Synthesis and SAR of Methoxyiminoacetate and Methoxyiminoacetamide Derivatives as Strobilurin Analogues

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Methoxyiminoacetate and methoxyiminoacetamide derivatives possessing 2,2-dichlorovinyl side chains, have been synthesized and their biological activities against six representative plant fungal pathogens have been evaluated. Five substances in this series (**3a**, **4a**, **3b**, **3d**, and **4d**) were found to exhibit potent fungicidal activities compared to those of the commercially available fungicides, azoxystrobin and fenarimol.

Key Words: Strobilurin, Fungicide, Methoxyiminoacetate, Methoxyiminoacetamide

Introduction

The strobilurins, first isolated by Anke and co-workers[1] in 1977 from fermentations of *Strobilurus tenacellus*, are one of the most important classes of agricultural fungicides. Strobilurin A-C and oudemansin A-B, possess a wide range of fungicidal activities as a consequence of their ability to inhibit electron transfer between mitochondrial cytochrome *b* and cytochrome c_1 through binding at the so-called Q_o site of cytochrome *b*.[2] Since their discovery, many strobilurin fungicides have been developed for the treatment of fungal pathogens and commercialized (Figure 1). However, a significant increase in strobilurin-resistant plant pathogens has occurred.[3]

A large effort focused on structurally modified strobilurins has been undertaken recently to overcome this problem. In this regard, strobilurin analogues that possess methoxyiminoacetate and methoxyiminoacetamide toxophores have attracted great attention[4] owing to their powerful fungicidal activities against resistant pathogens. In continuing efforts targeted at the development of new fungicides with low toxicities and broad ranges of fungicidal activity, we designed, synthesized and evaluated several novel strobilurin analogues that contain 2,2-dichlorovinyl side chain (Figure 2). The results of this effort are described below.

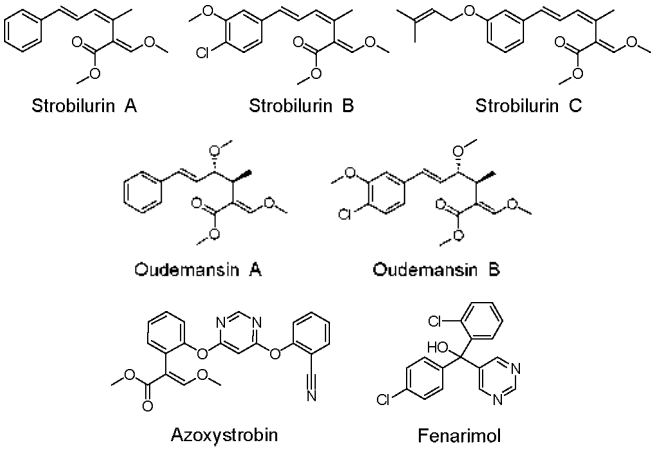


Figure 1. The structures of azoxystrobin, fenarimol, and two members of the strobilurin natural product family.

Chemistry

The strategy employed for the synthesis of methoxyiminoacetate analogues **3** involves nucleophilic aromatic substitution reaction of the corresponding benzyl bromide **1** with 2,2-dichlorovinyl derivatives **2** in the presence of K_2CO_3. This is followed by amidation of methoxyiminoacetate **3** with methylamine to provide the corresponding methoxyiminoacetamide **4** (Scheme 1).

Following this approach, phenol derivatives **2** (**2a** ~ **2h**), possessing 2,2-dicholorovinyl side chains, were synthesized by using a literature procedure (Scheme 2).[5] The routes begin with reductive addition of carbon tetrachloride to hydroxybenzaldehyde **5** in the presence of lead(II) bromide and aluminum that generates the trichloromethyl carbinols **6**, which are transformed to **2** by treatment with lead(II) bromide in aqueous hydrochloric acid .

