# Synthesis and Herbicidal Activity of 2-Cyano-3-(2-chlorothiazol-5-yl)methylaminoacrylates

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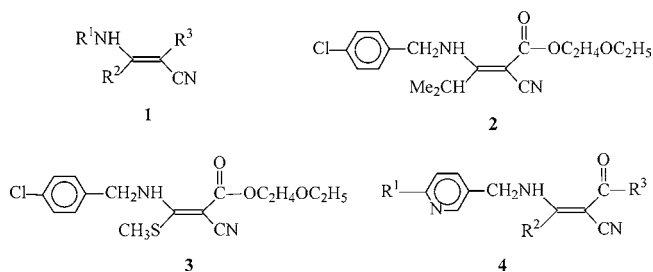
A series of 2-cyano-3-(2-chlorothiazol-5-yl)methylaminoacrylates were synthesized as herbicidal inhibitors of PSII electron transport. All of these compounds exhibited good herbicidal activities. In particular, (*Z*)-ethoxyethyl 2-cyano-3-isopropyl-3-(2-chlorothiazol-5-yl)methylaminoacrylate showed excellent herbicidal activities even at a dose of 75 g/ha. A suitable group at the 3-position of acrylate was essential for high herbicidal activity. 2-Cyanoacrylates containing a 2-chloro-5-thiazolyl group are a novel class of herbicides and display herbicidal activities comparable to existing analogues bearing chloropyridyl or chlorophenyl.

## INTRODUCTION

The herbicidal activity of cyanoacrylates has been the subject of intense interest for decades (*1−3*). A detailed study of compounds with general structure **1** revealed that cyanoacrylates are inhibitors of photosystem II (PSII) electron transport and inhibit the growth of weeds by disrupting photosynthetic electron transport at a common binding domain on the 32 kD polypeptide of the PSII reaction center. Among these cyanoacrylates, compund **2** exhibits the highest inhibitory activity of the Hill reaction yet reported (*4−6*). Bayer AG reported compound **3**, but little information was given on its herbicidal activity (*7*). It has been reported that the D1 protein of PSII is the herbicide binding site, where the benzyl group of cyanoacrylate fits into the hydrophobic domain of the site maximizing van der Waals ring stacking interactions with aromatic amino acids (Phe 211, Phe 255, Tyr 262) flanking this part of the binding domain (*8−10*). However, the complete nature and topography of this hydrophobic domain of the D1 protein are unknown, and cyanoacrylates have not commercialized as herbicides because of their high dose rates.

In our previous work, the cyanoacrylate structure **4** modified by the replacement of phenyl with pyridine heterocycles showed higher herbicidal activities than parent compounds **2** and **3** (*11*). Through the comparisons of structure and herbicidal activity, we concluded that a suitable substituent (chlorine or alkoxy) at the 2-position of pyridine ring and a well-fit group (methylthio or alkyl) at the 3-position of acrylate were essential for high herbicidal activity (*12*).

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Bioisosterism is an important concept of bioactive compound design. Substitution of a 2-chloro-5-pyridyl group by a 2-chloro-5-thiazolyl group represents a successful example of bioisosterism, as follows: Neonicotinoids are a new class of insecticides (*13*). The first successful member of this family is imidacloprid, developed by Nihon Bayer Agrochem KK in 1991 (*14*). As second and third neonicotinoids of the subclass chloronicotinyl compounds, nitenpyram from Takada Chemical Industries (*15*) and acetamiprid from Nippon Soda (*16*) have been brought to the market in 1995 and 1996, respectively. These three compounds possess 2-chloro-5-pyridyl groupa. However, thiamethoxam, possessing a 2-chloro-5-thiazolyl group, has exceptional insecticidal activity comparable to chloronicotinyl compounds and was introduced into the market by Novartis Crop Protection in 1997 (*17−18*). Takada have also developed acyclic nitroguanidine analogues with a thiazol-5-ylmethyl group (*19*). As a result, 2-chloro-5-thiazole is a bioisosteric analogue of 2-chloro-5-pyridine. Encouraged by these reports, we developed an idea that the replacement of 2-chloro-5-pyridyl with 2-chloro-5-thiazolyl in 2-cyanoacrylates could improve the herbicidal activities. Herein we are reporting the synthesis of a series of 2-cyano-3-(2-chlorothiazol-5-yl)-methylaminoacrylates and evaluation for herbicidal activity.

