Supplementary Materials. Lists of structure factors, anisotropic thermal parameters, coordinates of the H atoms and molecular dimensions of the phenyl rings are available from the author.

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References

1. D. J. Tipper and J. L. Strominger, *Proc. Natl. Acad. Sci. USA.*, **54**, 1133-1141 (1965).
2. A. Tomasz, *Annu. Rev. Microbiol.*, **33**, 113-137 (1979).
3. B. Lee, *J. Mol. Biol.*, **61**, 463-469 (1971).
4. J. A. Kelly, P. C. Moews, J. R. Knox, J. M. Frere, and J. M. Ghuysen, *Science*, **218**, 479-481 (1982).
5. P. Domiano, M. Nardelli, A. Balsamo, B. Macchia, and F. Macchia, *Acta Cryst.*, **B35**, 1363-1372 (1979).
6. N. C. Cohen, *J. Med. Chem.*, **26**, 259-264 (1983).
7. J. G. Christenson, D. L. Pruess, Talbot, M. K. and D. D. Keith, *Antimicrob. Agents Chemother.* **32**, 1005-1011 (1988).
8. S. Abrahamsson, D. C. Hodgkin, and E. N. Malslen, *Biochem. J.*, **86**, 514 (1963).
9. W. Shin and S. W. Cho, *Acta Cryst.*, **C48**, 1447-1449 (1992).
10. G. M. Sheldrick, *SHELXS86*, Program for the solution of crystal structures, Univ. of Göttingen, Germany (1986).
11. G. M. Sheldrick, *SHELX76*, Program for crystal structure determination. Univ. of Cambridge, England (1976).
12. *International Tables for X-ray Crystallography*, (1974). Vol. IV, p. 99. Birmingham: Kynoch Press (Present distributor: Kluwer Academic Publishers, Dordrecht).
13. R. M. Sweet and L. F. Dahl, *J. Am. Chem. Soc.*, **92**, 5489-5507 (1970).
14. C. Johnson, *ORTEPII*, Report ORNL-5138, Oak Ridge National Laboratory, Tennessee, USA (1976).

Synthesis and Herbicidal Activities of *N*-Phenyl Oxadiazolidinedione Derivatives

Hyung Jin Kim, Kwang-Jin Hwang, Chong-Hoe Park†, and Jae Hyun Lee*

Korea Research Institute of Chemical Technology
P.O. Box 9, Daedeog Danji, Taejon
†Department of Chemistry, Chung Nam National University, Taejon
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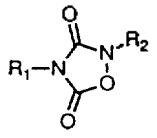
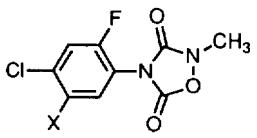
N-Phenyl oxadiazolidinedione derivatives **II** were synthesized and their herbicidal activities were measured against grass weeds. A parabolic relationship between molar refractivity (MR) of meta substituents of dione **II** and their herbicidal activities was observed. With the substituents having MR value = ~15, the higher activities were obtained. Especially, the highest herbicidal activity (97% inhibition of weeds at 0.25 kg/ha) was observed by propyne **IIr** containing propargyloxy group as meta substituent.

Introduction

Disubstituted oxadiazolidinedione derivatives **I**, a class of *N*-phenylimide, have been well known as their herbicidal activities.[1] The structural derivatization of oxadiazolidine **I** by modification of substituents R_1, R_2 and the heterocyclic ring itself affects their herbicidal activities and selectivity on the plants. The herbicidal activities of oxadiazolidine **I** are usually increased with the halogenated phenyl groups at R_1 and R_2. However, no clear structure activity relationship (SAR) is available yet. We have been interested in providing the SAR data of oxadiazolidine **I** since it is useful for the design of new herbicides such as *N*-phenyl pyrimidone and phthalimide derivatives. The herbicidal biomechanism of Methazole (**III**),[2] a well known oxadiazolidinedione, includes the cleavage of oxadiazolidine ring as a key step to give a potent urea **IV** (Scheme 1). When a phenyl ring is adjacent to the bond breaking or formation center, the electronic effect of meta substituent is not important on the reaction. Rather, it might have significant bulk effect on its binding to a receptor or an enzyme during the action as a biomolecule.

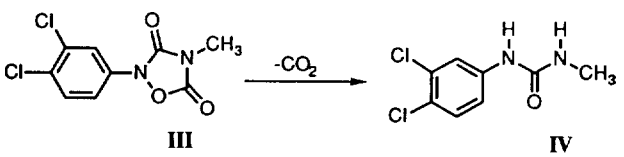


I



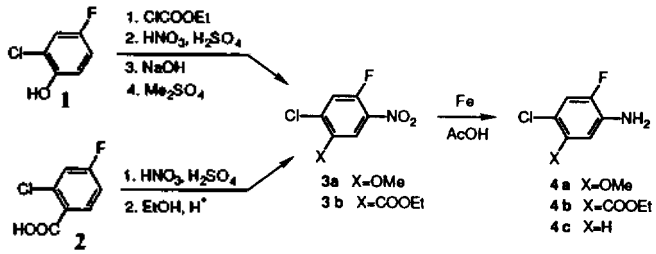
II

In this regard, we designed oxadiazolidine derivatives **II** in which *N*-2-fluoro-4-chlorophenyl group with various meta