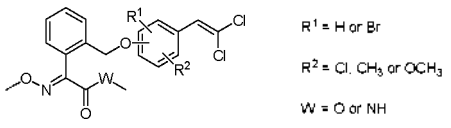
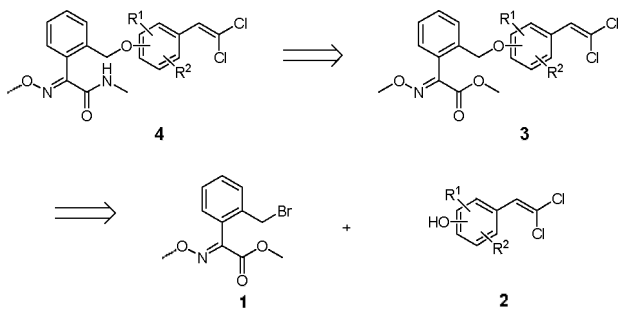
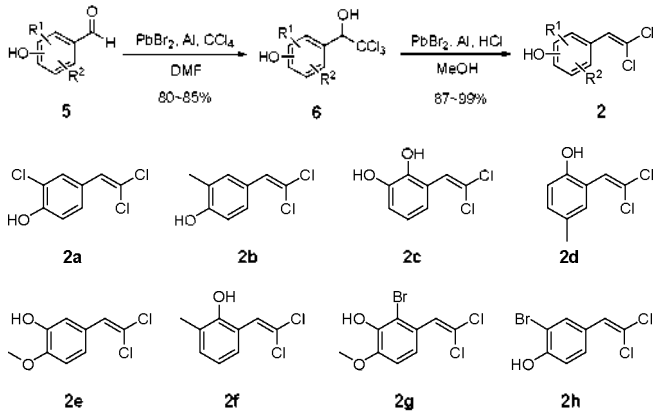


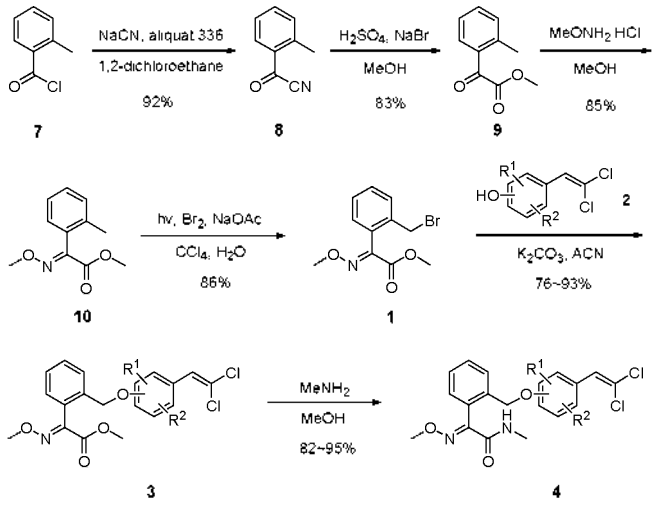
Figure 2. The structures of azoxystrobin, fenarimol, and two members of the strobilurin natural product family.



Scheme 1. Retrosynthetic approach for preparation of **3** and **4**.



Scheme 2. Synthesis of the 2,2-dichlorostyrene derivatives **2**.



Scheme 3. Preparation of methoxyiminoacetate analogues **3** and **4**.

The methoxyiminoacetate analogues **3** were prepared by employing a well-known literature procedure.[6] In these sequences, commercially available *o*-toluoyl chloride **7** is converted to bromo-methoxyiminoacetate **1** *via* a four-step route on a multigram scale without the need for chromatographic separations (Scheme 3). Cyanation of **7** with sodium cyanide and aliquat 336 in 1,2-dichloroethane quantitatively yields benzoyl cyanide **8**, which is converted to keto ester **9** by treatment with a methanolic solution of sodium bromide and sulfuric acid. (*E*)-Methyl 2-methoxyimino-2-*o*-tolylacetate **10**, formed in an *E*/*Z* ratio of 86:14 by reaction of **9** with *O*-methylhydroxylamine hydrochloride, undergoes bromination to yield bromo-methoxyiminoacetate **1** in good yield. *O*-Alkylation reactions of bromo-methoxyiminoacetate **1** with the dichlorostyrenes **2** generate the coupling products **3** in high yield. Finally, amidation of **3** is achieved by efficient reactions with methylamine at room temperature to provide amides **4**.