2-Cyano-3-(2-chlorothiazol-5-yl)methylaminoacrylates

*J. Agric. Food Chem.,* Vol. 52, No. 7, 2004  **1919**

## MATERIALS AND METHODS

**Synthetic Procedures.** Proton NMR spectra were obtained at 200 MHz using a Bruker AC-P 200 spectrometer. Chemical shift values ($\delta$) are given in ppm and were downfield from internal TMS. Infrared spectra were recorded on a Shimadzu-435 spectrometer. Elemental analyses were determined on an MT-3 elemental analyzer. Mass spectra were recorded with HP 5988A spectrometer using the EI method.

**Synthesis of 1,2,3-Trichloropropane (6).** A mixture of 3-chloro-1-propene (7.65 g, 0.1 mol) and a cat. mount of benzoyl peroxide in carbon tetrachloride (10 g) was heated to 85 °C. To the mixture, sulfuryl chloride (13.5 g, 0.1 mol) was added dropwise. Then, the mixture was stirred at 90 °C for 4 h. Carbon tetrachloride was distilled off, and the residue was distilled to give a colorless liquid (14.8 g) in 50.2% yield (bp 154−156 °C/760 mm Hg).

**Synthesis of 2,3-Dichloro-1-propene (7).** Aqueous sodium hydroxide (4.4 g, 0.11 mol, dissolved in 30 mL ethanol and 10 mL water) was added dropwise to 1,2,3-trichloropropane (14.8 g, 0.1 mol) at 100 °C. Then, the resulting mixture was refluxed for 4 h and distilled to collect the distillation cut of 72−76 °C. Water (30 mL) was added to the distillate, and the organic phase was washed with water (15 mL) and dried over anhydrous magnesium sulfate. After the solvent was distilled off, the residue was distilled, yielding 2,3-dichloro-1-propene (7.2 g) in 64.7% yield (bp 92−98 °C/760 mm Hg).

**Synthesis of 2-Chloro-2-propenyl Isothiocyanate (8).** Under a nitrogen atmosphere, a mixture of 2,3-dichloro-1-propene (11.1 g, 0.1 mol), potassium thiocyanate (9.7 g, 0.1 mol), and water (70 mL) was heated gradually to 104 °C and stirred for 10 h. Then, the resulting mixture was cooled to room temperature. The water phase was extracted three times with chloroform (10 mL). The extraction solvent was combined with the organic phase, washed two times with water (20 mL), and dried over anhydrous magnesium sulfate. Chloroform was distilled off, and the residue was heated to 120 °C and stirred for 2 h. Then, the residue was distilled under reduced pressure, yielding 2-chloro-2-propenyl isothiocyanate (7.5 g) in 56.2% yield (bp 64−67 °C/10 mm Hg). $^1$H NMR (CDCl$_3$) $\delta$: 4.21 (s, 2H, CH$_2$NCS), 5.40, 5.51 (d, 2H, =CH$_2$).

**Synthesis of 2-Chloro-5-chloromethylthiazole (9).** To a solution of 2-chloro-2-propenyl isothiocyanate (13.4 g, 0.1 mol) in chloroform (50 mL) was added dropwise sulfuryl chloride (16.2 g, 0.12 mol), while maintaining the temperature at 30 °C. Following the addition, the reaction mixture was stirred for 3 h at 36 °C. The solvent and the excess of sulfuryl chloride were removed by distillation. The residue was cooled to room temperature to give a yellow solid (15.9 g) in 94.6% yield. $^1$H NMR (CDCl$_3$) $\delta$: 4.69 (s, 2H, CH$_2$), 7.47 (s, 1H, thiazole).