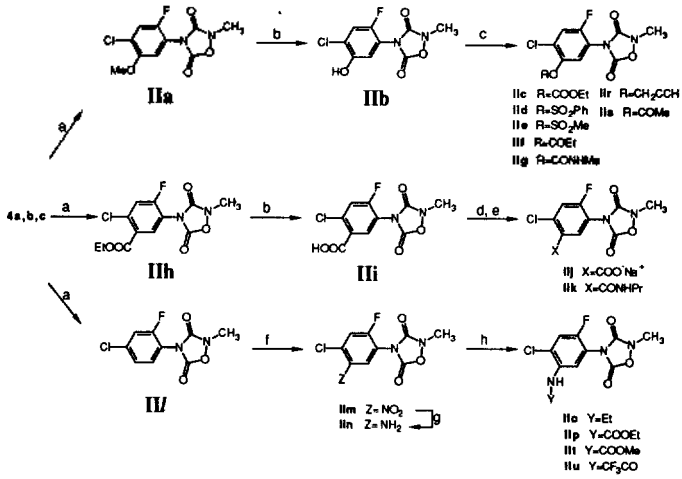


III **IV**

Scheme 1.



Scheme 2.



a) $COCl_2$, MeNHOH/ py then ClCOOEt/ NaOH; b) BBr_3/ CH_2Cl_2; c) E^+/ py; ClCOOEt (IIe), $ClSO_2Ph$ (IId), $ClSO_2Me$ (IIe), ClCOEt (IIf), MeNCO (IIg), $ClCH_2CCH$ (IIr), ClCOMe (IIs); d) Na_2CO_3; e) PCl_5, $PrNH_2$; f) HNO_3/ H_2SO_4; g) Fe/ AcOH; h) Et_3OBF_4, CH_2Cl_2 (IIo); ClCOOEt/ py, CH_3CN (IIp); ClCOOMe/ py, CH_2Cl_2 (IIt); $(CF_3CO)_2O$/ CH_2Cl_2 (IIu).

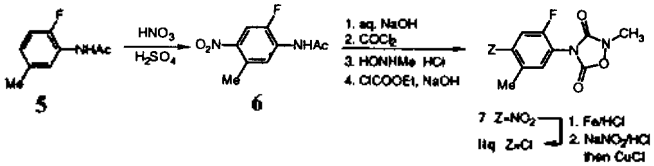
Scheme 3.

substituents was selected as a basic skeleton. In addition, methyl group was substituted at 2-position for the synthetic simplicity. Here, we wish to report the synthesis of oxadiazolidinedione derivatives **II** with variety of meta substituents and their herbicidal activities.

Synthesis

The synthetic endeavors in preparation of *N*-phenyl oxadiazolidinedione derivatives **II** are focused on the formation of oxadiazolidinedione ring and the introduction of functional groups on the phenyl ring as shown in Schemes 2, 3 and 4. The formation of oxadiazolidine rings was proceeded by the known procedure[3] with minor modification as a key step. The meta substituents on the phenyl rings of oxadiazolidine derivatives **II** were introduced before/after the formation of oxadiazolidine rings by the proper functional group manipulations.

The key intermediates oxadiazoles **IIa**, **IIh** and **IIl** were prepared from the corresponding amines **4a, b, c** by the reaction with phosgene, *N*-methylhydroxylamine and chloroformate subsequently (Scheme 3). To prepare oxazole derivatives with oxygen substituent, phenol **IIb** was obtained from anisole **IIa** in quantitative yield by the treatment with BBr_3 then reacted with appropriate electrophiles such as ClCOOEt, $ClSO_2Ph$, $ClSO_2CH_3$, ClCOEt, methyl isocyanate, $ClCH_2CCH$, and $ClCOCH_3$ in the presence of pyridine to give oxadiazoles **IIc-g**, **IIr** and **IIs** in high yields. Ester **IIh** was



Scheme 4.

also treated with BBr_3 to give acid **IIi** which was then neutralized with an equivalent of Na_2CO_3 to result sodium salt **IIj**. Amide **IIk** was readily obtained by the reaction of **IIi** with PCl_5 and propylamine subsequently.

To introduce a nitrogen substituent on the phenyl rings of oxadiazolidinedione **II**, oxadiazolidine **IIl** was treated with a mixture of nitric acid and sulfuric acid to give nitro oxadiazolidine **IIm**. Aniline **IIn** was generated from nitrooxadiazole **IIm** by the reduction with iron powder and acetic acid. The reaction of **IIn** with ClCOOEt, $ClCOOCH_3$, and $(CF_3CO)_2O$ provided oxadiazoles **IIp**, **IIt**, and **IIu** respectively. The ethylation of amine **IIn** was unsuccessful using EtI as an electrophile, however it was accomplished by treatment with $Et_3O^+BF_4^-$ to give ethylamine **IIo**.

In addition, other key intermediates anilines **4a, b** were prepared from the corresponding nitrobenzenes **3a, b** (Scheme 2). In order to introduce nitro group on meta position of phenol **1**, it was converted into ethyl carbonate then hydrolyzed and methylated to give anisole **3a**. Nitro compound **3a** was reduced to aniline **4a** with iron powder and acetic acid. Ester **3b** was formed from acid **2** by the nitration followed by an esterification.

Methyl substituted oxadiazolidine **IIq** was prepared from acetanilide **5**, which was formed from 2-fluoro-5-methylaniline (Scheme 4). The direct chlorination of anilide **5** with $AlCl_3/Cl_2$ was unsuccessful to give 2-fluoro-4-chloro-5-methylacetanilide. Thus, anilide **5** was initially nitrated to give nitrobenzene **6** then, forced to be cyclized to generate oxadiazolidine **7** by the same procedure as that of oxadiazolidine **IIa**. Reduction with Fe/HCl followed by Sandmeyer displacement with Cl converted nitro oxadiazolidine **7** into chlorooxadiazolidine **IIq** in good yield.

