FACULTY RESEARCH EDITION

of

The Savannah State College Bulletin

Published by

The Savannah State College

Volume 23, No. 2 Savannah, Georgia December, 1969

HOWARD JORDAN, JR., *President*

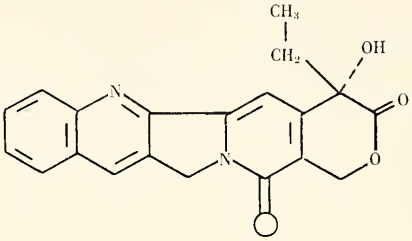
Articles are presented on the authority of their writers, and neither the Editorial Committee nor Savannah State College assumes responsibility for the views expressed by contributors.

Table of Contents

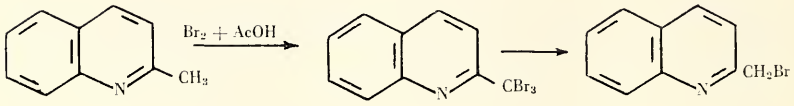
Studies In The Synthesis of Camptothecin Part I, Preparation of N-methylamino-2-quinanylmethane

By Kamalakar B. Raut

In 1966, Wall and co-workers isolated Camptothecin,[1] an alkaloid with a novel ring system exhibiting potent antilukemic and antitumor activities in animals from the tree *Camptotheca Acuminata, Nyssaceae.* In order to study the possibility of its synthesis it was necessary to prepare N-methylamino-2-quininylmethane. The present paper describes this preparation. The reactions are given below briefly.



I



The starting material was 2-methylquinoline (quinaldine) which was converted by bromine and acetic acid to w-tribromoquinaldine according to method of Hammick.[2] A number of methods is available for converting w-tribromoquinaldine to w-monobromoquinaldine. The most useful method was to heat w-tribromoquinaldine and tetralin.[3] The w-monobromoquinaldine was treated with methylamine and the hydrobromide of N-methylamino-2-quinonylmethane melting at 230° C was isolated.

---

[1]M. E. Wall, M. C. Wani, C. E. Cook, K. H. Palmer, A. T. McPhail, G. A. Sim, J.A.C.S. *88*, 3888 (1966).

[2]D. L. Hammick, J.C.S. *1923*, 2883.

[3]D. L. Hammick, C. N. Lammiman, E. D. Morgan and A. M. Roe, J.C.S. *1955*, 2436-41.

Experimental

W-Tribromoquinaldin. To a mixture of 50 grams of dry powdered sodium acetate, 100 grams of glacial acetic acid and 14 grams of pure quinaldine (1 Mol) at 70°, 48 grams of bromine (3 Mol) in 100 grams of acetic acid were added in the course of ten minutes the mixture being thoroughly shaken. The solution was boiled for a few minutes (until the separation of sodium bromide caused violent bumping) left for half an hour on the water bath, cooled and poured into water, and the faintly yellow crystalline precipitate washed and dried (weight 36 grams). After recrystallization from alcohol it gave m.p. 128. When ordinary quinaldine is used in the above preparation, the product obtained on pouring into water contains tarry matter difficult to remove. A good product is obtained, however, by allowing the acetic acid solution to cool and omitting the treatment with water. A mixture of sodium bromide and W-tribromoquinaldin separates, which is filtered, washed with cold glacial acetic acid and finally with water.

W-monobromoquinaldin. W-tribromoquinaldine (30 grams) was stirred in purified tetralin at 100° for 6 hours then 150° for 2 hours. The cooled solution was extracted with dil. H_2SO_4 (25% by volume) and the aqueous portion washed with a little chloroform to remove tetralin. The acid solution was then neutralized with aqueous ammonia, in an ice-bath. Crystallization of the precipitate from light petroleum gave 12.4 grams of W-monobromoquinaldine, m.p. 57.

N-*methylamino*-2-*quinonylmethane:* W-monobromoquinaldine, 0.2 grams was dissolved in ten ml. of benzene and methylamine was bubbled through the solution for 3 minutes. At the end of the reaction the solution was warmed on water bath and part of benzene removed. On cooling crystals of the hydrobromide of N-methylamino-2-quinonylmethane melting at 230° were separated. The compound has not been prepared before.