**Synthesis of 2-Chloro-5-aminomethylthiazoles (10).** To a mixture of hexamethylenetetramine (16.7 g, 0.11 mol) and chloroform (100 mL) was added dropwise 2-chloro-5-chloromethylthiazole (16.8 g, 0.1 mol) at refluxed temperature, then the resulting mixture was refluxed for 3 h. The solid was collected by filtration, and the filtrate was concentrated to obtain the solid again. The solid was combined and washed with chloroform. Finally, the yellow solid (30.1 g) was obtained in 96.7% yield. To the above solid, 100 g of 36% hydrochloric acid and 100 mL of ethanol were added. The mixture was stirred under reflux for 1 h then allowed to stand for 12 h. The solid was filtered off, and the filtrate was concentrated to about half of the original volume. The solid formed was filtered off again, and the filtrate was concentrated to dryness. To the residue was added 50 mL of acetone, and insoluble material was filtered off. To the filtrate was added 50 mL of water and 6 N aqueous sodium hydroxide to pH = 13. The mixture was extracted three times with dichloromethane, and the dichloromethane layer was washed with saturated aqueous sodium chloride and dried over anhydrous potassium carbonate. The solvent was removed by distillation to give a yellow solid (14.0 g) in 94.3% yield.

**General Synthetic Procedures for Esters 11a and b.** A mixture of cyanoacetic acid (25.5 g, 23.8 mmol), alkanol (31.5 mmol), sodium bisulfate monohydrate (0.7 g, 5.1 mmol) and toluene (15 mL) was placed in a flask equipped with a Dean Stark trap carrying a reflux condenser at its upper end and then heated under reflux. The reaction was not stopped until no more water was collected in appreciable

amount in the water separator. The mixture was filtered, and the filtration was washed with 10% sodium dicarbonate and brine, dried over anhydrous sodium sulfate, and distilled under reduced pressure to afford the corresponding esters.

**General Synthetic Procedures for 12a−d.** To a mixture of 2-cyanoacetate **7** (0.025 mol), triethylamine (5.05 g, 0.05 mol), magnesium chloride (2.37 g, 0.025 mol), and anhydrous acetonitrile (25 mL) was added acid chloride (0.025 mol) under an ice-salt bath. The reaction was continued for 5 h, and the solvent was evaporated. To the residue was added 5 N aqueous hydrochloric acid solution (20 mL) and ether (50 mL). The organic layer was separated, dried over anhydrous magnesium sulfate, filtered, and distilled under reduced pressure to give a colorless liquid (used without further purification).

The gas of diazomethane (0.013 mol) synthesized from 1.32 g of α-nitroso-α-methylurea according to the reported method (*20*) was dissolved in a solution of the above liquid (1.07 g, 0.005 mol) in anhydrous ether (10 mL). The reaction mixture was stirred for 12 h. Evaporation of the solvent afforded a yellow oil (used without further purification).

**General Synthetic Procedure for 2-Cyano-3,3-dimethylthioacry-late (13).** Compound **11b** (20 mmol) was added dropwise to a mixture of potassium hydroxide powder (2.24 g, 40 mmol) and anhydrous acetonitrile (30 mL) at 5 °C. The mixture was stirred for 0.5 h, then a solution of carbon disulfide (1.50 g, 20 mmol) in anhydrous acetonitrile (5 mL) was added over about 10 min. The reaction mixture was stirred for 3 h at room temperature. After the solution was cooled to 4 °C, dimethyl sulfate (5.04 g, 40 mmol) was added. The reaction mixture was stirred at room temperature for 4 h. The solvent was evaporated under reduced pressure, then water (25 mL) and ethyl acetate (50 mL) were added to the residue. The organic layer was separated and dried with anhydrous magnesium sulfate. Ethyl acetate was evaporated to afford corresponding **13**.

**General Synthetic Procedures for Target Compounds 14a−e.** The mixture of intermediate **12** or **13** (5 mmol), 2-chloro-5-aminomethyl-thiazoles **10** (6 mmol) and ethanol (12 mL) was refluxed for 3 h then evaporated under reduced pressure to give crude product. The product was purified by vacuum column chromatography on a silica gel.