Biological Results and Discussion

The methoxyiminoacetate analogues **3** and **4**, prepared in this manner, were evaluated for their fungicidal potency. For this purpose, 50 mL solutions of these substances in 10% aqueous acetone are applied to foliar of versatile host. The, wetting agent Tween-20 is added to the solution to give a concentration of 2,250 ppm of the controls or the methoxyiminoacetate analogues. After foliar application, the plants are allowed to stand for 24 h at room temperature, to enable evaporation of the solvent and water, and then incubated with six plant pathogenic fungi, including *Pyricularia oryzae* (RCB), *Rhizoctonia solani* (RSB), *Botrytis cinerea* (CGM), *Phytophthora infestants* (TLB), *Puccinia recondita* (WLR) and *Erysiphe graminis* (BPM). In order to judge the effectiveness of the synthesized compounds two commercial fungicides, azoxystrobin (Syngenta) and fenarimol (DowElanco), are used as positive controls. The preventive effects of the substances relative to the controls are expressed as [1-(Diseased rate in the treatment) / (Diseased rate in the control)] × 100, and the disease rate in plants treated with the control agents and the methoxyiminoacetate analogues are calculated by using the 'Evaluation method'.[7] The methoxyiminoacetate analogues that show 100% preventive effectiveness at 250 ppm are subjected to additional screenings at concentrations of 50, 10 and 2 ppm. The results of this biological screening against six plant pathogenic fungi are shown in Table 1.

Most of the methoxyiminoacetate analogues evaluated in this screen have either similar or greater fungicidal activities at 50, 10, and 2 ppm as compared to the control fenarimol. Select members of this family, including **3a**, **4a**, **3b**, **3d** and **4d** exhibit higher fungicidal activities than azoxystrobin against *Pyricularia oryzae*, *Rhizoctonia solani* and *Phytophthora infestants*, and all but **4e** and **4g** have similar activities as does the control azoxystrobin against *Puccinia recondite* and *Erysiphe graminis*. Finally, all of the methoxyiminoacetate analogues display no fungicidal activity against *Botrytis cinerea* (CGM) even at the highest concentrations employed. The observations made in this biological screen, demonstrate that methoxyiminoacetate derivatives that contain 2-chloro-4-(2,2-dichlorovinyl)phenoxy-(**3a**, **4a**) or 4-methyl-(**3d**, **4d**) substituents possess excellent fungicidal activities. However, methoxy- and bromo- derivatives (**3e**, **4e**, **3g**, **4g**, **3h** and **4h**) have slightly lower fungicidal activities.

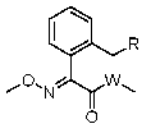
Conclusion

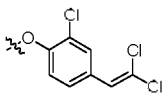
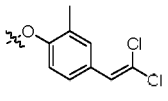
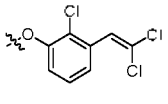
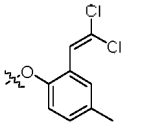
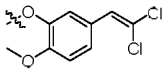
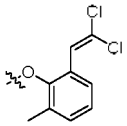
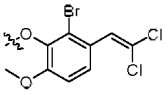
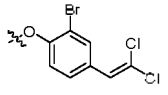
In summary, this effort has led to the synthesis and fungicidal SAR evaluation of 2,2-dichlorovinyl substituted methoxyiminoacetates and methoxyiminoacetamides. The results of this investigation demonstrate that, in comparisons with the control fungicides azoxystrobin and fenarimol, **3a**, **4a**, **3b**, **3d**, and **4d** have good preventive activity against five pathogens at concentrations as low as 2 ppm. Further studies, with structurally modified members of the methoxyiminoacetates and methoxyiminoacetamides families, are currently underway.

Experimental Section

All commercial reagents and solvents were used without further purification unless otherwise specified. Solvents and reagents were purchased from Aldrich (USA) and Merck Co. (Germany). Thin layer chromatography (TLC) was performed

Table 1. Fungicidal activity of methoxyiminoacetate analogues **3** and **4**.



