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3 Reprint requests to D.T., Laboratory of Organic Chemistry, Patras University, Patras (Greece).

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Identification and efficient synthesis of 6-methoxy-2-benzoxazolinone (MBOA), an insect antifeedant

I. Kubo and T. Kamikawa[1]

Division of Entomology and Parasitology, College of Natural Resources, University of California, Berkeley (California 94720, USA), and Faculty of Science, Osaka City University, Sugimoto-cho, Sumiyoshi-ku, Osaka 558 (Japan), October 13, 1982

Abstract. The identification and an efficient synthesis of 6-methoxy-2-benzoxazolinone (MBOA), an insect antifeedant in *Zea mays* is reported.

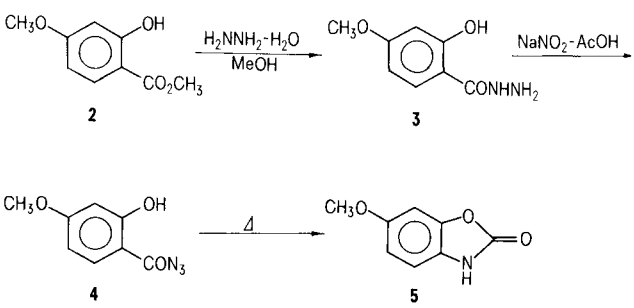
African armyworm, *Spodoptera exempta* larvae feed almost exclusively on graminaceous plants. Nevertheless, during our study some chromatographic fractions of a hexane extract of maize, *Zea mays*, a favored host plant for this insect species, actually deter feeding with leaf disk bioassay[2].

The active antifeedant principle, $C_8H_7O_3N$, m.p. 160–161 °C was identified as 6-methoxy-2-benzoxazolinone (MBOA) by spectroscopic data (UV, IR, MS and NMR). This compound was previously reported as a host plant resistant factor against European corn borer in *Z. mays*[3]. Possibly, this is also the case against African armyworm. ED_{50}-value of MBOA against this pest insect with a feeding assay is 500 ppm. MBOA also exhibits an inhibitory effect on growth of silkworm, *Bombyx mori* larvae with another feeding assay[4]. More recently, MBOA has been suggested to be a naturally occurring environmental cue affecting reproductive cycles in many mammals[5].

This simple chemical structure with unique biological activities is of primary synthetic interest for both determining the structure-activity relationships and elucidating mode of action at the biochemical and physiological levels.

Although the synthesis of MBOA is known[6–8], the reported overall yields are quite low, being 17% at best. In this paper, we report a synthetic scheme with which we were able to obtain 33% yield of MBOA.

In our scheme, commercially available 4-methoxysalicylic acid (**1**) is used as starting material. Brief treatment with diazomethane 1 gave the methyl ester (**2**), which was then converted to the hydrazide (**3**) with hydrazine hydrate in 60% yield. Diazatization of 3 with sodium nitrite gave the crystalline keto azide (**4**) (m.p. 96–97.5 °C) in 72% yield, which on pyrolysis in xylene afforded the isocyanate intermediate by Curtius rearrangement and proceeded with concomitant intramolecular addition of phenolic hydroxyl group to give 6-methoxy-2-benzoxyzolinone (**5**) (m.p. 168–170 °C) in 85% yield. The overall isolated yield of **5** was 33% from **1**. The synthetic products were identical in all respects with the natural product (m.p. and IR- and NMR-spectra).



2 **3** **4** **5**

1 This study was initiated since the hexane extract of *Z. mays* was found to induce biting responses without actual feeding (ingestion) responses. The authors thank A. Chapya and S. Asano for technical assistance.

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