*Data for 14a.* Yield, 80.3%; mp, 67−69 °C. $^1$H NMR (CDCl$_3$) $\delta$: 1.18 (t, $^3J_{HH}$ = 7 Hz, 3H, CH$_3$), 2.71 (s, 3H, SCH$_3$), 3.54 (q, $^3J_{HH}$ = 7 Hz, 2H, OCH$_2$), 3.66 (t, $^3J_{HH}$ = 5 Hz, 2H, CH$_2$O), 4.27 (t, $^3J_{HH}$ = 5 Hz, 2H, CO$_2$CH$_2$), 4.87 (d, $^3J_{HH}$ = 6 Hz, 2H, CH$_2$N), 7.44 (s, 1H, thiazole), 10.35 (s, 1H, NH). Anal. Calcd. for C$_{13}$H$_{16}$ClN$_3$O$_3$S$_2$: C, 43.15; H, 4.46; N, 11.61. IR (KBr, cm$^{-1}$) 3158, 2204, 1654, 1566, 1417, 1396, 1261, 1231. Found: C, 42.90; H, 4.39; N, 11.66. EIMS *m/z* (%): 361(M$^+$), 131.9(100).

*Data for 14b.* Yield, 78.9%; mp, 88−89 °C. $^1$H NMR (CDCl$_3$) $\delta$: 1.19 (t, $^3J_{HH}$ = 7 Hz, 3H, CH$_3$), 2.33 (s, 3H, =CCH$_3$), 3.53 (q, $^3J_{HH}$ = 7 Hz, 2H, OCH$_2$), 3.68 (t, $^3J_{HH}$ = 5 Hz, 2H, CH$_2$O), 4.27 (t, $^3J_{HH}$ = 5 Hz, 2H, CO$_2$CH$_2$), 4.64 (d, $^3J_{HH}$ = 6 Hz, 2H, CH$_2$N), 7.43 (s, 1H, thiazole), 10.15 (s, 1H, NH). Anal. Calcd. for C$_{13}$H$_{16}$ClN$_3$O$_3$S: C, 47.34; H, 4.89; N, 12.74. Found: C, 47.06; H,5.01; N, 12.84.

*Data for 14c.* Yield, 82.4%; mp, 79−81 °C. $^1$H NMR (CDCl$_3$) $\delta$: 1.08−1.24 (m, 6H, CH$_3$, CH$_3$), 2.59 (q, $^3J_{HH}$ = 6 Hz, 2H, CH$_2$), 3.47 (q, *J* = 7 Hz, 2H, OCH$_2$), 3.59 (t, $^3J_{HH}$ = 5 Hz, 2H, CH$_2$O), 4.20 (t, $^3J_{HH}$ = 5 Hz, 2H, CO$_2$CH$_2$), 4.63 (d, $^3J_{HH}$ = 6 Hz, 2H, CH$_2$N), 7.39 (s, 1H, thiazole), 10.05 (s, 1H, NH). Anal. Calcd. for C$_{14}$H$_{18}$ClN$_3$O$_3$S: C, 48.95; H, 5.28; N, 12.22. Found: C, 48.70; H, 5.29; N, 12.40.

*Data for 14d.* Yield, 79.6%; mp, 66−67 °C. $^1$H NMR (CDCl$_3$) $\delta$: 1.11 (t, $^3J_{HH}$ = 7 Hz, 3H, CH$_3$), 1.35 (d, $^3J_{HH}$ = 6 Hz, 6H, C(CH$_3$)$_2$), 3.20 (m, 1H, CH), 3.47 (q, $^3J_{HH}$ = 7 Hz, 2H, OCH$_2$), 3.61 (t, $^3J_{HH}$ = 5 Hz, 2H, CH$_2$O), 4.19 (t, $^3J_{HH}$ = 5 Hz, 2H, CO$_2$CH$_2$), 4.62 (d, $^3J_{HH}$ = 6 Hz, 2H, CH$_2$N), 7.17 (s, 1H, thiazole), 10.35 (s, 1H, NH). Anal. Calcd. for C$_{15}$H$_{20}$ClN$_3$O$_3$S: C, 50.35; H, 5.63; N, 11.74. Found: C, 50.34; H, 5.40; N, 11.75.

*Data for 14e.* Yield, 82.3%; mp, 58−60 °C. $^1$H NMR (CDCl$_3$) $\delta$: 2.33 (s, 3H, =CCH$_3$), 3.38 (s, 3H, OCH$_3$), 3.61 (t, $^3J_{HH}$ = 5 Hz, 2H, CH$_2$O), 4.28 (t, $^3J_{HH}$ = 5 Hz, 2H, CO$_2$CH$_2$), 4.63 (d, $^3J_{HH}$ = 6 Hz, 2H, CH$_2$N), 7.43 (s, 1H, thiazole),10.15 (s, 1H, NH). Anal. Calcd. for C$_{12}$H$_{14}$ClN$_3$O$_3$S: C, 41.43; H, 4.06; N, 12.08. Found: C, 41.51; H, 4.07; N, 11.99.

