Preparation and Plant Growth-Regulatory Activity of *N'*-Substituted *N*-Furfuryloxamides

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N'-Substituted *N*-furfuryloxamides (**4**) were prepared *via* condensation of potassium methyl oxalate (**8**) with furfurylamine (**5f**) using 1,1'-oxalyldiimidazole (**6**), followed by hydrolysis of the resulting amide-ester (**10**), and finally condensation with aliphatic or aromatic amines (**5**). The prepared compounds (**4**) were examined for activity as plant growth regulators using two kinds of plant seeds, namely, those of rape, *Brassica campestris* L. (Dicotyledoneae) and leek, *Allium tuberosum* ROTTLE (Monocotyledoneae). *N'*-Benzyl- and *N'*-phenyl-*N*-furfuryloxamides (**4b** and **4c**) and *N,N'*-difurfuryloxamide (**4f**) inhibited root growth in seedlings of both species.

Key words furan derivative; plant growth regulator; phytoactivity; seedling; 1,1'-oxalyldiimidazole; unsymmetrical oxamide

Oxamide derivatives are known to have plant growth-regulatory activities. For instance, *N,N'*-bis(2-phenylpyrimidin-5-yl)oxamide (**1**)¹⁾ stimulated root growth in oat seedlings, and a 3-substituted dialkylaminooxanilide (**2**)²⁾ caused severe injury to annual morning glory. In addition, *N,N'*-bis(2-propenyloxy)ethanediamide (**3**)³⁾ has been synthesized as a plant growth regulator. We therefore extended our earlier synthetic study of furan derivatives⁴⁾ to prepare various *N*-furfuryloxamide derivatives (**4**) with an aliphatic, an aromatic or a heterocyclic ring as the *N'*-substituent. The plant growth-regulatory properties of the synthesized compounds (**4**) were examined.

Preparation of *N'*-Substituted *N*-Furfuryloxamides (**4**)

In general, the synthesis of symmetrical oxamides, for example, *N,N'*-difurfuryloxamide (**4f**) was easily accomplished by the reaction of 2 eq of furfurylamine (**5f**) with 1 eq of 1,1'-oxalyldiimidazole (ODI; **6**).⁵⁾ The preparation of unsymmetrical oxamides (**4**) was more time-consuming. First, dimethyl oxalate (**7**) was hydrolyzed with equimolar water at 60 °C for 1 h in the presence of potassium acetate to form the potassium salt of oxalic acid monomethyl ester (**8**). To activate the carboxyl group, **8** was converted into *N*-(methoxyoxalyl)imidazole (**9**) using ODI (**6**). The mechanism of activation of **8** to **9** may involve nucleophilic attack of oxalic acid monomethyl ester (**14**) at the carbonyl carbon of ODI (**6**), followed by intramolecular rearrangement of an anhydride-type intermediate (**15**) with liberation of carbon dioxide and carbon monoxide, or nucleophilic attack of counter anion

of imidazole on the carbonyl carbon of **15** as shown in Chart 3. Subsequently, the reaction of **9** with furfurylamine (**5f**) proceeded smoothly to afford methyl *N*-furfuryloxamate (**10**) in 82% yield calculated on the basis of **8**. Hydrolysis of **10** in sodium hydroxide solution at room temperature afforded *N*-furfuryloxamic acid (**12**), which is an oily, hygroscopic material. Thus, we used the sodium salt (**11**) of **12** for the next reaction with various kinds of

Chart 1

i aq. CH_3COOK , ii $\text{CH}_3\text{SO}_3\text{H}$, and then ODI(**6**), iii furfurylamine(**5f**), iv NaOH, and then $\text{CH}_3\text{SO}_3\text{H}$, v ODI(**6**), vi RNH_2 (**5**)

Chart 2. Preparation of Symmetrical and Unsymmetrical Oxamides (**4f** and **4**)

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Chart 3

Table 1. Plant Growth-Regulatory Activities of *N'*-Substituted *N*-Furfuryloxamides (**4**)