compound	R	W	Rate (ppm)	RCB*	RSB	TLB	WLR	BPM
3a		O	50	100	100	100	100	100
			10	100	100	100	100	100
			2	100	100	100	100	100
4a		NH	50	100	100	100	100	100
			10	100	100	100	100	100
			2	100	100	100	100	100
3b		O	50	100	100	100	100	100
			10	100	100	100	100	100
			2	100	100	100	100	100
4b		NH	50	100	100	70	100	100
			10	100	100	-	100	100
			2	100	100	-	100	100
3c		O	50	100	100	100	100	100
			10	99	100	100	100	100
			2	90	90	100	100	100
4c		NH	50	100	100	100	100	100
			10	100	100	100	100	100
			2	100	90	95	100	100
3d		O	50	100	100	100	100	100
			10	100	100	98	100	100
			2	100	100	92	100	100
4d		NH	50	100	100	100	100	100
			10	100	100	100	100	100
			2	95	98	96	100	100
3e		O	50	100	100	100	100	100
			10	99	100	95	100	100
			2	80	95	85	100	100
4e		NH	50	100	100	100	100	100
			10	100	98	99	100	100
			2	90	95	70	100	99
3f		O	50	100	100	100	100	100
			10	100	98	99	100	100
			2	93	95	97	100	100
4f		NH	50	100	100	100	100	100
			10	98	98	99	100	100
			2	85	95	90	100	100
3g		O	50	100	100	100	100	100
			10	100	98	97	100	100
			2	90	90	90	100	100
4g		NH	50	100	100	100	100	100
			10	100	100	100	100	100
			2	70	95	95	100	99
3h		O	50	100	100	100	100	100
			10	97	98	99	100	100
			2	70	85	90	100	100
4h		NH	50	100	100	100	100	100
			10	90	98	95	100	100
			2	30	90	93	100	100
	Azoxystrobin		50	100	100	100	100	100
			10	100	100	98	100	100
			2	90	98	90	100	100
	Fenarimol		50	20	100	95	100	100
			10	0	85	80	100	100
			2	-	40	75	80	100

*RCB(Rice Blast. *Pyricularia oryzae*), RSB (Rice Sheath Blight. *Rhizoctonia solani*), TLB (Tomato Late Blight. *Phytophthora infestants*). WLR (Wheat Leaf Rust, *Puccinia recondita*), BPM (Barley Powdery Mildew, *Erysiphe graminis*). *All compounds showed no fungicidal acitivity against *Botrytis cinerea* (CGM, Cucumber Gray Mold).

on Merck 60 F-254 silica plates and visualized by UV. Flash column chromatography was performed on silica gel (Merck, 230-400 mesh ASTM). ^{1}H NMR spectra were obtained using a Varian Gemini 200 MHz NMR Spectrometer. GC-MS data were obtained using a Shimazu QP 1000 GC/MS and on a JEOL JMS-DX-305 high resolution mass spectrometer.

2-Oxo-2-*o*-tolylacetonitrile (8). To a mixture of sodium cyanide (5.4 g, 0.11 mol) in 1,2-dichloroethane (100 mL) and aliquat 336 (0.46 mL, 1 mmol) in water (20 mL) was added *o*-toluoyl chloride **7** (13.8 mL, 0.1 mol) dropwise at room temperature. The mixture was stirred for 1.5 h, and extracted with 1,2-dichloroethane. The combined organic layers were dried over magnesium sulfate and concentrated to give **8**. Yield 92%, dark red liquid. ^{1}H-NMR ($CDCl_3$, TMS) δ 2.65 (s, 3H), 7.36 (d, J = 7.62 Hz, 1H), 7.48 (dd, J = 15.9, 8.0 Hz, 1H), 7.62 (dd, J = 15.1, 7.5 Hz, 1H), 8.25 (d, J = 7.8 Hz, 1H); MS m/z 145.0 (M^-).

Methyl 2-Oxo-2-*o*-tolylacetate (9). To a mixture of 2-oxo-2-*o*-tolylacetonitrile **8** (15 mL, 0.1 mol) and sodium bromide (0.52 g, 5 mmol) was slowly added 85% sulfuric acid (12 mL, 0.19 mol) at room temperature, while maintaining the inner temperature at 32-35 °C (after stirring for 30-40 min, the inner temperature increases to 70 °C). The reaction mixture was cooled to 30-40 °C, and diluted with methanol (12 mL). Following stirring at reflux for 2 h, the mixture was cooled to room temperature, and extracted with 1,2-dichloroethane. The combined organic layers were dried over magnesium sulfate and concentrated to give **9**. Yield 83%, light green liquid. ^{1}H-NMR ($CDCl_3$, TMS) δ 2.61 (s, 3H), 3.96 (s, 3H), 7.26-7.35 (m, 2H), 7.50 (dd, J = 15, 7.6 Hz, 1H), 7.68 (d, J = 7.4 Hz, 1H); MS m/z 178.1 (M^-).