**1920** *J. Agric. Food Chem.,* Vol. 52, No. 7, 2004

Wang et al.
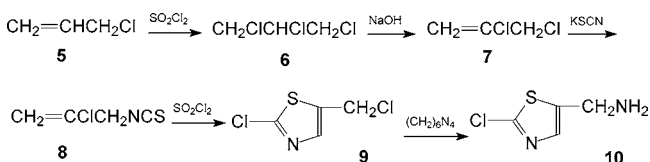
**Scheme 1**



**Scheme 2**
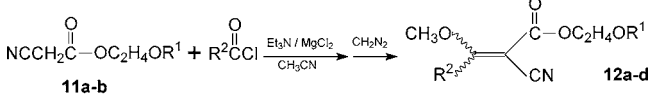


**11a-b:** $R^1$ = $CH_3$, $CH_3CH_2$;
**12a:** $R^1$ = $CH_3CH_2$, $R^2$ = $CH_3$;        **12b:** $R^1$ = $CH_3CH_2$, $R^2$ = $CH_3CH_2$;
**12c:** $R^1$ = $CH_3CH_2$, $R^2$ = $(CH_3)_2CH$;     **12d:** $R^1$ = $CH_3$, $R^2$ = $CH_3$;

**Biological Assay**. The herbicidal activities of the compounds **14a**−**e** and the reported compound **2** were evaluated using a previously reported procedure (*7, 12, 21*).

*Plant Material*. The three broadleaf species used to test the herbicidal activity of compounds were alfalfa (*Medicago sativa* L.), rape (*Brassica napus*), and amaranth pigweed (*Amaranthus retroflexus*). Seeds of *Amaranthus retroflexus* were reproduced outdoors and stored at room temperature. Seeds of alfalfa and rape were bought from the Institute of Crop, Tianjin Agriculture Science Academy.

*Culture Method*. Seeds were planted in 6-cm-diameter plastic boxes containing artificial mixed soil. Before plant emergence, the boxes were covered with plastic film to keep moist. Plants were grown in the green house. Fresh weight of the above ground tissues was measured 10 days after treatment. The inhibition percent is used to describe the control efficiency of the compounds.

*Treatment*. Dosage (activity ingredient) for each compound is 1.5 kg/ha. Purified compounds were dissolved in 100 ul *N,N*-dimethylformamide with the addition of a little Tween 20 and then were sprayed using a laboratory belt sprayer delivering at 750 L/ha-spray-volume. The mixture of same amount of water, *N,N*-dimethylformamide, and Tween 20 were sprayed as control. Triplicate each treatment. Activity numbers represent percent diplaying herbicidal damage as compared to control. Error of the experiments are 2%.

*Preemergence Treatment*. Compounds were sprayed immediately after seeds planting.

*Postemergence Treatment*. Compounds were sprayed after the expansion of the first true leaf.

## RESULTS AND DISCUSSION

**Synthesis.** To date, five synthetic routes for 2-chloro-5-chloromethylthiazole (**9**) have been published (*22−26*). We prepared this important synthetic intermediate **9** from 3-chloro-1-propene (**5**) as shown in **Scheme 1**. 3-Chloro-1-propene (**5**) was treated with sulfuryl chloride in the presence of benzoyl peroxide to obtain 1,2,3-trichloropropane (**6**). It was reacted with sodium hydroxide to give 2,3-dichloro-1-propene (**7**) Subsequent reaction with potassium thiocyanate yielded 2-chloro-2-propenyl isothiocyanate (**8**). Further reaction with sulfuryl chloride provided 2-chloro-5-chloromethylthiazole (**9**) in good yield. Compound **9** was converted into 2-chloro-5-aminomethylthiazoles (**10**) in excellent yield by its amination using hexamethylenetetramine.