Herbicidal Activities

The herbicidal activities of oxadiazole derivatives **II** were measured against various grass weeds and their results are shown in Table 1. The highest herbicidal activity of oxadiazolidinedione **II** was observed with the propargyloxy group at meta position of the phenyl ring (**IIr** in Table 1). However, the activities were very low with other OR substituents such as alkoxy (**IIa, IIv**), carbonyloxy (OCOR; **IIc, IIf, IIg** and **IIs**) groups. When the substituents were neutral such as H, CH_3, incapable of acting as H-bonding donor/acceptor, the activities were quite high (**IIl, IIq**). With NH_2, OH groups, the herbicidal activity of oxadiazolidine **II** was very low (**IIb, IIn**). Similarly, the activity of oxadiazolidine **II** was decreased by substitution with carboxyl group such as COONa, COOH (**IIi, IIj**). The substituents amide (CONHPr; **IIk**) and ester (COOEt, **IIh**) also showed good activities. The nitrogen substituents such as carbonylamine (NHCOOR; **IIp, IIt**) and secondary amine (NHEt, **IIo**) increased the activities of oxadiazolidine **II**.

Table 1. Physicochemical constants of the substituents X of oxadiazolidine **II** (all data are from the reference 8) and their herbicidal activities at 0.25 kg/ha: Pi; hydrophobic parameter, MR; molar refractivity, F; field effect

Compounds	Substituents	Pi(π)	MR	F	Activity[a]
IIa	OCH_3	−0.02	7.87	0.26	0
IIb	OH	−0.67	2.85	0.29	9
IIc	$OCOOC_2H_5$	[b]	18.74	[b]	10
IId	OSO_2Ph	0.93	36.70	0.36	13
IIe	OSO_2Me	−0.88	16.99	0.39	61
IIf	OCOEt	−0.10	17.12	0.41	3
IIg	OCONHMe	−0.42	15.29	[b]	1
IIh	COOEt	0.51	17.47	0.33	69
IIi	COOH	−0.32	6.93	0.33	10
IIj	COONa	−4.36	6.05	−0.15	11
IIk	CONHPr	−0.19	23.87	0.34	23
IIl	H	0.00	1.03	0.00	61
IIm	NO_2	−0.28	7.36	0.67	0
IIn	NH_2	−1.23	5.42	0.02	11
IIo	NHEt	0.08	14.98	−0.11	49
IIp	NHCOOEt	0.17	21.18	0.14	28
IIq	CH_3	0.56	5.65	−0.04	46
IIr	OCH_2CCH	[b]	14.93	[b]	97
IIs	OCOMe	−0.64	12.47	0.41	8
IIt	NHCOOMe	−0.37	16.53	0.14	56
IIu	$NHCOCF_3$	0.80	14.30	0.36	14
IIv	$OCH_2CH_2CH(Me)_2$	[b]	26.26	0.38	10

[a] inhibition of the weeds growth (%), [b] datus is not available.

There was no linear correspondence between the physicochemical parameters (Table 1) and herbicidal activity of oxadiazolidine **II**. However a parabolic relationship between MR (molar refractivity)[4] and herbicidal activity of oxadiazolidine **II** was observed.[5] With the substituents having MR = ~15, the herbicidal activities were higher than those of others. Because the herbicidal activity of oxadiazolidine **IIr** with propargyloxy substituent was the highest, its structure is carefully studied using the Sybyl molecular modeling program (Tripos silicon graphics).

In order to see if the propargyloxy group of propyne **IIr** interacts with the imide ring by certain spatial orientation, the conformation of propyne **IIr** having the lowest energy is searched by rotation of O-Ph, O-CH_2 and *N*-Ph bonds respectively and represented in Figure 1. The phenyl ring is tilted ($\theta = 53°$) to the imide plane instead of being parallel. This tilt breaks the conjugation of aromatic ring and imide plane. The propargyloxy group is oriented toward imide ring rather than outward.

Discussions

If we assume that oxadiazolidine **II** decompose biochemically to urea which is a potent component giving herbicidal activity (Scheme 1), then the electronic effect by a meta substituent on the phenyl ring of oxadiazolidine **II** might be not significant factor on the decomposition of the oxadiazolidine ring. Therefore, the electron donating or withdrawing effect of meta substituents on the phenyl ring should not be an important factor on the herbicidal activities of oxadiazolidine (**II**). This assumption is well proved by our experimental data.

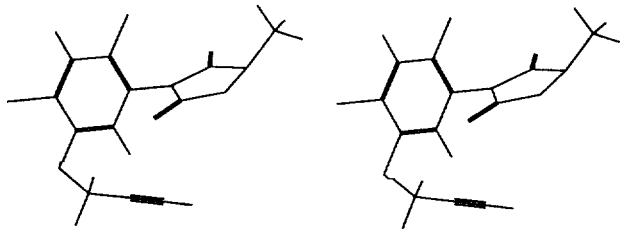


Figure 1. Stereoview of propyne **IIr** with the lowest energy generated by the Sybyl molecular modeling program.

The relatively high activities of oxadiazolidine **II** are observed with both electron donating (NHEt, NHCOOEt; **IIo, IIp**) and withdrawing groups (COOEt, **IIh**) as meta substituents. Similarly, both electron donating and withdrawing groups (OMe, **IIa**; COOH, **IIi**) give poor activities suggesting that the electronic effect of meta substituents is not crucial on the herbicidal activities of oxadiazolidin **II**.

