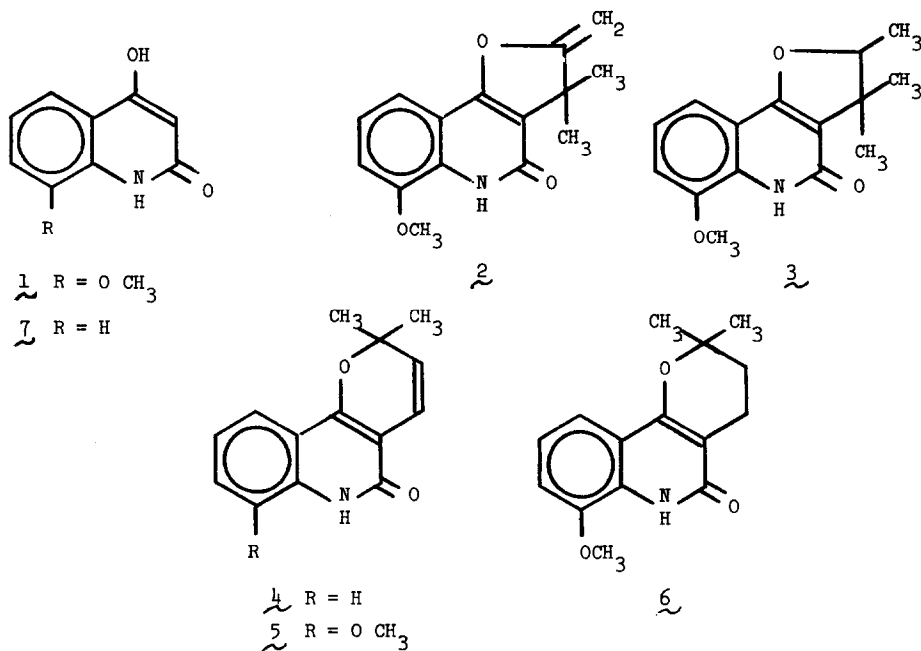


A One Step Synthesis of Flindersine¹

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The reaction of thallos salts of nonchelated β -diketones (e.g., dimedone) with alkyl halides has been reported to afford very high yields of the corresponding O-alkylated products.² In an effort to develop a new synthesis of furanoquinoline alkaloids, we had occasion to utilize this reaction in an attempt to prepare the 4-ether of 4-hydroxy-8-methoxy-2-quinolone (1) from the corresponding thallos salt and 3-chloro-3-methyl-1-butyne. This reaction gave two products A (21%) and B (35%), both of which had the molecular formula, $C_{15}H_{15}NO_3$,³ and neither of which was the desired ether. Compound A, mp 173-175° showed the infrared and ultraviolet spectra typical of a 4-alkoxy-

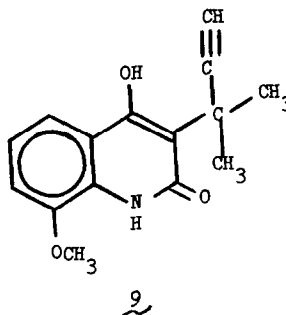
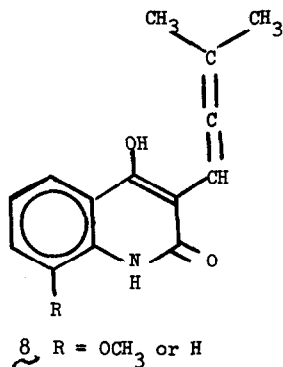


2-quinolone, however the nmr spectrum was clearly not consistent with that of the anticipated acetylenic ether and showed the presence of two vinyl protons at δ 4.35 and 4.80 with the coupling constant (3Hz) characteristic of a methylene group, and a six proton methyl singlet at δ 1.60. On the basis of these data, compound A was assigned structure 2, which was confirmed by reduction to a dihydro compound (3) mp 169-171° which showed a one proton quartet at δ 4.63 in the nmr^{3,4}.

Compound B, mp 165-167°, also lacked the spectral properties expected for the acetylenic ether, and in the nmr showed vinyl doublets at δ 6.78 and 5.58 with a coupling constant of 10Hz and a six proton methyl singlet at δ 1.56. These spectral data are remarkably similar to those reported for the alkaloid flindersine⁵ (4) and B was tentatively assigned the structure of a methoxyflindersine (5). This was confirmed by catalytic reduction to a dihydro compound (6)³, mp 165-167°, in which the vinyl protons had been replaced by an A₂B₂ pattern with triplets at δ 1.85 and 2.67.^{3,5}

Extension of this reaction to the thallos salt of 4-hydroxy quinolone (7) gave as the principal product (28%) flindersine (4), identical to an authentic sample^{6,7}. The isomer corresponding to 2 could be detected (tlc), but was not isolated. Although there have been two previously reported syntheses of flindersine^{7,8}, the interaction of the thallos salt of 4-hydroxy-2-quinolone and 3-chloro-3-methylbutyne constitutes a one step synthesis of this alkaloid and is significantly shorter than the other routes available. In addition, this seems to be a general method for the synthesis of alkaloids of this class.

Although the reaction of the thallos salts of 1 and 7 to give 5 and 4 respectively may proceed via the 4-ether, followed by anti-Markovnikoff cyclization, a more plausible mechanism involves C-alkylation by way of an S_N2' reaction to give 8, followed by cyclization to the angular pyranoquinoline. Furanoquinoline 2 is almost certainly formed by C-alkylation to 9 followed by cyclization, and was also obtained as the only isolable product from the reaction of 1 with 3-chloro-3-methyl-1-butyne and potassium carbonate in dimethyl formamide.



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