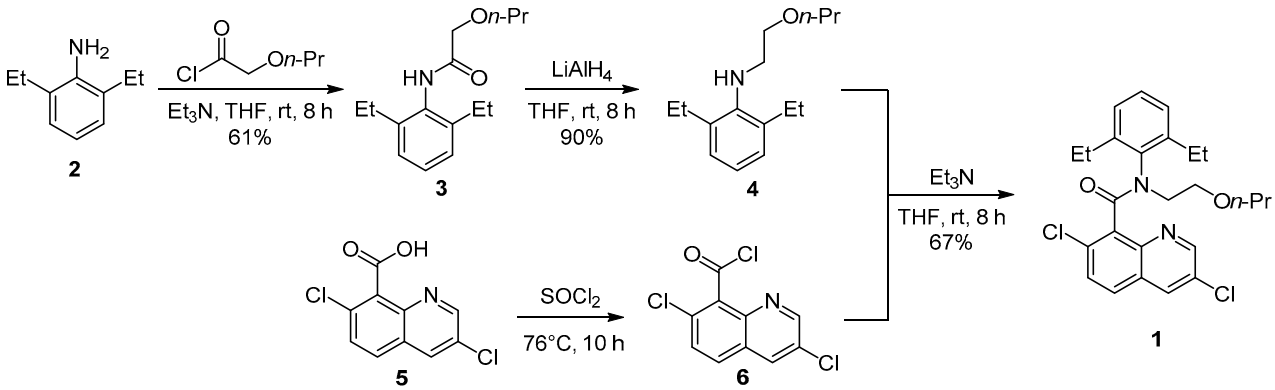
Methodology used in the synthesis of compound **1** is shown in Scheme 2. Using 2,6-diethylaniline (**2**) as the starting material, amide **3** was obtained *via* condensation with propoxyacetyl chloride in 61% yield. Then, secondary amine **4** was produced by reducing amide **3** with $LiAlH_4$ as a reduction reagent[40] in 90% yield. Acylchlorination[41] of quinclorac (**5**) then allowed us to afford 3,7-dichloro-quinoline-8-carbonyl chloride **6**. Finally, chloride **6** was amidated using imine **4** to obtain the target compound **1** in 67% yield.

The chemical structure of compound **1** was characterized using ^{1}H and ^{13}C NMR, FTIR, and high-resolution mass spectroscopy. The ^{1}H NMR spectra of compound **1** clearly showed the signals of quinoline protons appearing as four doublets in the chemical shift range of 7.63–8.87 ppm, and the protons of diethyl-substituted phenyl ring were observed as a multiplet at 7.23–7.28 ppm and a triplet at 7.33 ppm. Moreover, ^{1}H NMR signals of methyl groups were observed as triplets at 0.71, 1.34, and 1.39 ppm and those of methylene groups – as several multiplets in the range of 1.32–3.58 ppm. Meanwhile, the ^{13}C NMR spectrum, which also matched the proposed structure showed resonances of quinoline and phenyl rings at 126.9–150.6 ppm in the aromatic region, and the resonances of the alkyl group at 10.4–72.8 ppm in unsubstituted and substituted aliphatic regions. Notably, a singlet at 166.3 ppm corresponding to the carbonyl carbon atom was found in its characteristic region. Finally, the FTIR and HRMS data well matched with the expected values for the calculated brutto formula.

Compound **1** crystallized in the $P2_1/c$ space group of the monoclinical crystal system. The molecular structure is visualized in Figure 1, and selected molecular structure parameters, including bond lengths and bond angles, are listed in Table S1 of the Supplementary information file. The view of the crystal packing along the *b* crystallographic axis is shown in Figure S1 of the Supplementary information file.

The main bond lengths and bond angles of the quinoline ring and phenyl ring in the crystal structure of compound **1** are similar to those reported in the literature for compounds with similar structural motifs.[42–46] The molecule of

