Note

Novel Inhibitory Compounds against the Spore Germination of *Pyricularia oryzae*: 3-(ω -Amino)alkyl-4-hydroxy-5,5-dimethyl-4-phenyl-2-oxazolidinone Derivatives

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The utilization of carbon dioxide is an important and intriguing task, since CO_2 is nontoxic and the most common carbon resource. We have studied the synthesis of compounds having biological activities by reactions involving carbon dioxide incorporation into organic compounds. The reactions of oxiranes with carbon dioxide and aliphatic amines gave 2-oxazolidinones,¹⁾ tetrahydro-2H-1,3-oxazin-2-ones,²⁾ and other carbamate derivatives.^{2,3)} We recently reported that carbon dioxide reacted with oxiranes in the presence of α,ω -diamines to give bis(2-oxazolidinones)⁴⁾ and 3-(ω -amino)alkyl-2-oxazolidinones.⁴⁾ In this report, we synthesized novel 3-(ω -amino)alkyl-2-oxazolidinones bearing a long ω -aminoalkyl chain, and examined the inhibitory activities of these compounds against the spore germination of *Pyricularia oryzae*,⁵⁾ to find that 3-(ω -amino)alkyl-4-hydroxy-5,5-dimethyl-4-phenyl-2-oxazolidinones **1** are novel inhibitors.

3-(10-Amino)decyl-4-hydroxy-5,5-dimethyl-4-phenyl-2-oxazolidinone **1c** was synthesized by the reaction of 2-methoxy-3,3-dimethyl-2-phenyloxirane (**2**)¹⁾ with carbon dioxide and 1,10-diaminodecane in methanol (Fig. 1). The structure of **1c** was determined on the basis of the following physical data: The IR spectrum of **1c** gave an absorption at 3340 cm^{-1} , indicating the existence of a free amino group, and a carbonyl absorption at 1745 cm^{-1} corresponding to that of 2-oxazolidinones.¹⁾ The molecular formula and weight of **1c** were $\text{C}_{21}\text{H}_{34}\text{O}_3\text{N}_2$ and m/z

FIG. 1.

TABLE I. INHIBITORY ACTIVITY AGAINST THE SPORE GERMINATION OF *Pyricularia oryzae*

Compound	mp (°C)	Inhibitory activity ^a		
		Concentration (ppm)		
		50	100	200
1a	80~81	—	—	—
1b	79~80	—	++	++++
1c	83~84	+	++++	++++
1d	91~92	—	++	++++

^a Symbols show the ratio of spores not germinated + + + +, 100%; + + +, 99~91%; + +, 90~61%; +, 60~41%; —, under 40%.

363 ((M+1)⁺) respectively, by mass spectral analysis. Furthermore, the ^1H -NMR data supported that the structure was correct.

The oxazolidinones **1** were tested for inhibitory activity against the spore germination of *P. oryzae*. As shown in Table I, the length of the ω -aminoalkyl chain at the 3-position of **1** greatly influenced the inhibitory activity; namely, those derivatives having an ω -aminoalkyl chain length less than the C_6 methylene chain were found to have no activity, while **1b** having a C_8 -methylene chain showed moderate activity. The dodecamethylene compound **1c** showed the strongest activity, inhibiting 41~60% of the spore germination of *P. oryzae* at 50 ppm. The activity of **1d**, however, was slightly weaker than that of **1c**. Although shortening the methylene chain of the ω -aminoalkyl group of **1** tended to decrease the activity, the reason for this phenomena is not apparent. Bis(2-oxazolidinones) **3** obtained as by-products in the reaction did not show any activity. Also, **1c** showed the inhibitory activity against *Botrytis cinerea* and *Rhizoctonia solani*. The activity of **1** does not fully comply with that of other fungicides,⁶⁾ but **1** seems to have potential for developing new types of fungicides. It is interesting that useful compounds having inhibitory activity against the spore germination of *P. oryzae* have been obtained by re-

actions involving carbon dioxide incorporation into organic compounds under mild conditions.⁴⁾

EXPERIMENTAL

Melting points (mp) are uncorrected. IR spectra were recorded with a Perkin-Elmer 599 spectrophotometer by the KBr disk method. NMR spectra were measured on a JEOL FX-100 spectrometer using TMS as an internal standard. Mass spectra were recorded with a JEOL JMS-3000 mass spectrometer by the CI method.

