STUDIES ON THE SYNTHESIS OF HETEROANTHRACYCLINES

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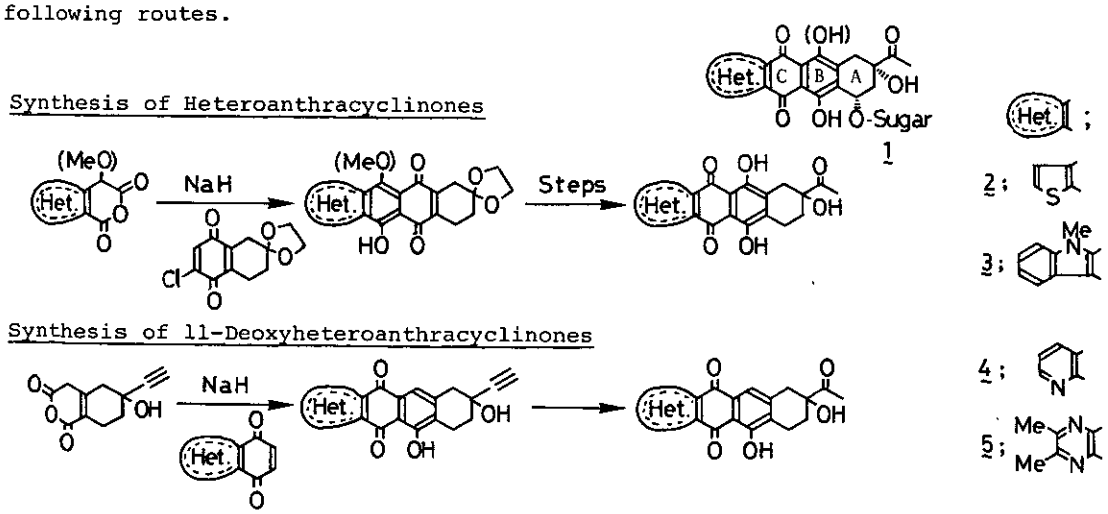
The anthracyclines are used widely in the clinical treatment of a range of human malignancies, but they have severe risk of cardiotoxity attending their administration. There is an urgent need to decrease side effects in these valuable agents by appropriate structural modification. In some clinical drugs, it has been known that heteroaromatic ring can bring about useful isosteric replacement of the benzene ring. Recently, we have reported[1] a short convergent synthesis of various types of anthracyclinones by using a strong base induced cycloaddition of homophthalic anhydrides and related anhydrides to appropriately functionalized quinones and now apply this method to a facile synthesis of late-stage key intermediates (2-5) for anthracycline isosters (1) modified at the D-ring as shown in the following routes.



1) Y. Tamura, A. Wada, M. Sasho, K. Fukunaga, H. Maeda, and Y. Kita, J. Org. Chem., 47, 4376 (1982); Y. Tamura, S. Akai, M. Sasho, and Y. Kita, Tetrahedron Lett., 25, 1167 (1984); Y. Tamura, M. Sasho, S. Akai, A. Wada, and Y. Kita, Tet., 40, 4539 (1984); Y. Tamura, M. Sasho, H. Ohe, S. Akai, and Y. Kita, Tetrahedron Lett., 26, 1549 (1985).