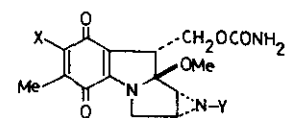


SYNTHETIC APPROACH TOWARD MITOMYCINS. NEW FACILE SYNTHESIS OF
3H-PYRROLO[1,2-*a*]INDOL-5,8-DIONES

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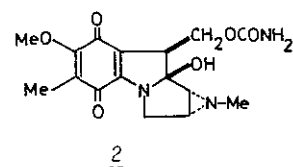
Since the first success on the isolation of mitomycin A (1), B (2), C (3), and porfiromycin (4) at the late 1950's, these unique quinones with complex functionality have attracted much attention of chemists.¹ Especially mitomycin C was shown to have the strongest and broadest activity against tumors and has been used in practice in cancer chemotherapy.² Development of a rapid entry to the general ring system is still urgent subject allowing for structural modification for the mitomycin skeleton. We recently developed a new and efficient route, which contains simultaneous double ring cyclization and leads to a shortening of reaction processes.



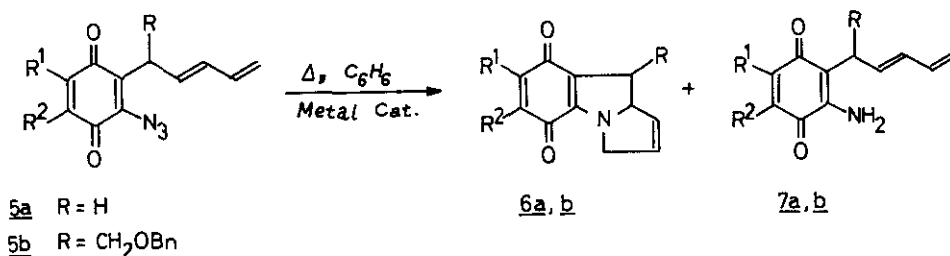
1: X=OMe, Y=H

3: X=NH₂, Y=H

4: X=NH₂, Y=Me



2-(2,4-Pentadienyl)-3-azido-1,4-quinones (5), which were easily prepared via either 2,4-pentadienylation of the corresponding quinones³ or Lewis acid catalyzed Claisen rearrangement of the corresponding 2,4-pentadienyl aryl ether, were heated under the presence of metal catalyst to afford the title compounds (6) and aminoquinones (7). Among various kinds of transition metal catalysts, Cu and Cu(acac)₂ afforded the best results and 6 (R=H, R¹=OMe, R²=Me) was isolated in 58% yield. The quinones 5b (R¹=OMe, R²=Me) with benzyloxymethyl group at the dienyl side chain also gave the desired pyrrolizidinoquinone 6b in a fair yield. This is the key compound for the total synthesis of mitomycins. Detail of the reactions and further results toward the total synthesis will be discussed.



¹ W.A.Remers, "The Chemistry of Antitumor Antibiotics", vol. 1, p. 221, Wiley, New York (1979).

² S.K.Carter and S.T.Crooke, eds., "Mitomycin C", Academic Press, New York (1979).

³ Y.Naruta, Y.Arita, N.Nagai, H.Uno, and K.Maruyama, Chem. Lett., 1982, 1859.