SHORT STEP SYNTHESSES OF (+)-DIPLODIATOXIN

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(+)-Diplodiatxin is a mycotoxin isolated from maize infected with *Diplodia maydis*, causal fungus of the disease "dry rot", which causes a disease, diplodiosis, among cattle and sheep in Southern Africa. The first symptoms of the disease are lachrymation, salivation and a slight quivering of the muscles of shoulder and flank, and the cause of death is muco-enteritis and nephritis (ref.1). The toxic principle, diplodiatxin, was extracted from the infected maize and the planar structure was elucidated on the basis of spectroscopic data and chemical reactions in 1972 (ref.2). Tentative configuration of the mycotoxin has been deduced as 1 from the known data and extensive comparison of ¹H NMR spectra of 1 with those of betaenone B (ref.3), and whole stereostructure including absolute configuration has been confirmed by the total syntheses of (+)-diplodiatxin according to the retrosynthesis shown in Fig.1 (ref.4).

The key step involves an intramolecular Diels-Alder reaction of a (E,E,E)-trienone 2. The trienone 2 may be divided into the three segments, (a), (b) and (c). Segments (a) and (c) are known or readily accessible compounds. Segment (b) has been derived from D-glucose through multi-steps in the first syntheses of 1. In search of new effective methods, we have developed short step syntheses of (+)-diplodiatxin through chiral cis-3,5-dimethyltetrahydropyran-2-ones, which are prepared by two methods.

i) By enzymatic oxidation; (3S,5R)-3,5-dimethyltetrahydropyran-2-one(3) was

prepared by known enzymatic oxidation of 2,4-dimethyl-1,5-pentandiol. The lactone 3a was converted to the aldehyde 4, segment (b) equivalent (Fig.2).

Fig. 2

ii) By optical resolution; treatment of the racemic lactone with D- α -phenethylamine gave a diastereomeric mixture 5. The mixture was converted to silylated derivatives, which were easily separated to diastereomers, 6a and 6b. After acid treatment, each of these 6a and 6b was transformed to the lactones 3a and 3b respectively (Fig.3). The enantiomeric lactone 3b was easily converted to segment (b) (Fig.4).

Fig. 3

Fig. 4

The latter method has made possible to provide sufficient amount of intermediates for the studies of structure-activity relationship and biosynthesis.

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