(*E*)-Methyl 2-Methoxyimino-2-*o*-tolylacetate (10). A solution of methyl 2-oxo-2-*o*-tolylacetate **9** (18 mL, 0.1 mol) in methanol containing *O*-methylhydroxylamine hydrochloride (9.1 g, 0.11 mol) was stirred at reflux for 15 h, cooled to room temperature, and extracted with ethyl acetate. The combined organic layers were dried over magnesium sulfate and concentrated to give *E* isomer of **10** as the major product (E/Z ratio = 86:14). To remove (*Z*) isomer, hexane was added and the resulting mixture was stirred for 1 h and filtered to give a precipitate that contained pure (*E*)-methyl 2-methoxyimino-2-*o*-tolylacetate (**10**). Yield 85%, white solid, mp 66-68 °C. ^{1}H-NMR ($CDCl_3$, TMS) δ : 2.19 (s, 3H), 3.87 (s, 3H), 4.05 (s, 3H), 7.10 (d, J = 7.4 Hz, 1H), 7.22-7.32 (m, 3H); MS m/z 207.1 (M^-).

(*E*)-Methyl 2-(2-(Bromomethyl)phenyl)-2-methoxyiminoacetate (1). To a stirred mixture of (*E*)-methyl 2-methoxyimino-2-*o*-tolylacetate (**10**) (62.2 g, 0.3 mol) in carbon tetrachloride (200 mL) was added bromine (50 g, 0.311 mol) and sodium acetate (24.6 g, 0.3 mol) in water. The solution was then irradiated by a 75 W fluorescent lamp for 5 h. The reaction mixture was extracted with carbon tetrachloride and combined organic layers were dried over magnesium sulfate and concentrated, giving a residue that was washed with hexane to give (*E*)-methyl 2-(2-(bromomethyl)phenyl)-2methoxyiminoacetate (**1**) as a green solid. Yield 86%, mp 45 - 48 °C. ^{1}H- NMR ($CDCl_3$, MS) δ 3.89 (s, 3H), 4.07 (s, 3H), 4.34 (s, 2H), 7.15 (d, J = 7.2 Hz, 1H), 7.34-7.52 (m, 3H); MS m/z 285.0 (M^+).

General Procedure for the Synthesis of 4-(2,2,2-Trichloro-1-hydroxyethyl)phenol (6). Carbon tetrachloride is added dropwise to a cooled (0 °C) suspension of 4-hydroxybenzaldehyde, lead bromide(II), and finely cut Al foil in DMF. The mixture was then stirred for 18 h and extracted with ethyl acetate. The combined extracts were washed with aqueous sodium bicarbonate and brine, dried over magnesium sulfate, and concentrated in vacuo to give a residue was subjected to column chromatography to give 4-(2,2,2-trichloro-1-hydroxyethyl)phenol (**6**). Yield 80%, dark brown liquid. ^{1}H-NMR ($CDCl_3$, TMS) δ 2.18 (s, 1H), 5.14 (s, 1H), 7.02 (d, J = 8.6 Hz, 1H), 7.42 (d, J = 8.2 Hz, 1H), 7.62 (s, 1H); MS m/z 273.9 (M^-).

Synthesis of 2-Chloro-4-(2,2-dichlorovinyl)phenol (2a). A mixture of trichloromethyl carbinol **6**, lead bromide(II), and finely cut Al foil, and aqueous 36% hydrochloric acid in methanol was heated at 50-60 °C for 6 h, cooled to room temperature, and concentrated in vacuo to remove methanol. The resulting solution was poured into ice-cold water and extracted with hexane-ether (1:1). The combined organic extracts were washed with sodium bicarbonate and brine, dried over magnesium sulfate and concentrated to give a residue which was subjected to column chromatography to yield 2-chloro-4-(2,2-dichlorovinyl)phenol (**2a**). Yield 84%, brown solid, mp 88-92 °C, ^{1}H-NMR ($CDCl_3$, TMS) δ 5.65 (s, 1H), 6.73 (s, 1H), 7.01 (d, J = 8.6 Hz, 1H), 7.33 (d, J = 8.6 Hz, 1H), 7.59 (s, 1H); MS m/z 221.9 (M^-).