Scheme 2



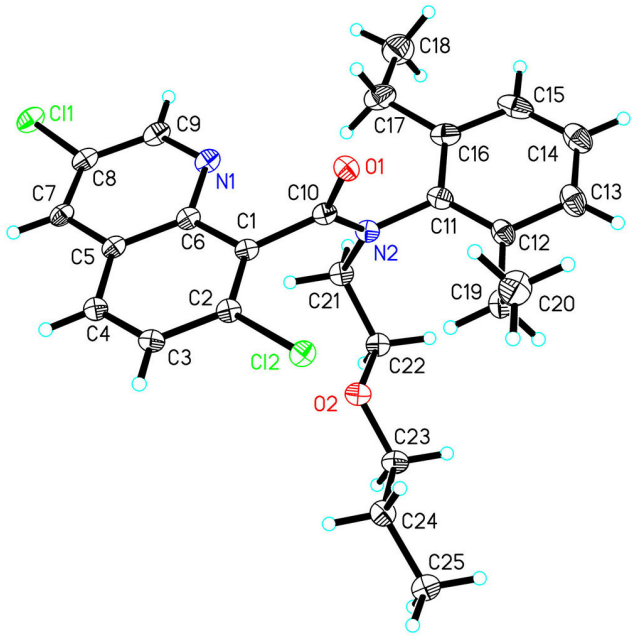


Figure 1. Molecular structure of compound **1** with atoms represented as thermal vibration ellipsoids of 50% probability.

compound **1** is comprised of four distinct moieties (a disubstituted phenyl ring, a chlorine-substituted quinoline ring, an amide moiety, and a 2-propoxyethyl moiety). The bond lengths of the amide moiety C(1)–C(10), C(10)–N(2), and N(2)–C(11) were found to have values 1.506(6), 1.346(5), and 1.455(5) Å, respectively. The valence angles of C(1)–C(10)–N(2) and C(10)–N(2)–C(11) were 119.0(3)° and 119.4(3)°. The bond length of C(10)–O(1) in the amide group was 1.241(5) Å, which is similar to what is generally reported for C=O bond, indicating that C(10)–O(1) has a fully double bond character.[36,42,47–49] The dihedral angle between the mean planes of phenyl ring and quinoline ring is 8.294(1)°, indicating the two rings are nearly coplanar in the synthesized compound.

In the whole structure, each molecule with CH_2 carbon atoms, C(19) and C(22), was found to participate in C–H···O hydrogen bonding interactions (symmetry code: *x*, *y*, –1 + *z*) (Table 1), which ultimately formed a three-dimensional network of molecules. The C···O distances between H-bond donor (D) and acceptor (A) atoms were 3.519(5) Å for C(22)–H(22)···O(1). In addition, weak intramolecular C–H···O and C–H···N hydrogen bonds also helped to stabilize the crystal structure.

The herbicidal activity of compound **1** was evaluated in an experimental greenhouse using four plant weeds: *Zinnia elegans*, *Abutilon theophrasti*, *Setaria glauca*, and *Echinochloa crus-galli* (Table 2). At 500 g a.i./hm^2, compound **1** demonstrated control efficiencies of 30.2 and 40.8% against *Z. elegans* and *A. theophrasti*, respectively. This was significantly better than herbicidal potency of quinclorac (**5**) (which demonstrated control efficiencies of 10.1 and 20.3%, respectively). At doses of 125 and 250 g a.i./hm^2, both compound **1** and quinclorac (**5**) were found to be nontoxic to *Z. elegans* and *A. theophrasti*. Furthermore, compound **1** was found to be more efficacious against *S. glauca* (100%), than quinclorac (**5**) (60%) at 500 g a.i./hm^2. Also, compound **1** demonstrated higher herbicidal activity against *E. crus-galli* (96.5%, 500 g a.i./hm^2) than quinclorac (**5**) (90.7%, 500 g a.i./hm^2), which is specifically active against *E. crus-galli*. Finally, we found that at decreased concentrations compound **1** always displays higher herbicidal activity than quinclorac (**5**) against *E. crus-galli*. The result indicated that the combination of the chloro-substituted quinoline group derived from quinclorac (**5**) and the *N*-alkylarylamine moiety derived from pretilachlor could enhance herbicide activity.