Compd. 4	R	Dicotyledoneae Rape; <i>Brassica campestris</i> L.				Monocotyledoneae Leek; <i>Allium tuberosum</i> ROTTLER			
		Growth (ratio) ^{a)} concentration (M)				Growth (ratio) ^{a)} concentration (M)			
		1.0×10^{-3}	5.0×10^{-4}	1.0×10^{-4}	5.0×10^{-5}	1.0×10^{-3}	5.0×10^{-4}	1.0×10^{-4}	5.0×10^{-5}
a	<i>n</i> -Butyl	93	79	99	73	100	75	83	102
b	Benzyl	85	83	63	92	58	55	56	52
c	Phenyl	43	33	48	45	64	78	47	67
d	4-Tolyl	85	70	76	101	108	87	127	114
e	-C ₆ H ₄ -COOMe (4)	63	70	68	93	150	120	115	115
f	Furfuryl	24	52	45	83	37	58	69	100
g	2-Thiazolyl	121	124	107	143	127	160	115	117
h	1,2,4-Triazin-3-yl	171	152	118	147	65	64	69	94
i	5-Me-1,3,4-thiadiazol-2-yl	84	90	108	108	103	80	82	95
j	2-Pyrimidinyl	94	92	135	110	142	200	150	215
k	4-Pyrimidinyl	88	122	109	113	82	101	68	78
l	2-Pyrazinyl	84	90	108	108	151	160	177	187
m	3-Quinoliny	91	101	128	86	100	125	119	88

a) Growth in control experiments after seven days (*A. tuberosum*: ten days) was taken as 100. Quantity of light: 8500 m⁻²·cd·Sr. Temperature 25 °C. Relative humidity of 60%. Experimental size: 20 seeds/group, 2 groups.

amines (**5**).

As illustrated in Chart 2, the above-mentioned hydrolysis-activation-amidation methodology was applied to the conversion of methyl *N*-furfuryloxamate (**10**) to *N'*-substituted *N*-furfuryloxamides (**4**) in yields of 84% to 13%. Among them, the yields of *N'*-(2-pyrimidinyl)- and *N'*-(4-pyrimidinyl)-*N*-furfuryloxamides (**4j** and **4k**) were only 13% and 28%, respectively. This may be due to the high solubility of **4j** and **4k** in water, so that they are not readily extractable from the aqueous solution. All thirteen of the prepared *N*-furfuryloxamide derivatives (**4a–m**) were examined for phytoactivity.

Phytogrowth Activity Tests Phytogrowth activity was assayed according to the method reported by Inamori *et al.*⁶⁾ using seeds of rape, *Brassica campestris* L. (Brassicaceae), as a dicotyledon and leek, *Allium tuberosum* ROTTLER (Liliaceae), as a monocotyledon. The results are summarized in Table 1. The root growth of rape and leek seedlings was inhibited by the *N'*-benzyl, *N'*-phenyl and *N'*-furfuryl derivatives (**4b**, **4c** and **4f**). The introduction of a methoxycarbonyl or methyl group onto the benzene ring of **4c** did not cause enhanced inhibitory activity compared with the parent compound **4c**.

It is noteworthy that **4h** exhibited different rooting activity depending on the kind of plant seed. Namely, it showed about 50% stimulatory activity on growth of rape

seedlings, but 30% inhibitory activity on root growth of leek seedlings. The 2-pyrimidinyl, 4-pyrimidinyl and 2-pyrazinyl derivatives (**4j**, **4k** and **4i**), containing two nitrogen atoms in an *N'*-substituted six-membered aromatic ring, did not exhibit any marked effect.

In summary, the synthetic method described here is convenient for the preparation of *N'*-substituted *N*-furfuryloxamides (**4**) under essentially neutral conditions. Preliminary evaluation of **4** revealed that *N'*-benzyl- and *N'*-phenyl-*N*-furfuryloxamides (**4b** and **4c**), and *N,N'*-difurfuryloxamide (**4f**) exhibit root growth-inhibitory activity in seedlings of rape and leek. Future work will concentrate on the synthesis and activity of *N'*-(halogenated phenyl)- or *N'*-(halogenated benzyl)-*N*-furfuryloxamides.

