BIOTECHNOLOGY

Edited by C. F. PHELPS and P. H. CLARKE

The fourteen contributions forming this volume were presented at a London meeting of the Biochemical Society including the Society’s Forty-Eighth Symposium “Biotechnology”, in December 1982. With today’s increasing pressures to develop latest laboratory findings into practical industrial processes as quickly as possible the chosen theme of this Symposium was a timely one. The papers represent up-to-date reports from international biochemists whose work is of direct relevance to the wide areas of interests concerned with biotechnology, together with glimpses of the early development of its techniques and a look at its exciting future.

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Macrolactonization (the synthesis of large-ring lactones) has become a subject of interest in recent years, due primarily to the presence of these ring systems (usually 12 to 16 carbons) in several important macrolide antibiotics. The most efficient macrolactonization methodology starts with an ω-hydroxy carboxylic acid which is treated with a reagent that induces ring closure (internal esterification) by activation of either the carboxyl or the hydroxyl group or both.

**Carboxyl-Group Activators:**

Treatment of ω-hydroxy carboxylic acids with 1,1'-carbonyldiimidazole (CDI) affords acylimidazolides which undergo internal alcoholsysis on treatment with base, e.g., the synthesis of (±)-pyrenophorin.

Acyl imidazolides have also been prepared from phenyl or 2,2,2-trifluoroethyl esters with N-(trimethylsilylimidazolide).

**2-Chloro-1-methylpyridinium iodide** in the presence of triethylamine effects cyclization in moderate yields.

**Mercuric trifluoroacetate**-induced cyclization of thiol esters has been applied to the syntheses of methymycin and zearalenone.

An equimolar mixture of 1-phenyl-1H-tetrazole-5-thiol and tert-butyl isocyanide has recently been reported to effect macrolactonization under mild conditions.

**Hydroydic-Group Activator:**

The Mitsunobu reaction [diethyl azodicarboxylate (DEAD), triphenylphosphine] affords lactones via OH-activation followed by nucleophilic attack of the carboxylate anion generated in situ, e.g., the synthesis of (±)-vermiculene.

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**Carboxyl-Hydroxyl Activator:**

The Corey-Nicolau "double-activation" method employing 2-pyridyl disulfide (Aldrithiol-2) effects faster macrolactonization under mild conditions. It affords good yields of lactones containing 12 to 21 carbon atoms and has been employed in the syntheses of several complex macrolides including carpaine, vertaline, erythronolide B, and brefeldin A.

2,2'-Dithiobis(4-tert-buty1-1-isopropylimidazole) affords higher yields of macroyclic lactones under milder conditions than with Aldrithiol-2.