The hydrogen bonding effect of substituents is not linearly correlated with the herbicidal activities of oxadiazolidine (**II**). Oxadiazolidine **IIq** (CH_3; neutral) and **IIt** (NHCOOMe; H-bonding donor/acceptor) show high activities. Rather, a certain size of MR value (~15) of substituent is relevant to relatively high herbicidal activity (over 50% inhibition of weeds at 0.25 kg/ha).

The high herbicidal activity of propyne **IIr** is very unusual and needs further study to interpret. Sato *et al.* reported that one of the mode of action of *N*-4-cloro-2-fluoro-5-propargyloxyphenyl-tetrahydrophthalimide is the inhibition of the photosynthetic CO_2 fixation in soybean.[6] Likewise, propyne **IIr** also inhibited the biosynthesis of chlorophyl in cotyledon disks of white cucumber.[7] This suggests us that oxadiazolidine **II** is also involved in the inhibition of chlorophyl biosynthesis resulting in their herbicidal activities.

Experimentals

Screening of Herbicidal Activities

Sterilized sandy loam soil was filled in plastic pots (348 cm^2). The seeds of common sorghum (*Sorghum bicolor*), barnyardgrass (*Echinochloa crus-galli*), large crabgrass (*Digitaria sanguinalis*), wheatgrass (*Agropyron smithii*), fall panicum (*Panicum dichotomiflorum*), bind weed (*Calystegia japonica*), common cocklebur (*Xanthium strumarium*), velvetleaf (*Abutilon avicenne*), Indian jointvetch (*Aeschnomene indica*), and black nightshade (*Solanum nigrum*) were placed on top of the soil and covered with the soil finely sieved. The plants were grown for 12 days in a greenhouse. A known amount of test compound was dissolved in a 50% acetone/water solution containing Tween-20. The solution was foliar-applied at a rate of 0.25 kg/ha and the pots were kept in the greenhouse for 2 weeks. The herbicidal activity was visually observed on the basis of morphological and physiological symptoms by percent scale, in which 0% represents no activity and 100% represents complete control.

Chemical Synthesis

Melting points were uncorrected. Infrared spectra were obtained on a Shimadzu IR-435 spectrophotometer. Proton NMR spectra were recorded at 60 MHz. Chemical shifts were reported im ppm (δ) relative to tetramethylsilane. Electron impact mass spectra were recorded at 70 or 20 eV. Column chromatography was performed using Merck Kieselgel 60 (230-400 mesh) as the stationary phase.

2-Methyl-4-(4′-chloro-2′-fluoro-5′-methoxyphenyl)-1,2,4-oxadiazolidine-3,5-dione (IIa). To a solution of 4-chloro-2-fluoro-methoxyaniline[9] (3.6 g, 20.51 mmol) in toluene (20 m*l*) was added a solution of phosgene in toluene (28.5 m*l*, 2.16 M, 61.5 mmol) for 30 min at room temperature. After being refluxed for 2 h, the reaction mixture was concentrated to remove excess phosgene under reduced pressure, then the residue was redissolved in CH_2Cl_2 (20 m*l*) and filtrated. The filtrate was added dropwise into the mixture of *N*-hydroxylamine hdrochloride (1.71 g, 20.5 mmol) and pyridine (1.62 g, 20.5 mmol) in CH_2Cl_2 (20 m*l*) at room temperature. After being stirred for 1 h, the reaction mixture was washed with water and dried ($MgSO_4$). Evaporation of solvent and recrystallization (*n*-hexane/EtOAc) afforded *N*-5-chloro-2-fluoro-5-methoxyphenyl-N′-hydroxy-N′-methylurea (2.4 g, 47% yield). mp. 163-165℃ ; ^{1}H NMR ($CDCl_3$+DMSO-d_6) δ 3.20 (s, 3H, CH_3), 3.80 (s, 3H, CH_3), 7.10 (d, 1H, Ph), 7.95 (d, 1H, Ph), 8.10 (br, 1H, NH), 9.70 (s, OH); MS m/e 248 (M^+), 201, 158, 147, 132, 47 (base). The above intermediate urea (2.0 g, 8.04 mmol) was dissolved in the mixture of 2 N NaOH (4 m*l*) and dioxane (10 m*l*). To this mixture was added ethylchloroformate (0.96 g, 8.84 mmol) with stirring at 0℃. After being stirred for 30 min, the reaction mixture was extracted with EtOAc (20 m*l*×2). The combined extracts were washed with brine and dried ($MgSO_4$). Evaporation and recrystallization from *n*-hexane/EtOAc afforded dione **IIa** as white solid (1.5 g, 68%): mp. 137℃ ; ^{1}H NMR ($CDCl_3$) δ 3.40 (s, 3H, NCH_3), 3.80 (s, 3H, CH_3), 6.85 (d, 1H, Ph), 7.25 (d, 1H, Ph); MS m/e 277 (M^++3, 81), 276 (M^++2, 100), 201 (65), 186 (29), 158 (58), 130 (26).

2-Methy-4-(4′-chloro-2′-fluoro-5′-hydroxyphenyl)-1,2,4-oxadiazolidine-3,5-dione (IIb). To a solution of dione **IIa** (9.0 g, 32.79 mmol) in CH_2Cl_2 (50 m*l*) was added BBr_3 (6 m*l*, 63.5 mmol) at 0℃. After being stirred for 1 h at room temperature, the reaction mixture was poured into ice-water. The organic layer was washed with water and brine, then dried ($MgSO_4$). Subsequent concentration *in vacuo* provided **IIb** (8.5 g, 100%): mp. 139-143℃ ; ^{1}H NMR ($CDCl_3$+DMSO-d_6) δ 3.40 (s, 3H, CH_3), 6.95 (d, 1H, Ph), 7.20 (d, 1H, Ph), 9.80 (br. s, OH); MS m/e 260 (M^+, 100), 187 (98), 159 (16), 145 (11).