As compound **1** contains both a quinoline moiety and an amide group that might be a core structure possessing fungicidal activity, we hypothesized that this compound might also have fungicidal activity. Therefore, its fungicidal activity against four plant pathogens (*Phytophthora capsici*, *Phytophthora sojae*, *Peronophthora litchii*, and *Phytophthora infestans*) was tested *in vitro* (Table 3). At 50 mg/l concentration, compared to the fungicidal activity of cyazofamid (a commercial fungicide), compound **1** was still found to demonstrate good fungicidal activity against *P. capsici*, *P. sojae*, and *P. infestans* and moderate fungicidal activity against *P. litchii*. To further investigate the fungicidal activities of compound **1**, the EC_{50} values of compound **1** and cyazofamid toward *P. capsici*, *P. sojae*, and *P. infestans* were compared (Tables 4). Although compound **1** displayed relatively weaker fungicidal activity than cyazofamid, it exhibited potential fungicidal activities against *P. capsici*, *P. sojae*, and *P. infestans*. What is more, the fungicidal activity of compound **1** against *P. capsici* (EC_{50} 0.8062 mg/l) is much

Table 1. Interatomic distances (*d*) and bond angles (<) of hydrogen bonding interactions in the crystal structure of compound **1**

D–H···A*	*d*(D–H), Å	*d*(H···A), Å	*d*(D···A), Å	<(DHA), deg
C(22)–H(22)···O(1)	0.97	2.58	3.519(5)	162
C(19)–H(19)···O(2)	0.97	2.50	3.385(5)	152
C(19)–H(19)···N(2)	0.97	2.51	2.942(6)	187

* Symmetry transformations used to generate the equivalent atoms: *x*, *y*, –1 + *z*.

Table 2. Herbicidal activity of compound **1** toward *Zinnia elegans*, *Abutilon theophrasti*, *Setaria glauca*, and *Echinochloa crus-galli* after 15-day treatment under greenhouse conditions*

Compounds	Dose, g a.i./hm^2	Weed destruction, %			
		Z. elegans	*A. theophrasti*	*S. glauca*	*E. crus-galli*
1	125	NT**	NT	NT	45.7 ± 4.0
	250	NT	NT	45.6 ± 3.7	75.9 ± 2.6
	500	30.2 ± 6.0	40.8 ± 5.6	100	96.5 ± 1.8
Quinclorac (**5**)	125	NT	NT	NT	35.9 ± 3.6
	250	NT	NT	NT	65.5 ± 1.9
	500	10.1 ± 3.7	20.3 ± 4.8	60.8 ± 6.1	90.7 ± 2.4

* The statistical analyses were carried out *via* the SPSS 22.0 software package, and all the mean values within each column are significantly different from each other at $P < 0.05$.
** NT – herbicidal activity was not tested.

Table 3. *In vitro* fungicidal activity of compound **1** compared to that of the fungicide cyazofamid, for the plant pathogens *Phytophthora capsici*, *Phytophthora sojae*, *Peronophthora litchi*, and *Phytophthora infestans* at 50 mg/l*

Compounds	Inhibition rate, %			
	P. capsici	*P. sojae*	*P. litchii*	*P. infestans*
1	92.7 ± 1.2	87.8 ± 0.7	53.5 ± 0.5	84.0 ± 2.0
Cyazofamid	100	100	95	100

* The statistical analyses were carried out *via* the SPSS 22.0 software package, and all the mean values within each column are significantly different from each other at $P < 0.05$.

Table 4. Median effective concentrations (EC_{50} values) of compound **1** compared to cyazofamid for the plant pathogen *Phytophthora capsici*, *Phytophthora sojae*, *and Phytophthora infestans* characterized in *in vitro* bioassays

Compounds	EC_{50}, mg/l	95% confidence interval	$y = a + bx$*
		Phytophthora capsici	
1	0.8062	0.6612–0.9831	$y = 5.1061 + 1.1347x$
Cyazofamid	0.1495	0.1151–0.1941	$y = 6.1342 + 1.3741x$
		Phytophthora sojae	
1	1.6002	1.1596–2.2081	$y = 4.8128 + 0.9171x$
Cyazofamid	0.3258	0.2858–0.3716	$y = 5.6285 + 1.2906x$
		Phytophthora infestans	
1	2.5923	2.1278–3.1583	$y = 4.5151 + 1.1722x$
Cyazofamid	0.5847	0.4909–0.6964	$y = 5.3055 + 1.3106x$

* The equation to calculate EC_{50} values, where y – dependent variable; a – longitudinal intercept; b – slope; x – independent variable.

better than that against *P. sojae* (EC_{50} 1.6002 mg/l) and *P. infestans* (EC_{50} 2.5923 mg/l). These results indicated that compound **1** can potentially be used to design novel fungicides, and further study on structure–activity relationship of compound **1** is underway.