*Inhibitory activity test for the spore germination of P. oryzae*⁷⁾: **1** (2 mg) was dissolved in ethanol (0.3 ml), and the ethanol solution was made up to 2 ml with a 100 ppm aqueous solution of Tween-80. This solution (a 1000 ppm solution of **1**) was diluted to prepare the desired concentration with a 100 ppm solution of Tween-80. The solution (1 ml) containing spores of *P. oryzae* (8×10^5 /ml) and the solution (1 ml) of **1** were mixed sufficiently, and the mixed solution was dropped on to slideglass that was then put in an incubator for 24 hr at 25°C. The number of spores of *P. oryzae* that had not germinated were finally counted under a microscope.

3-(10-Amino)decyl-4-hydroxy-5,5-dimethyl-4-phenyl-2-oxazolidinone **1c**, 3,3'-decamethylenebis[4-hydroxy-5,5-dimethyl-4-phenyl-2-oxazolidinone] **3c**, 3-(12-Amino)dodecyl-4-hydroxy-5,5-dimethyl-4-phenyl-2-oxazolidinone **1d**, and 3,3'-dodecylmethylenebis[4-hydroxy-5,5-dimethyl-4-phenyl-2-oxazolidinone] **3d**. These compounds were synthesized according to the procedure described for **1b** and **3b** in the previous paper.⁴⁾ **1c**. Yield 32%, mp 83~84°C (ethanol). Found: C, 69.33; H, 9.35; N, 7.35; MS (*m/z*), 363 ((*M*+1)⁺). Calcd. for C₂₁H₃₄O₃N₂: C, 69.58; H, 9.45; N, 7.73%. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3340 (NH, OH), 1745 (C=O). NMR (CDCl₃) δ : 0.89 (3H, s, -CH₃), 1.23 (14H, br. s, -(CH₂)₇-), 1.48 (3H, s, -CH₃), 1.60~1.98 (2H, m, NH₂-CH₂-CH₂-), 2.47~2.78 (2H, m, -N-CH₂-),

2.81~3.40 (2H, m, NH₂-CH₂-), 7.40 (5H, br. s, -Ph). **3c**. Yield 6%, mp 162~163°C (benzene-hexane). Found: C, 68.66; H, 7.91; N, 5.11%, MS (*m/z*), 553 ((*M*+1)⁺). Calcd. for C₃₂H₄₄O₆N₂: C, 69.54; H, 8.02; N, 5.07%. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1745 (C=O). **1d**. Yield 14%, mp 91~92°C (benzene-hexane), Found: C, 70.02; H, 9.61; N, 6.95%; MS (*m/z*), 391 ((*M*+1)⁺). Calcd. for C₂₃H₃₈O₃N₂: C, 70.73; H, 9.81; N, 7.17%. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3340 (NH, OH), 1740 (C=O). NMR (CDCl₃) δ : 0.89 (3H, s, -CH₃), 1.23 (18H, br. s, -(CH₂)₉-), 1.48 (3H, s, -CH₃), 1.60~2.04 (2H, m, NH₂-CH₂-CH₂-), 2.50~2.78 (2H, m, -N-CH₂-), 2.78~3.45 (2H, m, NH₂-CH₂-), 7.40 (5H, br. s, -Ph). **3d**. Yield 3%, mp 137~138°C. Found: C, 70.09; H, 8.10; N, 4.88; MS (*m/z*), 581 ((*M*+1)⁺). Calcd. for C₃₄H₄₈O₆N₂: C, 70.31; H, 8.33; N, 4.82%. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1740 (C=O).

REFERENCES AND NOTES

- 1) (a) T. Toda, *Chem. Lett.*, 1977, 975; (b) T. Toda, *Nippon Kagaku Kaishi*, **1982**, 282, and references therein.
- 2) (a) T. Asano, N. Saito, S. Ito, K. Hatakeda and T. Toda, *Chem. Lett.*, **1978**, 311; (b) N. Saito, K. Hatakeda, S. Ito, T. Asano and T. Toda, *Nippon Kagaku Kaishi*, **1986**, 1196.
- 3) (a) Y. Yoshida and S. Inoue, *Chem. Lett.*, **1977**, 1375; (b) Y. Yoshida and S. Inoue, *J. Chem. Soc., Perkin Trans. I*, **1979**, 3146.
- 4) N. Saito, K. Hatakeda, S. Ito, T. Asano and T. Toda, *Bull. Chem. Soc. Jpn.*, **59**, 1629 (1986).
- 5) A. Kamiyama and S. Tuda, "Seibutu no Bogyo Sayo," ed. by M. Nakazima, T. Goto and N. Takahashi, Kagaku Dozin, Tokyo, 1978, p. 66.
- 6) Isoprothiorane, Phthalide, Kasugamycin, *etc.* are well used to control rice blast disease.
- 7) S. Sato, M. Goto and H. Hori, "Syokubutu Byorigaku Zikken Hou," Kodansha, Tokyo, 1983, p. 214.