2-Methyl-4-(4′-chloro-2′-fluoro-5′-ethoxycarbonyloxyphenyl)-1,2,4-oxadiazolidine-3,5-dione (IIc). To a mixture of **IIb** (1.0 g, 3.84 mmol) and pyridine (0.364 g, 4.6 mmol) in CH_2Cl_2 (10 m*l*) was added ethylchloroformate (0.5 g, 4.6 mmol). After being stirred for 10 min at room temperature, the reaction mixture was diluted with EtOAc (20 m*l*), then washed with 10% HCl, water, and brine. The solution was dried ($MgSO_4$) and concentrated to give a crude product which was recrystallized from n-hexane/EtOAc to afford dione **IIc** (0.95 g, 74%): mp. 96-97.5℃ ; ^{1}H NMR ($CDCl_3$) δ 1.30 (t, *J*=6 Hz, 3H, CH_3), 3.30 (s, 3H, NCH_3), 4.20 (q, *J*=6 Hz, 2H, CH_2), 7.20 (s, 1H, Ph), 7.30 (d, 1H, Ph); MS m/e 333 (M^++1, 17), 260 (51), 187 (36).

2-Methyl-4-(4′-chloro-2′-fluoro-5′-phenylsulfonyloxyphenyl)-1,2,4-oxadiazolidine-3,5-dione (IId). The mixture of **IIb** (1.0 g, 3.84 mmol), pyridine (0.364 g, 4.6 mmol) and phenylsulfonyl chloride (0.813 g, 4.6 mmol) in CH_2Cl_2 (10 m*l*) was refluxed for 2 h. After being cooled, the reaction mixture was diluted with EtOAc (20 m*l*), washed with 10% HCl and water (10 m*l*). The solution was dried ($MgSO_4$) and concentrated *in vacuo*. Column chromatography on silica gel (*n*-hexane/EtOAc=3/1) provided dione **IId** (1.4 g, 91%) as a yellowish oil: ^{1}H NMR ($CDCl_3$) δ 3.50 (s, 3H, CH_3), 7.10-7.90 (m, 7H, Ph); MS (20 eV) m/e 402 (M^-+2, 17), 141 (47).

2-Methyl-4-(4′-chloro-2′-fluoro-5′-methanesulfonyloxyphenyl)-1,2,4-oxadiazolidine-3,5-dione (IIe). was prepared from **IIb**, pyridine, and methanesulfonyl chloride in a similar procedure described for **IId** in 95% yield: ^{1}H NMR ($CDCl_3$) δ 3.20 (s, 3H, SO_2CH_3), 3.35 (s, 3H, NCH_3), 7.35 (d, 1H, Ph), 7.50 (d, 1H, Ph); MS m/e 338 (M^+, 50), 260 (97), 187 (35), 158 (53).

2-Methyl-4-(4′-chloro-2′-fluoro-5′-propionyloxyphenyl)-1,2,4-oxadiazolidine-3,5-dione (IIf). was prepared from **IIb** (0.80 g, 3.07 mmol), pyridine (0.29 g, 3.68 mmol), and propionyl chloride (0.34 g, 3.68 mmol) in a similar manner to that described for **IIc**. Yield 0.82 g (85%). mp. 117-118℃ (*n*-hexane/EtOAc). ^{1}H NMR ($CDCl_3$) δ 1.20 (t, *J*=6 Hz, 3H, CH_3), 2.55 (q, *J*=6 Hz, 2H, CH_2), 3.40 (s, 3H, NCH_3), 7.15 (d, 1H, Ph), 7.25 (d, 1H, Ph); MS m/e 316 (M^+, 0.5), 260 (5), 187 (0.5), 173 (0.5).

2-Methyl-4-(4′-chloro-2′-fluoro-5′-methylcarbamoyloxyphenyl)-1,2,4-oxadiazolidine-3,5-dione (IIg). The mixture of **IIb** (1.0 g, 3.48 mmol) and methylisocyanate (0.219 g, 3.84 mmol) in THF (10 m*l*) with a few drops of Et_3N was stirred for 20 min at room temperature. The reaction mixture was concentrated *in vacuo* and the residue was crystallized from n-hexane/THF to give **IIg** (1.13 g, 93%): mp 132-135℃ ; ^{1}H NMR ($CECl_3$) δ 2.85 (d, *J*=5 Hz, 3H, CH_3), 3.40 (s, 3H, CH_3), 5.30 (br, 1H, NH), 7.30 (s, 1H, Ph), 7.40 (s, 1H, Ph); MS m/e 318 (M^++1, 18), 260 (100), 187 (60), 173 (21), 159 (16).

2-Methyl-4-(4′-chloro-2′-fluoro-5′-ethoxycarbonylphenyl)-1,2,4-oxadiazolidine-3,5-dione (IIh). was prepared from 4-chloro-5-ethoxycarbonyl-2-fluoroaniline in a same manner to that described for **IIa**. Yield (54%): mp. 95-98℃ (*n*-hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 1.35 (t, *J*=6 Hz, 3H, CH_3), 3.40 (s, 3H, CH_3), 4.35 (q, *J*=6 Hz, 2H, CH_2), 7.35 (1H, Ph), 7.90 (d, 1H, Ph); MS m/e 316 (M^+, 33), 288 (51), 271 (100), 198 (65), 157 (19).