Experimental

Oxalyl chloride, imidazole, DMSO, were purchased from commercial sources and used as received. ODI (**6**) was prepared according to the reported procedure.⁵⁾ Melting points were taken on a Yanagimoto melting point apparatus. All melting points are uncorrected. IR spectra were measured on a Hitachi model 270-30 IR spectrophotometer. NMR spectra were measured on a Bruker AM-400 spectrometer (400 MHz) using tetramethylsilane as an internal reference, and chemical shifts were recorded as δ -values.

Potassium Methyl Oxalate (8) The preparation of **8** was carried out according to the method of Efimovsky.⁷⁾ A mixture of methanol (118 g, 3.6 mol) and dimethyl oxalate (118 g, 1 mol) was added dropwise to a

stirred mixture of potassium acetate (98 g, 1 mol) and water (98 g, 5.4 mol). The resultant mixture was refluxed at 60 °C for 1 h, and then concentrated *in vacuo* at 40 °C to one-half of its original volume. The residue was triturated with a mixed solution of ethanol (40 ml) and ether (80 ml) to give 114 g (80%) of **8**, mp 194–197 °C (lit.⁷⁾ 197 °C). The product (**8**) was dried in a vacuum desiccator over phosphorus pentoxide at room temperature, and used without further purification.

Methyl *N*-Furfuryloxamate (10) Oxalyl chloride (1.3 g, 10 mmol) was added dropwise to an ice-cold, stirred solution of imidazole (2.8 g, 40 mmol) in acetonitrile (80 ml). The mixture was stirred at room temperature for 5 min, then a suspension of potassium methyl oxalate (**8**) (1.4 g, 10 mmol) and methanesulfonic acid (1 g, 10 mmol) in acetonitrile (10 ml) was added rapidly in a single portion. The mixture was stirred at room temperature for 20 min, and then furfurylamine (**5f**) (1 g, 10 mmol) was added dropwise at room temperature. The resultant mixture was stirred for 1 h at room temperature. The solvent was removed *in vacuo*, and the resultant residue was poured into ice-cooled water and extracted with ethyl acetate. Washing of the ethyl acetate extract with 1% citric acid and water, followed by drying and evaporation of the solvent left the crude product (**10**), which was recrystallized from ether/ethyl acetate to afford 1.5 g (82%) of **10**, mp 39–40 °C. IR (KBr) cm^{-1} : 1742, 1695 (CO). ¹H-NMR (CDCl₃): 3.3 (s, 3H, –CH₃), 4.3 (d, $J=6$ Hz, 2H, –CH₂–), 6.0–7.3 (m × 3, 1H × 3, furan-4H, -3H, -5H) and 9.3 (t, 1H, –NH–). Anal. Calcd for C₈H₉NO₄: C, 52.46; H, 4.92; N, 7.65. Found: C, 52.62; H, 4.82; N, 7.73.

***N*-Furfuryloxamic Acid Sodium Salt (11)** A 4% sodium hydroxide solution (100 ml) was added to a methanol solution (100 ml) of methyl *N*-furfuryloxamate (**10**) (18.3 g, 0.1 mol), and the resulting mixture was stirred for 1 h at room temperature. The reaction mixture was concentrated to one-third of its original volume *in vacuo*, and the resultant residue was poured onto ice, then extracted with ethyl acetate. The aqueous layer was evaporated to dryness *in vacuo* to afford 12 g (82% yield) of *N*-furfuryloxamic acid sodium salt (**11**), which was used for the preparation of *N*'-substituted *N*-furfuryloxamide (**4**) without further purification.

***N*-Furfuryloxamic Acid (12)** A mixture of *N*-furfuryloxamic acid sodium salt (**11**) (21 g, 0.1 mol) and methanesulfonic acid (10 g, 0.1 mol) in acetonitrile (100 ml) was stirred at room temperature for 30 min. Most of the solvent was distilled off *in vacuo*, and the remainder was added to a mixture of ethyl acetate (100 ml) and ice-cooled water (30 ml). The organic layer was collected, and dried over anhydrous sodium sulfate. The organic layer was concentrated by distillation and the residue was distilled to afford 8.1 g (53%) of the crude free acid (**12**), which was sufficiently pure for preparative purposes, bp 170–175 °C (1 mmHg). IR (neat) cm^{-1} : 3310 (NH); 1764, 1683 (CO). ¹H-NMR (*d*₆-DMSO) δ : 4.2 (d, $J=5.6$ Hz, 2H, –CH₂–), 6.2–7.4 (m × 3, 1H × 3, furan-4H, -3H, -5H), 8.3 (br s, 1H, –CH₂NHCO–).