In this study, 3,7-dichloro-*N*-(2,6-diethylphenyl)-*N*-(2-propoxyethyl)quinoline-8-carboxamide was synthesized by combining a chloro-substituted quinoline group derived from quinclorac with a substituted amide moiety derived from pretilachlor using the active substructure splicing method. The chemical structure of the synthesized compound was subsequently characterized using standard spectroscopic methods and X-ray crystallography. The product displayed excellent control efficiency against the weed plant *E. crus-galli* which was better than that of quinclorac, as well as good fungicidal activity *in vitro* against three fungal species (*P. capsici*, *P. sojae*, and *P. infestans*). This research provides a foundation for the design of a novel herbicide product, using chemical moieties derived from known herbicides and highlights the potential for use of herbicidal compounds in the synthesis and screening of new fungicide products.

Experimental

The IR spectra were obtained on a PerkinElmer Spectrum 100 FTIR spectrometer in KBr pellets. ^{1}H and ^{13}C NMR spectra were obtained on a Bruker Avance AV-400-WB spectrometer (400 and 100 MHz, respectively) in $CDCl_3$, internal standard TMS (^{1}H) or solvent signal (^{13}C, δ 77.0 ppm). High-resolution ESI mass spectra were recorded on an Agilent Technologies 6230 TOF LC/MS system. The melting point was determined using a Hanon MP100 automatic melting point apparatus with an open capillary tube.

Methods for preparing 3,7-dichloro-*N*-(2,6-diethylphenyl)-*N*-(2-propoxyethyl)quinoline-8-carboxamide (**1**) are described in literature[50–52] and used here with indicated modifications. The commercially available 2,6-diethylaniline, THF, and Et_3N were used without further purification.

***N*-(2,6-Diethylphenyl)-2-propoxyacetamide (3)**. 2,6-Diethylaniline (**2**) (0.75 g, 5.00 mmol) and Et_3N (0.76 g, 7.50 mmol, 1.04 ml) were dissolved in anhydrous THF (20 ml), and then propoxyacetyl chloride (0.68 g, 5 mmol) in anhydrous THF (15 ml) was added. The reaction mixture was stirred for 8 h at room temperature until the starting material disappeared (as indicated by TLC). The solvent was evaporated under reduced pressure (20 mm Hg) at 40°C. The obtained residue was dissolved in EtOAc (30 ml), washed with 10% brine (3×60 ml). The organic layer was then separated from the aqueous layer, and dried by anhydrous $MgSO_4$. The solvent was removed under reduced pressure (20 mm Hg) at 35°C. The residue was further purified using silica gel (eluent petroleum ether – EtOAc, 5:1). Yield 0.76 g (61%), white solid. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.02 (3H, t, *J* = 7.4, $OCH_2CH_2C\underline{H}_3$); 1.23 (6H, t, *J* = 7.5, $2ArCH_2C\underline{H}_3$); 1.69–1.77 (2H, m, $OCH_2C\underline{H}_2CH_3$,); 2.64 (4H, q, *J* = 7.4, $2ArC\underline{H}_2CH_3$); 3.62 (2H, t, *J* = 6.5, $OC\underline{H}_2CH_2CH_3$); 4.16 (2H, s, OCH_2CO); 7.14 (2H, d, *J* = 7.6, H Ar); 7.26 (1H, dd, *J* = 8.4, *J* = 6.7, H Ar); 10.0 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 10.5; 14.4; 22.9; 24.9; 70.4; 73.6; 126.4; 128.0; 131.9; 141.4; 169.0 (C=O). Found, *m*/*z*: 205.1809 $[M+H]^+$. $C_{15}H_{23}NO_2$. Calculated, *m*/*z*: 205.1802.