2-Methyl-4-(4′-chloro-2′-fluoro-5′-carboxyphenyl)-1,2,4-oxadiazolidine-3,5-dione (IIi). To a solution of **IIh** (9.0 g, 28.44 mmol) in CH_2Cl_2 (80 m*l*) was added boron tribromide (10.68 g, 42.66 mmol) at 0℃. After being stirred for 1 h at room temperature, the reaction mixture was poured into ice-water (60 m*l*). The aqueous layer was extracted with EtOAc (30 m*l*×3) and combined organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was crystallized from n-hexane/EtOAc to give dione **IIi** (7.1 g, 87%): mp. 181-185℃ ; ^{1}H NMR ($CDCl_3$+DMSO-d_6) δ 3.40 (s, 3H, CH_3), 7.35 (d, 1H, Ph), 8.05 (d, 1H, Ph), 10.05 (br s, 1H, COOH); MS m/e 288 (M^+, 42), 215 (25), 198 (40).

2-Methyl-4-(4′-chloro-2′-fluoro-5′-propylaminocar-

bonylphenyl)-1,2,4-oxadiazolidine-3,5-dione (IIk). The mixture of **IIi** (1.0 g, 347 mmol) and phosphorous pentachloride (0.72 g, 3.47 mmol) in phosphorous oxychloride (10 m*l*) was heated for 30 min at 80℃ then distilled to remove phosphorous oxychloride. Bulb to bulb distillation of the residue under reduced pressure gave 2-methyl-4-(4'-chloro-2'-fluoro-5'-chlorocarbonylphenyl)-1,2,4-oxadiazolidine-3,5-dione (0.84 g, 79%): bp 180-200℃/0.1 mmHg; ^{1}H NMR ($CDCl_3$) δ 3.45 (s, 3H, NCH_3), 7.40 (d, 1H, Ph), 8.20 (d, 1H, Ph); MS m/e 306 (M^+), 271 (base), 198, 157, 142, 47. This acetyl chloride (0.84 g, 2.73 mmol) with *n*-propylamine (0.326 g, 5.46 mmol) in CH_2Cl_2 (10 m*l*) was stirred for 30 min at room temperature. The reaction mixture was washed with water, then dried ($MgSO_4$) and concentrated. Crystallization from n-hexane/EtOAc gave dione **IIk** (0.72 g, 81%): mp. 165-167℃; ^{1}H NMR ($CDCl_3$) δ 1.00 (t, 3H, CH_3), 1.35-1.90 (m, 2H, CH_2), 3.20-3.55 (m, 2H, CH_2), 3.45 (s, 3H, CH_3), 6.45 (br s, 1H, NH), 7.25 (d, 1H, Ph), 7.60 (d, 1H, Ph); MS m/e 330 (M^-+1, 8), 329 (M^+, 14), 294 (7), 271 (100), 198 (29).

2-Methyl-4-(4'-chloro-2'-fluorophenyl)-1,2,4-oxadiazolidine-3,5-dione (IIl). was prepared from 4-chloro-2-fluoroaniline by the same procedure as described for **IIa** in 35% yield overall: mp. 110-111℃ (*n*-hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.40 (s, 3H, CH_3), 7.10-7.20 (m, 2H, Ph), 7.25-7.40 (m, 1H, Ph); MS m/e 244 (M^+, 49), 171 (49), 157 (23), 143 (39).

2-Methyl-4-(4'-chloro-2'-fluoro-5'-nitrophenyl)-1,2,4-oxadiazolidine-3,5-dione (IIm). To a solution of **IIl** (11.0 g, 45.0 mmol) in con-H_2SO_4 (15 m*l*) was dropped a mixture of 60% nitric acid (9.45 g) and con-H_2SO_4 (15 m*l*) at 0℃. After completion of the addition, the mixture was stirred for 20 min at 0℃ and then poured into ice-water to afford a yellow solid. Recrystallization from n-hexane/EtOAc gave nitrobenzene **IIm** (9.3 g, 71%): mp. 133-135℃; ^{1}H NMR ($CDCl_3$ +DMSO-d_6) δ 3.45 (s, 3H, CH_3), 7.50 (d, 1H, Ph), 8.20 (d, 1H, Ph); MS m/e 289 (M^+, 22), 216 (2), 202 (11).

2-Methyl-4-(4'-chloro-2'-fluoro-5'-aminophenyl)-1,2,4-oxadiazolidine-3,5-dione (IIn). The mixture of nitrobenzene **IIm** (1.5 g, 4.18 mmol), iron powder (0.87 g, 15.54 mmol) in 50% EtOH (20 m*l*) was heated at 80℃. At this temperature, a mixture of conc. HCl and 50% EtOH (10 m*l*) was added, then the resulting mixture was refluxed for 30 min. After being cooled to room temperature, the mixture was filtered, dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography (*n*-hexane /EtOAc, 3/1) to give amine **IIn** (0.65 g, 48%): mp. 162-164℃; ^{1}H NMR ($CDCl_3$+DMSO-d_6) δ 3.40 (s, 3H, CH_3), 4.60 (br s, 2H, NH_2), 6.80 (d, 1H, Ph), 7.10 (d, 1H, Ph); MS m/e 259 (M^+, 100), 186 (89), 172 (19), 157 (21); IR (KBr) 3436, 3332 cm^{-1} (NH_2).

