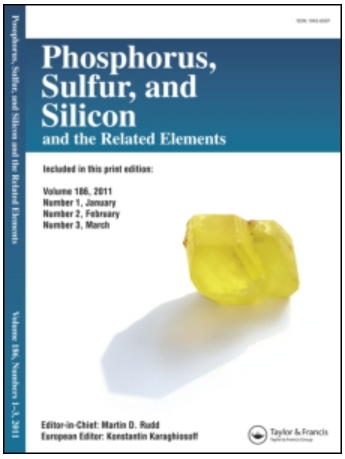

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Synthesis and Biological Activities of Methyl 1-(5-Methyl Isoxazol-3-oxy Acetoxy) Alkyl Methyl Phosphinates

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SYNTHESIS AND BIOLOGICAL ACTIVITIES OF METHYL 1-(5-METHYL ISOXAZOL-3-OXY ACETOXY) ALKYL METHYL PHOSPHINATES

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Methyl 1-(5-methyl isoxazol-3-oxy acetoxy) alkyl methyl phosphinates were synthesized by the condensation of O-methyl methyl 1-hydroxyalkyl phosphinates moiety with 5-methyl isoxazol-3-oxy acetyl chloride and were tested for plant growth regulatory activity and herbicidal activity. Some compounds exhibited notable plant regulatory activity and herbicidal activity.

Keywords: Herbicidal activity; isoxazole-substituted phosphinates; plant regulatory activity; synthesis

INTRODUCTION

The useful biological properties of compounds containing the isoxazole ring have received special attention. There are several naturally occurring isoxazoles with important biological activity, such as Musimol and 4-Hydroxy isoxazole, which is a seed-germination inhibitor.[1] Their structure has been used as the basis for the design of a number of synthetic isoxazole derivatives, which were developed as commercial agrochemicals.[2]

In our previous work, it was shown that certain aryloxy acetoxy alkyl phosphonates or phosphinates possess good herbicide activities and plant growth regulatory activity.[3,4] In order to find new phosphinates with better pesticide activity, the isoxazole structural unit is introduced into their molecules, so a novel series of methyl 1-(5-methyl isoxazol-3-oxy acetoxy) alkyl methyl phosphinates were synthesized and screened for their plant growth regulatory activity and herbicidal activity.

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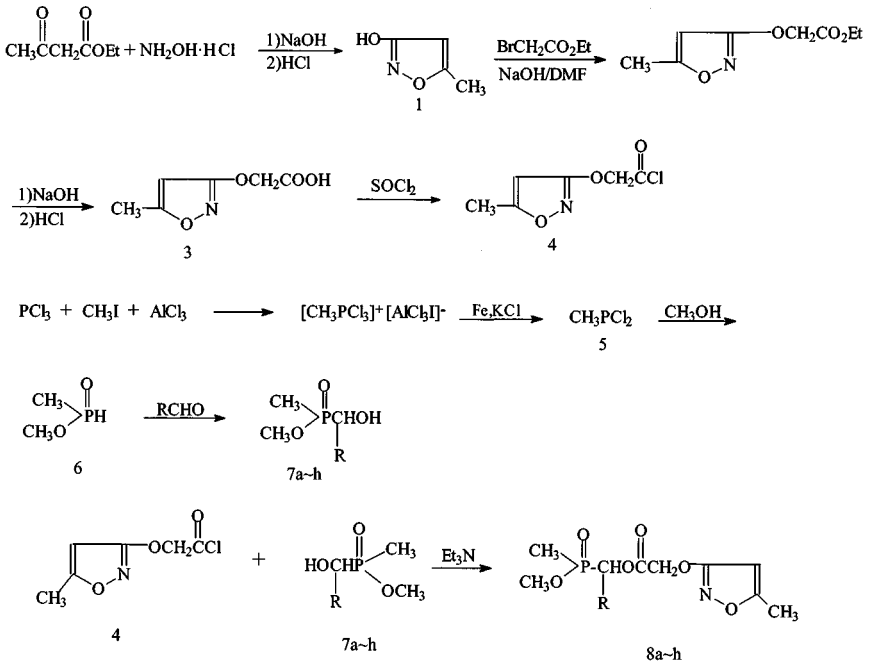
RESULTS AND DISCUSSIONS

Synthesis of Methyl 1-(5-methyl Isoxazol-3-oxy Acetoxy) Alkyl Methyl Phosphinates

The title compounds were synthesized by means of the multistep procedure outlined in Scheme 1.



SCHEME 1 R = —Ph, p-MePh, o-ClPh, p-MeOPh, m-NO_2Ph, —Pr, —Et, —Me.