2,6-Diethyl-*N*-(2-propoxyethyl)aniline (4).[53] *N*-(2,6-Diethylphenyl)-2-propoxyacetamide (**3**) (1.25 g, 5.00 mmol) was dissolved in anhydrous THF (20 ml) under a nitrogen atmosphere of 2 Mpa. The reaction mixture was then cooled at 0°C in an ice water bath, and 2.50 M $LiAlH_4$ solution in THF (4.55 g, 4.40 ml, 12 mmol) was added. The reaction mixture was subsequently warmed to room temperature and stirred for 8 h at room temperature until the starting material disappeared (as indicated by TLC). The mixture was quenched with H_2O (10 ml), and the solvent was evaporated under reduced pressure (20 mmHg) at 40°C. The residue was extracted with EtOAc (2×30 ml), and the extract was washed with 10% brine (3×60 ml). The organic layer was then dried over anhydrous $MgSO_4$, and the solvent was subsequently evaporated under reduced pressure (20 mmHg) at 35°C. The crude material was then purified by flash chromatography on silica gel (eluent petroleum ether – EtOAc, 6:1). Yield 1.06 g (90%), colorless liquid. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.03 (3H, t, *J* = 7.4, $OCH_2CH_2C\underline{H}_3$); 1.23 (6H, t, *J* = 7.6, $2ArCH_2C\underline{H}_3$); 1.70–1.77 (2H, m, $OCH_2C\underline{H}_2CH_3$); 2.63 (4H, q, *J* = 7.5, $2ArC\underline{H}_2CH_3$); 3.35 (2H, t, *J* = 7.4, NCH_2); 3.46 (2H, t, *J* = 6.5, $OC\underline{H}_2CH_2CH_3$); 3.64 (2H, t, *J* = 7.5, OCH_2); 7.16 (2H, d, *J* = 7.5, H Ar); 7.25 (1H, dd, *J* = 8.3, *J* = 6.8, H Ar); 7.91 (1H, s, NH).

3,7-Dichloroquinoline-8-carbonyl chloride (6). Quinclorac (**5**) (0.80 g, 3.31 mmol) was dissolved in $SOCl_2$ (50 ml) and refluxed for 10 h (76°C). The reaction mixture was distilled under reduced pressure to obtain crude 3,7-dichloroquinoline-8-carbonyl chloride (**6**) which was subsequently used in the next step without further purification.

3,7-Dichloro-*N*-(2,6-diethylphenyl)-*N*-(2-propoxyethyl)-quinoline-8-carboxamide (1). *N*-(2,6-Diethylphenyl)-2-propoxyacetamide (**4**) (0.59 g, 2.50 mmol), dissolved in anhydrous THF (15 ml), was added dropwise to a solution of 3,7-dichloroquinoline-8-carbonyl chloride (**6**) (0.61 g, 2.50 mmol) and Et_3N (0.76 g, 7.50 mmol, 1.04 ml) in THF (15 ml). The reaction mixture was stirred for 8 h at room temperature (25°C) until the reaction had completed as monitored by TLC. The solvent was then evaporated, and the residue was taken up in EtOAc (30 ml), washed with 10% aqueous HCl solution (2 × 50 ml), $NaHCO_3$ solution (2×50 ml, 1 M), and, finally, 10% brine (3×60 ml). The organic layer was dried over anhydrous $MgSO_4$. The solvent was then evaporated under reduced pressure (20 mmHg) at 40°C. The crude product was purified on silica gel (eluent petroleum ether – EtOAc, 7:1). Yield 0.77 g (67%), white solid, mp 293–294°C. IR spectrum, ν, cm^{-1}: 1786 (C=O), 1589 (C=N), 1472 (C=N), 1308 (C–N), 1165, 1138 (C–O), 1097, 1064, 923, 893 (C–H), 806, 642, 481. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.71 (3H, t, *J* = 7.4, $OCH_2CH_2C\underline{H}_3$); 1.32–1.41 (2H, m, $OCH_2C\underline{H}_2CH_3$); 1.34 (3H, t, *J* = 7.4, $ArCH_2C\underline{H}_3$); 1.39 (3H, t, *J* = 7.4, $ArCH_2C\underline{H}_3$); 2.72–2.81 (1H, m, $ArC\underline{H}_2CH_3$); 2.84–2.93 (1H, m, $ArC\underline{H}_2CH_3$); 2.97–3.09 (3H, m, NCH_2, $ArC\underline{H}_2CH_3$); 3.20–3.26 (1H, m, NCH_2); 3.28–3.36 (2H, m, $OC\underline{H}_2CH_2CH_3$); 3.41–3.48 (1H, m, OCH_2); 3.51–3.58 (1H, m, OCH_2); 7.23–7.28 (2H, m, H Ar); 7.33 (1H, t, *J* = 7.5, H Ar); 7.63 (1H, d, *J* = 8.8, H quinoline); 7.75 (1H, d, *J* = 8.8, H quinoline); 8.16 (1H, d, *J* = 2.4, H quinoline); 8.87 (1H, d, *J* = 2.4, H quinoline). ^{13}C NMR spectrum, δ, ppm: 10.4; 18.5; 18.9; 22.7; 50.3; 67.4; 72.8; 126.9; 128.0; 128.5; 128.7; 129.1; 129.4; 129.5; 132.2; 133.9; 135.4; 136.7; 136.8; 138.0; 143.8; 150.6; 166.3 (C=O). Found, *m*/*z*: 459.1610 $[M+H]^+$. $C_{25}H_{28}Cl_2N_2O_2$. Calculated, *m*/*z*: 459.1601.