Esters **11** were prepared conveniently from cyanoacetic acid and primary alcohols in the presence of a catalytic amount of sodium bisulfate monohydrate (*27*). Intermediate 2-cyano-3-methoxyacrylates **12** (*Z* and *E* mixture) were synthesized by treating ester **11** with acid chloride followed by methylation with diazomethane in good yields (**Scheme 2**) (*28*).

Intermediate 2-cyano-3,3-dimethylthioacrylate **13** was achieved by treating corresponding ester **11b** with carbon disulfide and
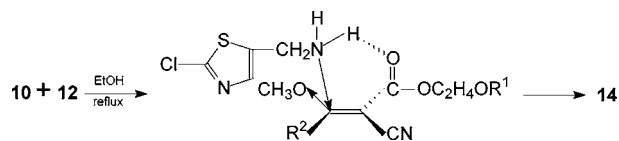
**Scheme 3**
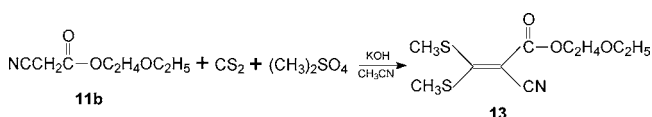


**Scheme 4**
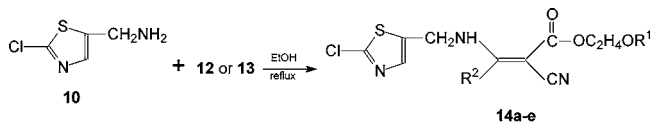


**14a:** $R^1$ = $CH_3CH_2$, $R^2$ = $CH_3S$;
**14b-d:** $R^1$ = $CH_3CH_2$, $R^2$ = $CH_3$, $CH_3CH_2$, $(CH_3)_2CH$;
**14e:** $R^1$ = $CH_3$, $R^2$ = $CH_3$;

**Scheme 5**



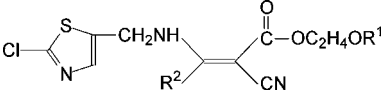two moles of dimethyl sulfate in a one-pot reaction using potassium hydroxide as alkali (**Scheme 3**).

Intermediates **12** or **13** were reacted with 2-chloro-5-aminomethylthiazole (**10**) in refluxing absolute ethanol to give the target compounds **14** in good yields (**Scheme 4**). This reaction is assumed to go through a nucleophilic addition and elimination reaction (**Scheme 5**). The amine attached the α,β-unsaturated double bond to form a transition state in which the orientation of thiazolemethylamino and ester carbonyl is cis because of the presence of an intramolecular hydrogen bonding. We confirmed configuration of existing analogue bearing chloropyridyl by X-ray and demonstrated the presence of a planar core stablized by an intramolecular hydrogen bond between the ester carbonyl oxygen and the pyridinemethylamino hydrogen atom (*11, 29*). All compounds were confirmed by $^1$H NMR, elemental, IR, and mass spectrum analyses.

**Structure−Activity Relationship.** In our previous work, the cyanoacrylate structure modified by the replacement of phenyl with substituted pyridyl showed higher herbicidal activities than the parent compound (*11*).

To further amplify the interaction of these cyanoacrylates with the lipophilic binding domain of the PSII reaction center, pyridyl was replaced by thiazole heterocycles in 2-cyanoacrylates, and all of the products **14** showed good herbicidal activities (**Table 1**). Most of the compounds **14** showed greater herbicidal activities in post-emergence treatment than in preemergence treatment as seen for substituted-pyridinemethylaminoacrylates. Compound **14b** showed excellent activities to alfalfa and amaranth pigweed. By comparing herbicidal activities of **14** and (*Z*)-ethoxyethyl 2-cyano-3-isopropyl-3- (4-chlorophenyl)methaneaminoacrylate (**2**), we found that 2-cyanoacrylates containing the 2-chloro-5-thiazolyl group provides higher herbicidal activities than compounds containing phenyl.

At the rate of 750 g/ha, compounds **14a**, **14b,** and **14d** exhibited good herbicidal activities (**Table 2**). Their activities to amaranth pigweed decreased remarkably when the dose was reduced. At the rate of 187.5 g/ha, compound **14d** still exhibited excellent herbicidal activity to rape.