Preparation of *N*'-Substituted *N*-Furfuryloxamides (4) A General Method. A solution of oxalyl chloride (0.64 g, 5 mmol) in acetonitrile (5 ml) was added dropwise to an ice-cold, stirred solution of imidazole (1.35 g, 20 mmol) in acetonitrile (80 ml). The mixture was stirred at room temperature for 5 min, then a suspension of *N*-furfuryloxamic acid sodium salt (**11**) (0.88 g, 5 mmol) and methanesulfonic acid (0.5 g, 5 mmol) in acetonitrile (5 ml) was added rapidly in a single portion. The mixture was stirred at room temperature for 20 min, and then a solution of an amine (**5**) (5 mmol) in acetonitrile (5 ml) was added dropwise at room temperature. The resultant mixture was stirred for 3 h at 40 °C. The solvent was removed *in vacuo*, and the resultant residue was poured onto ice and extracted with ethyl acetate. Washing of the ethyl acetate extract with 1% citric acid and water, followed by drying and evaporation of the solvent left the crude product (**4**).

***N*'-Butyl-*N*-furfuryloxamide (4a)** was prepared as above from the reaction of **11** with *n*-butylamine (**5a**) in 56% yield. Recrystallization from ethyl acetate gave **4a**, mp 148–150 °C. IR (KBr) cm^{-1} : 1656 (CO). ¹H-NMR (*d*₆-DMSO) δ : 0.93 (t, 3H, –CH₃), 1.3–3.3 (m, 6H, –(CH₂)₃–), 6.2–7.4 (m × 3, 1H × 3, furan-4H, -3H, -5H), 7.5 (br s, 1H, –NHCO–), 7.8 (br s, 1H, –NHCO–). Anal. Calcd for C₁₁H₁₆N₂O₃: C, 58.91; H, 7.11; N, 12.49. Found: C, 58.94; H, 7.22; N, 12.58.

***N*'-Benzyl-*N*-furfuryloxamide (4b)** was prepared as above from the reaction of **11** with benzylamine (**5b**) in 83% yield. Recrystallization from toluene gave **4b**, mp 172–174 °C. IR (KBr) cm^{-1} : 1656 (CO). ¹H-NMR (*d*₆-DMSO) δ : 4.4 (s, 2H, –NHCH₂–), 4.5 (s, 2H, –NHCH₂–), 6.3–7.4 (m × 3, 1H × 3, furan-4H, -3H, -5H), 7.2–7.4 (m, 5H, C₆H₅–), 7.8 (br s, 1H × 2, –NHCO– × 2). Anal. Calcd for C₁₄H₁₄N₂O₃: C, 65.11;

H, 5.46; N, 10.58. Found: C, 65.15; H, 4.49; N, 10.91.

***N*'-Phenyl-*N*-furfuryloxamide (4c)** was prepared as above from the reaction of **11** with aniline (**5c**) in 46% yield. Recrystallization from ethyl acetate gave **4c**, mp 151–153 °C. IR (KBr) cm^{-1} : 1656, 1627 (CO). ¹H-NMR (*d*₆-DMSO) δ : 4.4 (d, $J=6$ Hz, 2H, –CH₂NH–), 6.2–7.5 (m × 3, 1H × 3, furan-4H, -3H, -5H), 7.3–7.8 (m, 5H, C₆H₅–), 9.4 (t, 1H, –CH₂NH–), 10.6 (br s, 1H, –CONH–). Anal. Calcd for C₁₃H₁₂N₂O₃: C, 63.92; H, 4.93; N, 11.47. Found: C, 64.08; H, 5.03; N, 11.45.