X-ray structural investigation of compound 1. A colorless single crystal of compound **1** was obtained by recrystallization from a dilute EtOH solution. X-ray single crystal structure data were collected using a Rigaku SuperNova dual wavelength diffractometer, equipped with an AtlasS2 CCD area detector; MoKα radiation (λ 1.54184 Å) at 100.01(10) K. Data was processed using the SHELXL program, the crystal structure was solved by the direct method using Olex2[54] and ShelXT[55] structure solution programs and refined by the least squares method using the ShelXL refinement package.[56] The complete crystallographic information on compound **1** has been deposited at the Cambridge Crystallographic Data Center (deposit CCDC 1878381).

Herbicidal activity assay.[57] Four weed species were used in the herbicide bioassays: *Z. elegans*, *A. theophrasti*, *S. glauca*, and *E. crus-galli*. Weeds were grown in paper flowerpots (diameter 7 cm) that contained loamy sand (substrate: ~3.0% humus). The seeds of the test weeds were sown separately, according to the species. The test weeds were grown to heights of 3–15 cm (depending on individual weed species) before herbicide treatment. Active ingredients (compound **1** and quinclorac (**5**)) were suspended or emulsified in H_2O and applied using a tracked crop sprayer (Engineer Research Ltd., UK). *Z. elegans* and *A. theophrasti* were used when in the 2 leaf stage, while *S. glauca* and *E. crus-galli* were grown to 2–3 leaf stages before the treatment. Compound **1** and quinclorac (**5**) were applied at doses of 500, 250, and 125 g a.i./hm^2. Following the treatment, the weeds were naturally dried and kept at 10–25 or 20–35°C (depending on the species) in a greenhouse. The plants were gathered and their reactions to the individual treatments were evaluated 15 days after the treatment. Toxicological evaluations were based on a percentage scale, where 100% was defined as no weed emergence or the complete destruction of the above ground parts and 0% was defined as no damage or normal weed growth. Each experiment was replicated three times.

Fungicidal activity assay. The *in vitro* fungicidal activity of compound **1** was tested using the mycelium growth rate method.[58–60] Plant pathogen species used were *P. capsici*, *P. sojae*, *P. litchii*, and *P. infestans*. To prepare 10 mg/ml solution, compound **1** (10 mg) was weighed and dissolved in DMSO (1 ml). This solution was then mixed with boiling hot potato dextrose agar (PDA) (199 ml). Medium containing compound **1** (used for initial screening) in 50 mg/l concentration was poured into sterile Petri dishes (diameter 9 cm). After all the dishes were cooled down to 60–70°C, 0.5 cm diameter mycelia disks were inoculated onto the center of the Petri dishes for 3–8 days (representing the exposure period) and then incubated at 25°C. DMSO was used as the negative control. Hypha diameter was measured using the cross bracketing method. The commercial fungicide cyazofamid was used as the positive control. Each experiment was replicated for three times. The *in vitro* inhibition rate of compound **1** against fungi was calculated as $(C - T)/(C - 0.5)\times100\%$ where *C* represents the average diameter of fungal hypha on untreated PDA (in cm), and *T* represents the average diameter of fungal hypha on PDA treated with the test compound (in cm). The test concentrations used for calculating EC_{50} values were 10, 5, 2.5, 1.25, and 0.625 mg/l respectively. The EC_{50} values were calculated using log-probit analysis.

Statistical analyses. All the statistical analyses were carried out using the SPSS 22.0 software package (IBM, NY, USA). Data were represented by the standard deviations (values ± SD) and analyzed for statistical significance by means of ordinary one-way analysis of variance, and $P < 0.05$ was considered to indicate the statistically significant difference.

Supplementary information file containing ^{1}H and ^{13}C NMR and mass spectra as well as X-ray data of compound **1** is available at the journal website at http://link.springer.com/journal/10593.

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