2-Methyl-4-(4'-chloro-2'-fluoro-5'-ethylaminophenyl)-1,2,4-oxadiazolidine-3,5-dione (IIo). The mixture of **IIn** (0.43 g, 1.09 mmol) and Et_3OBF_4 (1 M CH_2Cl_2 solution, 2 m*l*) in CH_2Cl_2 (10 m*l*) was stirred for 1 h at room temperature. To remove excess Et_3OBF_4, $NaHCO_3$ (satd., 10 m*l*) was added into the reaction mixture with stirring. The organic layer was washed with water (10 m*l*), dried ($MgSO_4$), and concentrated. Column chromatography (*n*-hexane/EtOAc=2/1) gave **IIo** (53 mg, 17%): mp. 79.5-80.5℃; ^{1}H NMR ($CDCl_3$) δ 1.25 (t, J=7 Hz, 3H, CH_3), 2.80-3.20 (m, 2H, CH_2), 4.15 (br, 1H, NH), 6.45 (d, 1H, Ph), 7.10 (d, 1H, Ph); MS m/e 287 (M^+, 29), 272 (62), 199 (20).

2-Methyl-4-(4'-chloro-2'-fluoro-5'-ethoxycarbamidophenyl)-1,2,4-oxadiazolidine-3,5-dione (IIp). To a mixture of amine **IIn** (0.608 g, 2.34 mmol) and pyridine (0.222 g, 2.808 mmol) in CH_3CN (15 m*l*) was added ethylchloroformate (0.305 g, 2.81 mmol) and stirred for 20 min at room temperature. The reaction mixture was concentrated *in vacuo*, and purified by column chromatography (*n*-hexane/EtOAc=2/1) to give **IIp** (0.59 g, 76%): mp. 105-109℃; ^{1}H NMR ($CDCl_3$) δ 1.25 (t, J=7 Hz, 3H, CH_3), 3.35 (s, 3H, CH_3), 4.15 (q, J=7 Hz, 2H, CH_2), 7.05 (s, 1H, NH), 7.20 (d, 1H, Ph), 8.20 (d, 1H, Ph); MS m/e 331 (M^+, 83), 296 (46), 186 (62).

2-Methyl-4-(4'-chloro-2'-fluoro-5'-methylphenyl)-1,2,4-oxadiazolidine-3,5-dione (IIq). The mixture of nitrobenzene 7 (1.13 g, 4.20 mmol)[10] and iron powder (0.70 g, 4.20 mmol) in EtOH (10 m*l*) with a catalytic amount of HCl was refluxed for 30 min. After being cooled to room temperature, the reaction mixture was filtered off and the filtrate was concentrated. The residue was dissolved in conc. HCl (10 m*l*) and then added sodium nitrite (0.35 g, 5.0 mmol) in water (5 m*l*) dropwise at 0℃. After being stirred for 10 min, the reaction mixture was filtered. The filtrate was treated with an aqueous $CuCl_2$ solution (0.49 g, 5.0 mmol, 1 m*l* of water) at 50℃ for 30 min. The mixture was extracted with EtOAc (20 m*l*×3) and then the extract was dried ($MgSO_4$), concentrated. The residue was purified by column chromatography (*n*-hexane/EtOAc=4/1) to afford **IIq** (0.63 g, 58%): mp. 93℃; ^{1}H NMR ($CDCl_3$) δ 2.35 (s, 3H, CH_3), 3.45 (s, 1H, CH_3), 7.20 (d, 1H, Ph), 7.25 (d, 1H, Ph); MS m/e 258 (M^+, 100), 185 (37), 171 (24), 157 (23).

2-Methyl-4-(4'-chloro-2'-fluoro-5'-propargyloxyphenyl)-1,2,4-oxadiazolidine-3,5-dione (IIr). was prepared from **IIb** (1.0 g, 3.84 mmol), pyridine (0.364 g, 4.6 mmol) and propargyl chloride (0.34 g, 4.6 mmol) in a similar manner to that described for **IIc**: Yield 70%; mp. 139-142℃ (*n*-hexane/EtOAc); ^{1}H-NMR ($CDCl_3$) δ 2.58 (t, J=2 Hz, 1H, CCH), 3.45 (s, 3H, CH_3), 4.71 (d, J=2 Hz, 2H, OCH_2CC), 7.07 (d, 1H, Ph), 7.32 (d, 1H, Ph); MS m/e 298 (M^+, 100), 263 (24), 225 (31).

2-Methyl-4-(4'-chloro-2'-fluoro-5'-acetyloxyphenyl)-1,2,4-oxadiazolidine-3,5-dione (IIs). was prepared from **IIb** (0.5 g, 1.92 mmol), pyridine (0.18 g, 2.28 mmol) and acetyl chloride (0.17 g, 2.7 mmol) in a similar manner to that described for **IIc**: Yield 88%; mp. 92-93℃ (*n*-hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 2.30 (s, 3H, CH_3), 3.45 (s, 3H, CH_3), 7.20 (d, 1H, Ph), 7.35 (d, 1H, Ph); MS m/e 302 (M^+, 1.2), 260 (47), 187 (12).

2-Methyl-4-(4'-chloro-2'-fluoro-5'-methoxycarbamidophenyl)-1,2,4-oxadiazolidine-3,5-dione (IIt). The mixture of aniline **IIn** (0.4 g, 1.54 mmol), methyl chloroformate (0.175 g, 1.86 mmol) and pyridine (0.24 g, 3.0 mmol) in CH_2Cl_2 (12 m*l*) was stirred for 3 h at room temperature. The reaction mixture was washed with water (15 m*l*), dried ($MgSO_4$), and concentrated *in vacuo* to give **IIt** (0.42 g, 86%): mp 110-112℃; ^{1}H NMR ($CDCl_3$) δ 3.50 (s, 3H, CH_3), 3.80 (s, 3H, CH_3), 7.20 (br, 1H, NH), 7.40 (d, 1H, Ph), 8.40 (d, 1H, Ph); MS m/e 317 (M^+, 29), 282 (100), 209 (22), 185 (5).