***N*'-(4-Tolyl)-*N*-furfuryloxamide (4d)** was prepared as above from the reaction of **11** with 4-tolylamine (**5d**) in 84% yield. Recrystallization from toluene gave **4d**, mp 168–172 °C. IR (KBr) cm^{-1} : 1665 (CO). ¹H-NMR (*d*₆-DMSO) δ : 2.2 (s, 3H, –CH₃), 4.3 (s, 2H, –CH₂NH–), 6.3–7.4 (m × 3, 1H × 3, furan-4H, -3H, -5H), 7.1–7.7 (d × 2, each $J=8$ Hz, 2H × 2, Ph-2H, -6H and Ph-3H, -5H), 9.3 (t, 1H, –CH₂NH–), 10.5 (br s, 1H, –CONH–). Anal. Calcd for C₁₄H₁₄N₂O₃: C, 65.11; H, 5.46; N, 10.58. Found: C, 65.25; H, 5.55; N, 10.69.

***N*'-(4-Methoxycarbonylphenyl)-*N*-furfuryloxamide (4e)** was prepared as above from the reaction of **11** with 4-methoxycarbonylaniline (**5e**) in 62% yield. Recrystallization from ethyl acetate gave **4e**, mp 201–202 °C. IR (KBr) cm^{-1} : 1728, 1674 (CO). ¹H-NMR (*d*₆-DMSO) δ : 3.8 (s, 3H, –CH₃), 4.4 (d, $J=6$ Hz, 2H, –NHCH₂–), 6.3–7.6 (m × 3, 1H × 3, furan-4H, -3H, -5H), 7.2–7.4 (d × 2, each $J=8$ Hz, 2H × 2, Ph-2H, -6H and Ph-3H, -5H), 9.4 (t, 1H, –CH₂NH–), 11.0 (br s, 1H, –CONH–). Anal. Calcd for C₁₅H₁₄N₂O₅: C, 59.60; H, 4.64; N, 9.27. Found: C, 59.37; H, 4.67; N, 9.06.

***N,N'*-Difurfuryloxamide (4f)** was prepared as above from the reaction of **11** with furfurylamine (**5f**) in 93% yield. Recrystallization from ethyl acetate gave **4f**, mp 168–170 °C. IR (KBr) cm^{-1} : 1650 (CO). ¹H-NMR (*d*₆-DMSO) δ : 4.4 (d, $J=6$ Hz, 2H, –CH₂NH–), 6.2–7.3 (m × 3, 1H × 3, furan-4H, -3H, -5H), 7.7 (br s, 1H, –NH–). Anal. Calcd for C₁₂H₁₂N₂O₄: C, 58.06; H, 4.83; N, 11.29. Found: C, 57.90; H, 4.74; N, 11.30.

***N*'-(2-Thiazolyl)-*N*-furfuryloxamide (4g)** was prepared as above from the reaction of **11** with 2-aminothiazole (**5g**) in 68% yield. Recrystallization from water gave **4g**, mp 209–212 °C. IR (KBr) cm^{-1} : 1704, 1671 (CO). ¹H-NMR (*d*₆-DMSO) δ : 4.3 (d, $J=6$ Hz, 2H, –CH₂NH–), 6.2–7.5 (m × 3, 1H × 3, furan-4H, -3H, -5H), 7.3–7.5 (d × 2, each $J=3.5$ Hz, 1H × 2, thiazole-4H, -5H), 9.5 (t, 1H, –CH₂NH–), 12.5 (br s, 1H, –CONH–). Anal. Calcd for C₁₀H₉N₃O₃S: C, 47.80; H, 3.61; N, 16.72. Found: C, 47.64; H, 3.66; N, 16.77.

***N*'-(1,2,4-Triazin-3-yl)-*N*-furfuryloxamide (4h)** was prepared as above from the reaction of **11** with 3-amino-1,2,4-triazine (**5h**) in 34% yield. Recrystallization from *N,N*-dimethylformamide (DMF) gave **4h**, mp 264–266 °C. IR (KBr) cm^{-1} : 1671 (CO). ¹H-NMR (*d*₆-DMSO) δ : 4.3 (d, 2H, –CH₂NH–), 6.2–7.5 (m × 3, 1H × 3, furan-4H, -3H, -5H), 7.9 (s, 1H, triazine-5H), 9.4 (br t, 1H, –CH₂NH–), 13.8 (br s, 1H, –CONH–). Anal. Calcd for C₉H₈N₅O₃: C, 45.96; H, 3.86; N, 29.78. Found: C, 46.14; H, 3.91; N, 30.04.