4-(2,2-Dichlorovinyl)-2-methylphenol (2b). Yield 83%, light brown solid, mp 113-115 °C, ^{1}H-NMR($CDCl_3$, TMS) δ 2.31 (s, 3H) 5.49 (s, 1H), 6.72 (s, 1H), 7.18 (d, J = 8.4 Hz, 1H), 7.24 (d, J = 8.6 Hz, 1H), 7.27 (s, 1H); MS m/z 202.0 (M^-).

2-Chloro-3-(2,2-dichlorovinyl)phenol (2c). Yield 78%, gray solid, mp 98-102 °C, ^{1}H-NMR ($CDCl_3$, TMS) δ 5.26 (s, 1H), 6.63 (s, 1H), 7.01 (d, J = 8.6 Hz, 1H), 7.43 (d, J = 8.6 Hz, 1H), 7.59(s, 1H); MS m/z 221.9 (M^+).

2-(2,2-Dichlorovinyl)-4-methylphenol (2d). Yield 90%, yellow solid, mp 118-127 °C, ^{1}H-NMR($CDCl_3$, TMS) δ 2.34 (s, 3H) 5.48 (s, 1H), 6.75 (s, 1H), 7.32 (d, J = 8.6 Hz, 1H), 7.38 (d, J = 8.6 Hz, 1H), 7.42 (s, 1H); MS m/z 202.1 (M^-).

5-(2,2-Dichlorovinyl)-2-methoxyphenol (2e). Yield 88%, white solid, mp 77-86 °C, ^{1}H-NMR ($CDCl_3$, TMS) δ 3.62(s, 3H), 5.65 (s, 1H), 6.74 (s, 1H), 7.11 (d, J = 8.6 Hz, 1H), 7.31 (d, J = 8.6 Hz, 1H), 7.50 (s, 1H); MS m/z 218.0 (M^-).

2-(2,2-Dichlorovinyl)-6-methylphenol (2f). Yield 94%, dark brown solid, mp 109-110 °C. ^{1}H-NMR ($CDCl_3$, TMS) δ 2.27 (s, 3H), 5.63 (s, 1H), 6.52 (s, 1H), 7.28 (d, J = 8.6 Hz, 1H), 7.48 (d, J = 8.6 Hz, 1H), 7.51 (s, 1H); MS m/z 202.0 (M^-).

2-Bromo-3-(2,2-dichlorovinyl)-6-methoxyphenol (2g). Yield 74%, light yellow solid, mp 67-76 °C, ^{1}H-NMR ($CDCl_3$, TMS) δ 3.54 (s, 3H), 5.35 (s, 1H), 6.34 (s, 1H), 7.21 (d, J = 8.4 Hz, 1H), 7.44 (d, J = 8.6 Hz, 1H), 7.54 (s, 1H); MS m/z 296.0 (M^-).

2-Bromo-4-(2,2-dichlorovinyl)phenol (2h). Yield 77%, brown solid, mp 52-55 °C, ^{1}H-NMR ($CDCl_3$, TMS) δ 3.63 (s, 3H), 5.23 (s, 1H), 6.73 (s, 1H), 7.31 (d, J = 8.6 Hz, 1H), 7.39 (d, J = 8.6 Hz, 1H), 7.69 (s, 1H); MS m/z 265.9 (M^+).

(*E*)-Methyl 2-(2-((2-Chloro-4-(2,2-dichlorovinyl)phenoxy)methyl)phenyl)-2-methoxyiminoacetate (3a). A solution of

(*E*)-methyl 2-(2-(bromomethyl)phenyl)-2-methoxyiminoacetate (**1**) in anhydrous acetonitrile containing 4-(2,2-dichlorovinyl)phenol was stirred at reflux for 12 h, cooled to room temperature, was and extracted with ethyl acetate. The extracts were dried over magnesium sulfate and concentrated in vacuo to give a residue which was subjected to column chromatography to yield **3a** in 88% yield as a white solid, mp 97-98 °C. ^{1}H-NMR ($CDCl_3$, TMS) δ 3.86 (s, 3H), 4.03 (s, 3H), 5.04 (s, 2H), 6.71 (s, 1H), 6.85 (d, J = 8.6 Hz, 1H), 7.19-7.61 (m, 6H); MS m/z 427.0 (M^-).

