STUDIES DIRECTED TOWARD THE TOTAL SYNTHESIS OF (+)-GRISEOVIRIDIN

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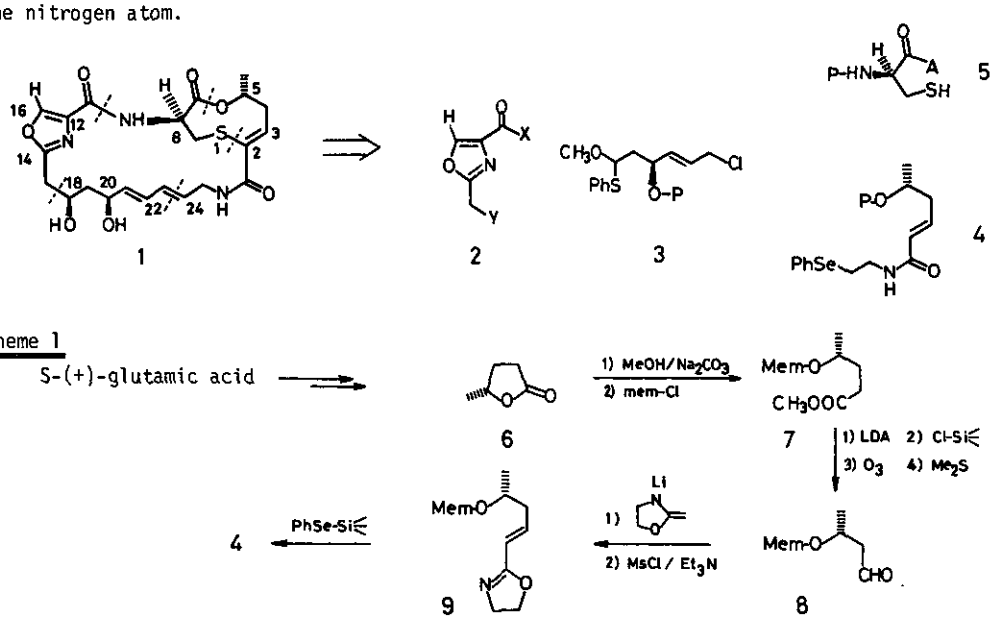
Recent approaches to the convergent total synthesis of (+)-griseoviridin (1), one of the streptogramin family of antibiotics, which requires four fragments 2, 3, 4, and 5, are described. The fragment 4 corresponding to O(6)-C(5)–C(2)-C(27)–C(24) framework was prepared as outlined in Scheme 1, starting from (S)-(+)-glutamic acid as chiral template. An optically pure γ-methyl-γ-butyrolactone, derived from the amino acid through well-known procedures, was successfully converted to aldehyde 8, which was subsequently condensed with lithio-oxazoline to afford key intermediate 9. The final step in Scheme 1 can be realized in terms of an imidatonium-initiated nucleophilic ring opening reaction by $PhSe^-$ anion. This reaction has been developed recently in our laboratory as a convenient method for the synthesis of secondary amide carrying a functionalized substituent on the nitrogen atom.



The fragment 3 was also elaborated by the use of glutamic acid as chiral template. Easily available γ-hydroxymethyl-γ-butyrolactone from R-(-)-glutamic acid was converted to the desired fragment 3 in eight steps. Not only a detail for such transformation but also a chemistry about combination between the fragments 3 and 4 will be presented.