***N*'-(5-Methyl-1,3,4-thiadiazol-2-yl)-*N*-furfuryloxamide (4i)** was prepared as above from the reaction of **11** with 2-amino-5-methyl-1,3,4-thiazazole (**5i**) in 51% yield. Recrystallization from DMF gave **4i**, mp 237–239 °C. IR (KBr) cm^{-1} : 1722, 1680 (CO). ¹H-NMR (*d*₆-DMSO) δ : 2.6 (s, 3H, –CH₃), 4.3 (d, $J=6$ Hz, 2H, –CH₂NH–), 6.2–7.5 (m × 3, 1H × 3, furan-4H, -3H, -5H), 9.6 (t, 1H, –CH₂NH–), 12.9 (br s, 1H, –CONH–). Anal. Calcd for C₁₀H₁₀N₄O₃S: C, 45.10; H, 3.79; N, 21.04. Found: C, 45.24; H, 3.79; N, 21.17.

***N*'-(2-Pyrimidinyl)-*N*-furfuryloxamide (4j)** was prepared as above from the reaction of **11** with 2-aminopyrimidine (**5j**) in 13% yield. Recrystallization from ethyl acetate gave **4j**, mp 124–126 °C. IR (KBr) cm^{-1} : 1722, 1685 (CO). ¹H-NMR (*d*₆-DMSO) δ : 4.3 (d, $J=6$ Hz, 2H, –CH₂NH–), 6.2–7.3 (m × 3, 1H × 3, furan-4H, -3H, -5H), 7.5–8.7 (m, 1H × 3, pyrimidine-4H, -5H, -6H), 9.4 (t, 1H, –CH₂NH–), 11.0 (br s, 1H, –CONH–). Anal. Calcd for C₁₁H₁₀N₂O₃: C, 53.66; H, 4.09; N, 22.76. Found: C, 53.71; H, 3.99; N, 22.89.

***N*'-(4-Pyrimidinyl)-*N*-furfuryloxamide (4k)** was prepared as above from the reaction of **11** with 4-aminopyrimidine (**5k**) in 28% yield. Recrystallization from ethyl acetate gave **4k**, mp 154–156 °C. IR (KBr) cm^{-1} : 1722, 1685 (CO). ¹H-NMR (*d*₆-DMSO) δ : 4.4 (d, $J=6$ Hz, 2H, –CH₂NH–), 6.3–7.5 (m × 3, 1H × 3, furan-4H, -3H, -5H), 8.0–8.9 (m, 1H × 3, pyrimidine-2H, -5H, -6H), 9.4 (t, 1H, –CH₂NH–), 10.4 (br s, 1H, –CONH–). Anal. Calcd for C₁₁H₁₀N₄O₃: C, 53.66; H, 4.09; N, 22.76. Found: C, 53.76; H, 4.13; N, 22.76.

***N*'-(2-Pyrazinyl)-*N*-furfuryloxamide (4l)** was prepared as above from the reaction of **11** with 2-aminopyrazine (**5l**) in 30% yield. Recrystallization from ethyl acetate gave **4l**, mp 147–149 °C. IR (KBr)

cm^{-1} : 1722, 1683 (CO). $^1\text{H-NMR}$ (d_6 -DMSO) δ : 4.4 (d, $J=6$ Hz, 2H, $-\text{CH}_2\text{NH}-$), 6.3—7.5 (m $\times$ 3, 1H $\times$ 3, furan-4H, -3H, -5H), 8.4—9.2 (m $\times$ 3, 1H $\times$ 3, pyrazine-3H, -5H, -6H), 9.5 (t, 1H, $-\text{CH}_2\text{NH}-$), 10.6 (br s, 1H, $-\text{CONH}-$). *Anal.* Calcd for $\text{C}_{11}\text{H}_{10}\text{N}_4\text{O}_3$: C, 53.66; H, 4.09; N, 22.76. Found: C, 53.71; H, 3.98; N, 22.96.