(*E*)-2-(2-((2-Chloro-4-(2,2-dichlorovinyl)phenoxy)methyl) phenyl)-2-methoxyimino-*N*-methylacetamide (4a). A solution of **1** in methanol containing 40% aqueous methyl amine was stirred for 18 h at room temperature and concentrated in vacuo. The residue was dissolved in dichloromethane, dried over magnesium sulfate, and concentrated. Column chromatography (ethyl acetate-hexane as an eluent) of the residue gave **4a**. Yield 94%, white solid, mp 118-120 °C. ^{1}H-NMR ($CDCl_3$, TMS) δ 2.89 (d, J = 5.0 Hz, 3H), 3.93 (s, 3H), 5.07 (s, 2H), 6.70 (s, 1H), 6.76 (s, 1H), 6.78-7.61 (m, 7H); MS m/z 426.0 (M^-).

(*E*)-Methyl 2-(2-((4-(2,2-Dichlorovinyl)-2-methylphenoxy) methyl)phenyl)-2-methoxyiminoacetate (3b). Yield 91%, white solid, mp 67-68 °C. ^{1}H-NMR ($CDCl_3$, TMS) δ 2.24 (s, 3H), 3.82 (s, 3H), 4.02 (s, 3H), 4.98 (s, 2H), 6.74 (s, 1H), 6.77-7.56 (m, 7H); MS m/z 407.1 (M^-).

(*E*)-2-(2-((4-(2,2-Dichlorovinyl)-2-methylphenoxy)methyl) phenyl)-2-methoxyimino-*N*-methylacetamide (4b). Yield 86%, white solid, mp 83-84 °C. ^{1}H-NMR ($CDCl_3$, TMS) δ 2.23 (s, 3H), 2.88 (d, J = 5.0 Hz, 3H), 3.94 (s, 3H), 4.98 (s, 2H), 6.73 (s, 1H), 6.71-6.79 (m, 2H), 7.20-7.54 (m, 6H); MS m/z 406.0 (M^-).

(*E*)-Methyl 2-(2-((2-Chloro-3-(2,2-dichlorovinyl)phenoxy) methyl)phenyl)-2-methoxyiminoacetate (3c). Yield 87%, white solid, mp 102-107 °C, ^{1}H-NMR ($CDCl_3$, TMS) δ 3.85 (s, 3H), 4.03 (s, 3H), 5.02 (s, 2H), 6.83(d, J = 8.2 Hz, 1H), 7.05 (s, 1H), 7.13-7.61 (m, 6H); MS m/z 427.0 (M^-).

(*E*)-2-(2-((2-Chloro-3-(2,2-dichlorovinyl)phenoxy)methyl) phenyl)-2-methoxyimino-*N*-methylacetamide (4c). Yield 88%, light yellow solid, mp 127-130 °C, ^{1}H-NMR ($CDCl_3$, TMS) δ 2.88 (d, J = 5.0 Hz, 3H), 3.96 (s, 3H), 5.06 (s, 2H), 6.74 (s, 1H), 6.84-6.88 (m, 1H), 7.05 (s, 1H), 7.13-7.45 (m, 6H); MS m/z 426.0 (M^+).

(*E*)-Methyl 2-(2-((2-(2,2-Dichlorovinyl)-4-methylphenoxy) methyl)phenyl)-2-methoxyiminoacetate (3d). Yield 93%, light pink solid, mp 113-115 °C. ^{1}H-NMR ($CDCl_3$, TMS) δ 2.28 (s, 3H), 3.89 (s, 3H), 4.03 (s, 3H), 5.01 (s, 2H), 6.70 (s, 1H), 6.84-7.61 (m, 7H); MS m/z 407.1 (M^+).

(*E*)-2-(2-((2-(2,2-Dichlorovinyl)-4-methylphenoxy)methyl) phenyl)-2-methoxyimino-*N*-methylacetamide (4d). Yield 95%, white solid, mp 92-95 °C. ^{1}H-NMR ($CDCl_3$, TMS) δ 2.28 (s, 3H), 2.87 (d, J = 5.0, Hz, 3H), 3.92 (s, 3H), 4.97 (s, 2H), 6.71-6.74 (m, 2H), 7.07 (s, 1H), 7.00-7.56 (m, 6H); MS m/z 406.1 (M^-).

