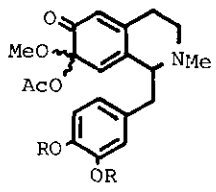
# SYNTHESIS OF (±)-1,2-DIACETOXYAPORPHINE VIA AN o-QUINOL ACETATE

Osamu Hoshino, Minoru Ohtani, and Bunsuke Umezawa*
Faculty of Pharmaceutical Sciences, Science University of Tokyo,
Shinjuku-ku, Tokyo, 162, Japan

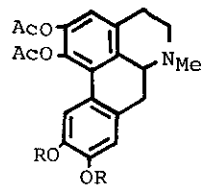
Abstract———Treatment with conc. $H_2SO_4$-$Ac_2O$ of a solution of o-quinol acetates (1) in $CH_3CN$ gave (±)-1,2-diacetoxyaporphines (2) in good yields.

In continuation of our work on aporphine synthesis via an o-quinol acetate (o-QA)[1], we found that o-QA (1a) in $CH_2Cl_2$ was treated with conc. $H_2SO_4$-$Ac_2O$ to give unexpectedly (±)-1,2-diacetoxy-9,10-dimethoxyaporphine (2a)[2], m.p. 147-148°, in 13.2% yield, accompanied with (±)-O-acetylpredicentrine (3)[1] (oil, 18.5%). The present communication deals with the structure of 2a and an improved method for its synthesis.

The spectral data [IR $\nu(CHCl_3)$: 1780 (sh), 1770 $cm^{-1}$; NMR $\delta(CDCl_3)$: 2.28, 2.31 (each 3H, s, 2 x $CH_3COO$), 2.56 (3H, s, $NCH_3$), 3.90, 3.93 (each 3H, s, 2 x $OCH_3$), 6.80, 6.88, 7.49 (each 1H, s, 3 x arom. H); MS m/z: 411 ($M^+$)] and the chemical transformations by methylation[3] and hydrolysis to (±)-glaucine (4), m.p. 134-135.5° (lit.[4], 136-138°), and the known (±)-1,2-dihydroxyaporphine (5) [HCl salt, m.p. 193-195° (lit.[5], 197-198°)] confirmed the structure of 2a.



1 a; R = Me
b; R + R = $CH_2$



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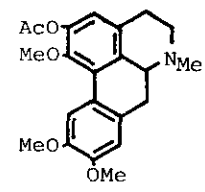

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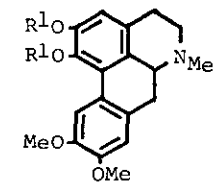
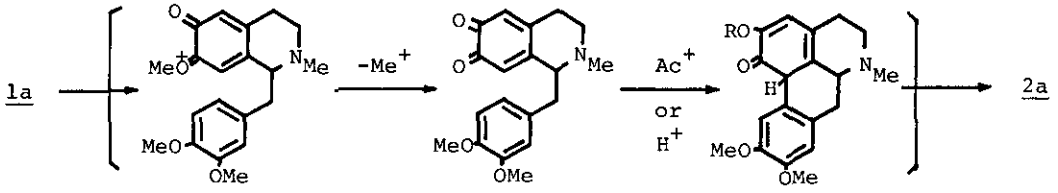


4 $R^1$ = Me
5 $R^1$ = H

A probable explanation for the formation of 2a was as follows. Namely, deacetoxylation by acetylium cation or proton occurred to give an o-quinonoid intermediate (A), the methyl cation of which was captured by the surrounding solvent molecule, leav-

ing an o-quinone (B)[6]. The intramolecular Michael reaction and the concomitant enolization of B produced 2a.




A B R = Ac or H

Accordingly, $CH_3CN$ was used as the more polar solvent to ensure an effective capture of the methyl cation. Thus, when 1a was treated with the reagent in 20 ml of $CH_3CN$, the yield of 2a was raised to 52%, together with 15% yield of 3. On the other hand, 2a was produced as a sole product in 63.3% yield, when the same reaction was conducted in 50 ml of the solvent.

Similarly, 1b was converted to 2b[7], m.p. 195-197°, in 70.9% yield.

A typical procedure: The o-QA (1a) prepared from the 6-phenolic tetrahydroisoquinoline (100 mg) as described previously[1] was dissolved in $CH_3CN$ (50 ml). To the ice-cold, stirred solution, $Ac_2O$ (1 ml) and conc. $H_2SO_4$ (0.1 ml, drop by drop) were added successively and stirring was continued at room temperature for 2 hr. Usual work-up of the reaction mixture gave an amorphous mass (113 mg), whose purification by preparative TLC gave 2a (76 mg, 63.3%), m.p. 147-148° (benzene-n-hexane).

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