2-Methyl-4-(4'-chloro-2'-fluoro-5'-trifluoroacetamidophenyl)-1,2,4-oxadiazolidine-3,5-dione (IIu). The mixture of aniline **IIn** (0.4 g, 1.54 mmol) and trifluoroacetic

anhydride (0.42 g, 2.0 mmol) in CH_2Cl_2 (12 m*l*) was stirred for 5 h at room temperature. The reaction mixture was washed with water (15 m*l*), dried ($MgSO_4$), and concentrated *in vacuo* to give anilide **IIu** (0.49 g, 92%): mp. 47-49℃ ; ^{1}H NMR ($CDCl_3$) δ 3.40 (s, 3H, CH_3), 7.30 (d, 1H, Ph), 8.40 (d, 1H, Ph); MS m/e 355 (M^+, 30), 320 (85), 247 (100).

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References

1. (a) G. Matolcsy, M. Nadasy, and V. Andriska, *Pesticide Chemistry*, Elsevier, Studies in Environmental Science 32 (1988); (b) D. R. Baker, J. G. Fenyes, and W. K. Moberg, *Synthesis and Chemistry of Agrochemicals II*, ACS Symposium Series 443, American Chemical Society, Washington D. C. (1991).
2. Methazole is a common name of 4-(3,4-dichlorophenyl)-2-methyl-oxadiazolidinone: for its metabolism see the references; (a) D. W. Jones and G. L. Foy, *Pestic. Biochem. Physiol.*, **2**, 8 (1972); (b) H. W. Dorough, R. A. Cardona, R. A. Cardona, and Lolmough, S. C.: *Drug Metabol. Disposition*, **2**, 129 (1974).
3. J. Kreuzer, US Patent 3437664; *Chem. Abstr.*, **71**, 38972x (1969).
4. L. Pauling and D. Pressman, *J. Am. Chem. Soc.*, **67**, 1003 (1945).
5. Activity (1 kg/ha) = 0.009 MR^3 − 0.697 MR^2 + 14.811 MR − 6.051.
6. G. Sato, E. Nagao, H. Oshio, and K. Kamoshita, *Pestic. Biochem. Physiol.*, **28**, 194 (1987).
7. in preparation and will be published elsewhere.
8. C. Hansch and A. Leo, *Substituent Constants for Correlation Analysis in Chemistry and Biology*, Wiley, New York (1979).
9. E. Nagao, S. Hashimoto, R. Yoshida, H. Matsumoto, H. Oshino, and K. Kamoshita, Europe Patent 61741 (1982); *Chem. Abstr.*, **98**, 71924p (1983).
10. 2-Methyl-4-(2'-fluoro-4'-nitro-5'-methylphenyl)-1,2,4-oxadiazolidine-3,5-dione **7** was prepared from (2-fluoro-4-nitro-5-methyl-acetanilide **5** in a same manner to that described for (**IIa**).

Di- and Triorganotin(IV) Complexes of Sulfur-containing Ylidenemalonates

Ok-Sang Jung*, Young-A Lee, Jongki Hong†, Jong Hwa Jeong‡, and Youn Soo Sohn*

Inorganic Chemistry Laboratory
†Advanced Analysis Center, Korea Institute of Science & Technology, Seoul 130-650
‡Department of Chemistry, Kyungpook National University, Taegu 702-701
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Organotin(IV) complexes of ylidenemalonates $(R_xSn)_{x-1}(O_2C)_2C=C(SR')_2$ (R = n-C_4H_9, C_6H_5, cyclo-C_6H_{11}, $CH_3OOCCH_2CH_2$; x=2,3; R' = CH_3, R_2' = -$CHCH$-, -CH_2CH_2-) have been synthesized and characterized by means of various spectroscopic methods. The X-ray crystal structure of $(Ph_3Sn)_2(O_2C)_2C=C(SCH_3)_2$ has been determined (Pi; a = 9.704(2) Å, b = 14.412 (1) Å, c = 14.760(3) Å, α = 74.26(1)°, β = 99.38(1)°, γ = 79.09(1)°, V = 1950.7(7) Å^3) and refined to R = 0.045. The crystal structure discloses a discrete molecule with bidentate-like carboxylate ligand. For diorganotin analogues, the structures are discussed in terms of IR, ^{1}H-NMR, ^{13}C-NMR, and FAB mass spectrometry. The mass spectrum indicates that the diorganotin complexes of ylidenemalonates are dimeric.

Introduction

Organotin carboxylates have received considerable attention because of industrial applicability such as homogeneous catalysts, agricultural biocides, and pharmaceutical properties[1-5] and in part because of various bonding modes of carboxylate ligands[6-8]. Even though a variety of papers on the organotin compounds of monocarboxylate ligand have been reported, dicarboxylate analogs have not been investigated extensively so far. In order to expand this chemistry this paper will describe the preparation and spectroscopic properties of the di- and triorganotin complexes of sulfur-containing ylidenemalonate ligands.

Experimental

Materials and Instruments. Organotin compounds were purchased from Alfa or Strem chemicals and used without further purification. $(CH_3OOCCH_2CH_2)_2SnCl_2$ was prepared by the literature method[9]. $(EtO_2C)_2C=C(SR)_2$(R = CH_3 R_2 = -CH_2CH_2-, -$CHCH$-) were also prepared according to the known procedure[10,11] and hydrolyzed by the standard method.

Chemical analyses were carried out by the Advanced Analysis Center at KIST. Melting points were measured on