(*E*)-Methyl 2-(2-((5-(2,2-Dichlorovinyl)-2-methoxyphenoxy) methyl)phenyl)-2-methoxyiminoacetate (3e). Yield 76%, light green solid, mp 88-94 °C, ^{1}H-NMR ($CDCl_3$, TMS) δ 3.85 (s, 3H), 3.88 (s, 3H), 4.05 (s, 3H), 5.01 (s, 2H), 6.69 (s, 1H), 6.84-7.57 (m, 7H); MS m/z 423.1 (M^+).

(*E*)-2-(2-((5-(2,2-Dichlorovinyl)-2-methoxyphenoxy)methyl) phenyl)-2-methoxyimino-*N*-methylacetamide (4e) Yield 83%, white solid, mp 76-78 °C, ^{1}H-NMR ($CDCl_3$, TMS) δ 2.90 (d, J = 5.0 Hz, 3H), 3.88 (s, 3H), 3.95 (s, 3H), 5.02 (s, 2H), 6.72 (s, 1H), 6.75-7.55 (m, 8H); MS m/z 422.0 (M^+).

(*E*)-Methyl 2-(2-((2-(2,2-Dichlorovinyl)-6-methylphenoxy) methyl)phenyl)-2-methoxyiminoacetate (3f). Yield 78%, light yellow liquid. ^{1}H-NMR ($CDCl_3$, TMS) δ 2.21 (s, 3H), 3.83 (s, 3H), 4.03 (s, 3H), 4.66 (s, 2H), 7.00 (s, 1H), 7.03-7.66 (m, 7H); MS m/z 407.0 (M^+).

(*E*)-2-(2-((2-(2,2-Dichlorovinyl)-6-methylphenoxy)methyl) phenyl)-2-methoxyimino-*N*-methylacetamide (4f). Yield 89%, white brown solid, mp 152-160 °C, ^{1}H-NMR ($CDCl_3$, TMS) δ 2.23 (s, 3H), 2.90 (d, J = 5.0 Hz, 3H), 3.95 (s, 3H), 4.66 (s, 2H), 6.77 (s, 1H), 7.02 (s, 1H), 7.05-7.67 (m, 7H); MS m/z 406.9 (M^-).

(*E*)-Methyl 2-(2-((2-Bromo-3-(2,2-dichlorovinyl)-6-methoxyphenoxy)methyl)phenyl)-2-methoxyiminoacetate (3g). Yield 81%, white solid, mp 131-133 °C, ^{1}H-NMR ($CDCl_3$, TMS) δ 3.84 (s, 3H), 3.86 (s, 3H), 4.02 (s, 3H), 4.83 (s, 2H), 6.90 (s, 1H), 6.87-7.88 (m, 6H); MS m/z 500.8 (M^-).

(*E*)-2-(2-((2-Bromo-3-(2,2-dichlorovinyl)-6-methoxyphenoxy)methyl)phenyl)-2-methoxyimino-*N*-methylacetamide (4g). Yield 82%, white solid, mp 92-95 °C. ^{1}H-NMR($CDCl_3$, TMS) δ 2.89 (d, J = 5.0 Hz, 3H), 3.83 (s, 3H), 3.94 (s, 3H), 4.85 (s, 2H), 6.67 (s, 1H), 6.90 (s, 1H), 6.87-7.82 (m, 6H); MS m/z 499.9 (M^+).

(*E*)-Methyl 2-(2-((2-Bromo-4-(2,2-dichlorovinyl)phenoxy) methyl)phenyl)-2-methoxyiminoacetate (3h). Yield 78%, white solid, mp 155-170 °C. ^{1}H-NMR ($CDCl_3$, TMS) δ 3.87 (s, 3H), 4.04 (s, 3H), 5.04 (s, 2H), 6.71 (s, 1H), 6.80-7.77 (m, 7H); MS m/z 472.9 (M^+).

(*E*)-2-(2-((2-Bromo-4-(2,2-dichlorovinyl)phenoxy)methyl) phenyl)-2-methoxyimino-*N*-methylacetamide (4h). Yield 91%, white solid, mp 120-124 °C. ^{1}H-NMR ($CDCl_3$, TMS) δ 2.90 (d, J = 5.0 Hz, 3H), 3.94 (s, 3H), 5.07 (s, 2H), 6.70 (s, 1H), 6.77-7.77 (m, 8H); MS m/z 471.8 (M^+).

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