$N'-(3\text{-Quinoliny})\text{-}N\text{-furfuryloxamide}$ (**4m**) was prepared as above from the reaction of **11** with 2-aminoquinoline (**5m**) in 31% yield. Recrystallization from ethyl acetate gave **4m**, mp 212—216°C. IR (KBr) cm^{-1} : 1758, 1668 (CO). $^1\text{H-NMR}$ (d_6 -DMSO) δ : 4.4 (d, $J=6$ Hz, 2H, $-\text{CH}_2\text{NH}-$), 6.3—7.7 (m $\times$ 3, 1H $\times$ 3, furan-4H, -3H, -5H), 7.5—9.2 (m, 1H $\times$ 6, quinoline-2H, -4H, -5H, -6H, -7H, -8H), 9.5 (t, 1H, $-\text{CH}_2\text{NH}-$), 11.2 (br s, 1H, $-\text{CONH}-$). *Anal.* Calcd for $\text{C}_{16}\text{H}_{13}\text{N}_3\text{O}_3$: C, 65.08; H, 4.44; N, 14.23. Found: C, 65.37; H, 4.52; N, 14.28.

Phytogrowth-Inhibitory Activity Test This test was carried out according to the method reported by Inamori *et al.*⁶⁾ Dimethyl sulfoxide (DMSO) solution (1.0 ml) containing an oxamide derivative (**4a—m**) or DMSO alone (1.0 ml) as a control was diluted in 100 ml of sterilized agar (0.8%, Nacalai Tesque, Inc.) to give concentrations of 5×10^{-5} M, 1.0×10^{-4} M, 5×10^{-4} M and 1.0×10^{-3} M. The agar containing a test chemical or DMSO as a control was poured into a sterilized culture jar of 500 ml. Then 20 seeds of each of the plant species, sterilized with 70% ethanol and 1% NaClO, were put on the agar and left for seven days (*A. tuberosum*; ten days) at 25°C under a relative humidity of 60% and a light intensity of $8500 \text{ m}^{-2} \cdot \text{cd} \cdot \text{Sr}$. The phytogrowth-inhibitory activity was expressed as the ratio of the root length in seedlings exposed to a test chemical to that of the control (100). The results are summarized in Table 1.

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References and Notes

- 1) Vladimirtsev I. F., Zhuravskaya N. I., Boldyrev I. V., Cherkasov V. M., Remennikov G. Y., Samolyuk L. I., Borisenko V. P., *Fiziol. Akt. Veshchestva* **8**, 101—103 (1976) [*Chem. Abstr.*, **86**, 182433v (1977)].
- 2) Wong R. Y., U.S. Patent, 4406692 [*Chem. Abstr.*, **100**, 6112t (1984)].
- 3) Rentzea C., Keil M., Harreus A., Rademacher W., Eur. Patent. Appl. EP 469423 [*Chem. Abstr.*, **116**, 214016x (1992)].
- 4) Kitagawa T., Akiyama N., *Chem. Pharm. Bull.*, **45**, 1865—1866 (1997).
- 5) ODI (**6**) was easily prepared from the reaction of imidazole with oxalyl chloride in acetonitrile according to the method reported by Murata; a) Murata S., *Chem. Lett.*, **1983**, 1819—1820; b) Murata S., *Bull. Chem. Soc. Jpn.*, **57**, 3597—3598 (1984).
- 6) General references; a) Inamori Y., Muro C., Yamanaka H., Osaka K., Hachiken H., Tsujibo H., Miki Y., *Biosci. Biotech. Biochem.*, **58**, 1150—1152 (1994); b) Arimoto M., Matsuura S., Muro C., Tsujibo H., Matsumura E., Yamaguchi H., Inamori Y., *ibid.*, **58**, 189—190 (1994).
- 7) Efimovsky O., *J. Recherches Centre Natl. Recherche Sci.*, **47**, 147—190 (1959) [*Chem. Abstr.*, **56**, 4742f (1962)].