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PREFACE

The anthracyclines were first encountered by chemists nearly a half century ago and the earliest efforts at structural characterization appeared in the literature in the 1950's; but it is only within the past ten or so years that the anthracyclines have captured the attention of the synthetic community. The principal events which spawned such enormous interest in anthracycline synthesis are the discovery of Adriamycin (doxorubicin) and the recognition of its broad efficacy in the treatment of human cancers.

The first reports of Adriamycin's structure and chemotherapeutic potential were published in 1969. Clinical vindication of its promise soon followed and the usually cautious Federal Drug Administration (FDA) approved it as a prescription drug in the U.S. in 1974. Initially dubbed the "Red Death" by physicians as a consequence of its severe toxicity, modified administration regimes and advances in combination therapy have propelled Adriamycin's annual worldwide sales to $150,000,000 (1983). Nonetheless, the toxicity problems attending Adriamycin have also stimulated a quest for second generation analogs which retain the efficacy of Adriamycin but lack some of its drawbacks.

Like Gaul, the synthesis of anthracyclines is divisible into three parts: fabrication of the aglycone, preparation of the sugar residue and coupling of the two. All three elements of the problem have provoked noteworthy responses, but it is the synthesis of the aglycones—the anthracyclinones—which has particularly engaged the interest of synthetic organic chemists. It is that aspect of anthracycline chemistry which is the topic of this Symposium.

Since its infancy only ten years ago, the field of anthracyclinone synthesis has developed rapidly. The synthetic challenge posed by anthracyclinones has evoked numerous solutions which are both conceptually innovative and experimentally challenging. It seems safe to say that anthracyclinone synthesis has now attained a certain maturity. This Symposium was undertaken with three principal goals: (1) to assemble in one place a selection of the diverse synthetic approaches that lead to anthracyclinones; (2) to provide a forum for the contribution of recent, previously unpublished developments and (3) to offer an opportunity—and perhaps an incentive—for those who have previously confined their reports to brief communications to expand on the strategic and tactical considerations which underlie their approaches and to elaborate on the experimental details of their execution.

I would like to take this opportunity to thank all who are participating in the Symposium for their contributions and their cooperation.

June, 1984

T. Ross Kelly