5-Methyl-isoxazol-3-oxy acetyl chloride **4** was prepared by four-step procedure using acetyl pyruvate and hydroxylamine hydrochloride as starting material. Hydroxylammonium chloride dissolved in sodium hydroxide reacted with acetyl pyruvate below 0°C for 1 h keeping pH = 10, then dealt with by ice-cooled concentrated hydrochloric acid to give 5-methyl-3-isoxazolol in 70% yield.[5] 5-Methyl-isoxazol-3-oxy acetic ester **2** prepared by the reaction of sodium 5-methyl-3-isoxazolate with bromoacetic ester in DMF for 3 h at 0~5°C. In order to complete the reaction, the mixture was left overnight at room temperature. Intermediate **2** was converted to 5-methyl-isoxazol-3-oxy acetic acid **3** in 48% overall yield by using 5% sodium hydroxide followed by 10% hydrochloric acid. 5-Methyl-isoxazol-3-oxy acetyl chloride **4** can be

easily obtained in 80% yield by treating the compound **3** with thionyl chloride.

O-methyl methyl 1-hydroxy alkyl phosphinates **7** were prepared by addition of dimethyl phosphinate **6** and several kinds of aliphatic aldehydes, aromatic aldehydes using triethylamine as catalyst.[6] 7a∼h were obtained in 53∼69% yields. Preparation of dimethyl phosphinate **6** was accomplished in two-step sequence starting from phosphorus trichloride, methyl iodide, and aluminium trichloride.[7] Thus, methyl 1-(5-methyl isoxazol-3-oxy acetoxy) alkyl methyl phosphinates **8** were synthesized by the condensation of 5-methyl isoxazol-3-oxy acetyl chloride **4** with O-methyl methyl 1-hydroxy alkyl phosphinates **7**. The reaction mixture of compound **7** (0.05 mol) and **4** (0.06 mol) was stirred cooled in an ice-water bath and triethylamin added dropwise below 0°C, then stirring at room temperature for 4∼6 h to give title compounds 8a∼h in 33∼65% yields, and all compounds have been identified by ^{1}H-NMR, IR and elemental analysis.

Biological Activities

Title compounds **8**a∼h were tested for plant growth regulatory by wheat (*Triticum aestivum L.*) coleoptile and cucumber (*cucumis satival L.*) cotyledon test.[8] As seen from Table I, most of the compounds had stimulating activity to the growth of wheat coleoptile and cucumber cotyledon root at 10 ppm and 100 ppm. The compound 8a, 8e inhibited the growth

TABLE I Growth Regulatory Activity of 8a∼h

	Wheat coleoptile		Cucumber cotyledon root
No.	100 ppm (%)	10 ppm (%)	10 ppm (%)
8a	−0.5	+3.8	−75
8b	−13.5	+18.9	+12.5
8c	+16.8	+40.5	+50
8d	+5.9	+12.4	+50
8e	+28.6	+12.4	−100
8f	+13.5	+8.1	+75.0
8g	+21.1	−2.7	+87.5
8h	+14.6	+21.1	+37.5
IAA		+14.3	+150
ABA	−16.3		

+, Stimulation; −, inhibition.

IAA—Indole acetic acid; ABA—abscisic acid.

The rates were determined by percentages of the averaged lengths of wheat coleoptile or root of treated plants to those of controls at 3-day growth.

of cucumber cotyledon root at 10 ppm, and 8b, 8c, 8h exhibited higher stimulating activity to the growth of wheat coleoptile than IAA at 10 ppm, but their stimulating activity to the growth of cucumber cotyledon root at 10 ppm was somewhat lower compared with that of IAA.

The herbicidal activity of compounds 8a∼h was also evaluated in a set of experiments in a greenhouse. They were tested for pre-emergence and post-emergence herbicidal activity on *Triticum aestirum L.* (wheat), *Digitaria sanguinalis scop* (ascendent crabgrass), *Echinochloa crusgalli* (barngard grass), *Brassica campestris L.* (rape), *Cucumis satvba L.* (cucumber), *Lactuca sativa L.C., V. sacramento* (lettuce), and *cirsium japonicum D. C*. (setose thistle).

Plastic pots were packed with sandy clay loam soil and water was added up to 3 cm in depth. In the pre, seeds of plant were sown, a diluted suspension of each compound containing acetone and Tween 80 were applied into the pots at 2,250 a.i. g/ha. Fifteen days later, the pre-emergence herbicidal activity against each weed was visually evaluated, and the solution of the chemicals tested was applied to the foliage of plants grown at 2 to 3 leaves stage with a sprayer at the rate of 2,250 a.i. g/ha with a spelling volume of 1000 L/ha. Visual assessment was conducted 15 days after treatment on a scale of values of zero (no effect) to 100 (dead). The post-emergence herbicidal activity against each weed was evaluated. The results showed that the compounds 8a and 8e (pre and post) displayed 100% inhibitory effect against *curcumas sativa L.*; 8a and 8b had 100% (post), and 8e and 8g had 82∼90% (pre) inhibitory effect against *cirsium juponicum D. C.*; 8b also displayed 100% post inhibitory effect against *Digitaria sanguinalis scop.* and 8a displayed 100% (pre and post) inhibitory effect against *Lactuca sativa L.C., V. sacramento.*

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