(*Z*)-ethoxyethyl 2-cyano-3-methylthio-3-(2-chloro-5-pyridyl)-methaneaminoacrylate (**4a**) was prepared for comparison of herbicidal activity with **14d**. This comparison (**Table 3**) clearly showed consistently better activity, with compound **14d** having a higher level of herbicidal activity against rape than compound

2-Cyano-3-(2-chlorothiazol-5-yl)methylaminoacrylates

*J. Agric. Food Chem.,* Vol. 52, No. 7, 2004  **1921**

**Table 1.** Herbicidal Activities of Products **14a**–e and **2** (1.5 kg/ha)[a]



| | R[1] | R[2] | postemergence treatment | | | preemergence treatment | | |
|---|---|---|---|---|---|---|---|---|
| | | | alfalfa | amaranth pigweed | rape | alfalfa | amaranth pigweed | rape |
| **14a** | CH₃CH₂ | CH₃S | 49 | 78 | 100 | 28 | 76 | 40 |
| **14b** | CH₃CH₂ | CH₃ | 94 | 100 | 95 | 47 | 87 | 93 |
| **14c** | CH₃CH₂ | C₂H₅ | 70 | 83 | 100 | 46 | 70 | 91 |
| **14d** | CH₃CH₂ | CH(CH₃)₂ | 19 | 96 | 100 | 16 | 54 | 96 |
| **14e** | CH₃ | CH₃ | 26 | 81 | 100 | 0 | 45 | 78 |
| **2** | | | 28 | 94 | 96 | 0 | 52 | 0 |

[a] Triplicate each treatment. Activity numbers represent percent diplaying herbicidal damage as compared to control. 0 mean no activity. Error of these numbers is 2%.

**Table 2.** Herbicidal Activities of Products **14a**–d[a]

| compd. | rate g/ha | postemergence treatment | |
|---|---|---|---|
| | | rape | amaranth pigweed |
| **14a** | 187.5 | 48 | 41 |
| | 375 | 57 | 48 |
| | 750 | 100 | 91 |
| **14b** | 187.5 | 39 | 73 |
| | 375 | 59 | 78 |
| | 750 | 96 | 98 |
| **14c** | 187.5 | 29 | 42 |
| | 375 | 60 | 50 |
| | 750 | 69 | 57 |
| **14d** | 187.5 | 100 | 67 |
| | 375 | 100 | 81 |
| | 750 | 100 | 100 |

[a] Triplicate each treatment. Activity numbers represent percent diplaying herbicidal damage as compared to control. Error of these numbers is 2%.

**Table 3.** Herbicidal Activities of Products **14d** and **4a** against Rape (Post-emergence treatment)[a]

| rate (g/ha) | 4a | 14d |
|---|---|---|
| 18.75 | 11 | 15 |
| 37.5 | 45 | 52 |
| 75.0 | 77 | 98 |
| 150.0 | 95 | 100 |
| 300.0 | 100 | 100 |

[a] Triplicate each treatment. Activity numbers represent percent diplaying herbicidal damage as compared to control. Error of these numbers is 2%.

**4a**. At the rate of 75 g/ha, compound **14d** still showed excellent herbicidal activity, whereas herbicidal activity of compound **4a** began to reduce significantly.



**4a**
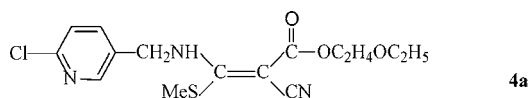
In conclusion, we have demonstrated that 2-cyanoacrylates containing a 2-chloro-5-thiazole ring presented excellent herbicidal activity, and their structure—activity relationships were studied. All of these compounds exhibited good herbicidal activities. In particular, (*Z*)-ethoxyethyl 2-cyano-3-isopropyl-3-(2-chlorothiazol-5-yl)methylaminoacrylate showed excellent herbicidal activities even at a dose of 75 g/ha. It was found that a suitable group at the 3-position of acrylate was essential for high herbicidal activity. 2-Cyanoacrylates containing 2-chloro-5-thiazolyl groups are a novel class of herbicides and display herbicidal activities comparable to existing analogues bearing chloropyridyl or chlorophenyl group.

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**1922** *J. Agric. Food Chem.,* Vol. 52, No. 7, 2004

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