

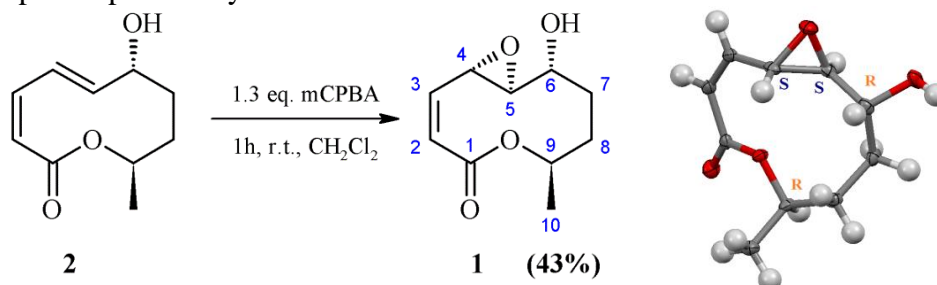
PR-11
SEMI-SYNTHETIC PREPARATION AND STRUCTURE CLARIFICATION
OF CURVULIDE A

Slukin A. P.,¹ Fedorov A.N.,^{1,2} Stukalova M. P.,² Dubovik V. R.,² Dalinova A. A.²

¹*Saint-Petersburg State University of Industrial Technologies and Design,*
198095, Russia, St. Petersburg, 4 Ivana Chernykh St.;

²*All-Russian Institute of Plant Protection, 196608, Russia, St.Petersburg, 3Podbelskogo highway*
 E-mail: anton.slukin@bk.ru

Abstract. Toxic secondary metabolites of phytopathogenic microorganisms are promising candidates for development of biorational herbicides. Among such compounds ten-membered lactones (nonenolides) represent significant potential as models for the development of herbicides with mechanisms of action different from widely used agrochemicals. Members of this extensive family of fungal secondary metabolites have a relatively simple structure and at the same time possess a wide range of biological activity¹. Phytotoxic nonenolide curvulide A **1** previously isolated from *Curvularia sp.*² was also found in the culture filtrate of the phytopathogenic fungus *Stagonospora cirsii* S-47. This compound has been little studied in terms of biological activity due to its low yield from fungal cultures. Structurally related analogue of compound **1** stagonolide E **2** is also produced by fungus *S. cirsii* with a higher yield, which makes this compound a convenient precursor for semi-synthetic curvulide A. For this purpose we developed stereoselective epoxidation of **2** using simpler and faster Prilezhaev method instead of Sharpless method reported previously.³



The synthesis was carried out using 30% excess of *m*-chloroperoxybenzoic acid in dichloromethane solution. Based on chromatographic and spectral data we found that only *syn*-epoxide was formed during the reaction. *Syn*-epoxidation of in this case can be explained by the Henbest phenomenon.⁴ Analysis of the reaction mixture composition and purification of the oxidation product was performed by HPLC. Semi-synthetic curvulide A was obtained in 43% yield and its structure was confirmed by spectral methods (1D/2D NMR) as well as XRC. The crystal structure of curvulide A along with crucial *J*(H5–H6) coupling constants gives absolute configurations of stereogenic centers as 4*S*, 5*S*, 6*R*, 9*R* that disproves previously proposed hypothesis³ about configuration of C4 and C5.

References

1. Sun P., Lu S., Ree V., et al. Nonanolides of Natural Origin: Structure, Synthesis, and Biological Activity. *Current Medicinal Chemistry*. 2012, v. 19, iss. 20, pp. 3417–3455.
2. Greve H., Schupp P. J., Eguereva E. et al. Ten-Membered Lactones from the Marine-Derived Fungus *Curvularia sp.* *Journal of Natural Products*, 2008, v. 71, iss 9, pp. 1651–1653.
3. Schmidt B., Kunz O. Bidirectional cross metathesis and ring-closing metathesis/ring opening of a C₂-symmetric building block: a strategy for the synthesis of decanolide natural products. *Beilstein J. Org. Chem.* 2013, v. 9, pp. 2544–2555.
4. Davies S. G., Fletcher A. M., Thomson J. E. Hydrogen bond directed epoxidation: diastereoselective olefinic oxidation of allylic alcohols and amines. *Organic & Biomolecular Chemistry*, 2014, v. 12, iss. 26, p. 4544.

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