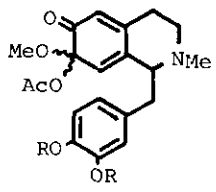
SYNTHESIS OF (±)-1,2-DIACETOXYAPORPHINE VIA AN o-QUINOL ACETATE

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

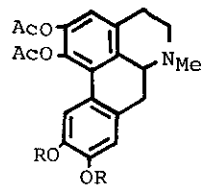
Abstract———Treatment with conc. H_2SO_4-Ac_2O of a solution of o-quinol acetates (1) in CH_3CN gave (±)-1,2-diacetoxyaporphines (2) in good yields.

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.

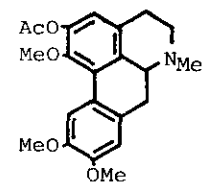
The spectral data [IR $\nu(CHCl_3)$: 1780 (sh), 1770 cm^{-1}; NMR $\delta(CDCl_3)$: 2.28, 2.31 (each 3H, s, 2 x CH_3COO), 2.56 (3H, s, NCH_3), 3.90, 3.93 (each 3H, s, 2 x OCH_3), 6.80, 6.88, 7.49 (each 1H, s, 3 x arom. H); MS m/z: 411 (M^+)] and the chemical transformations by methylation[3] and hydrolysis 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.



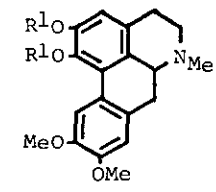
1 a; R = Me
b; R + R = CH_2



2



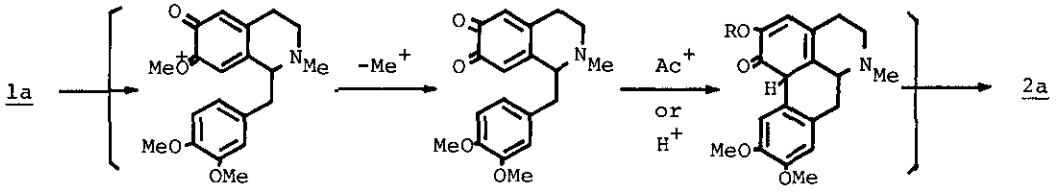
3



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).

ACKNOWLEDGEMENT The authors are indebted to Miss N. Sawabe of this Faculty and Sankyo Co., Ltd. for NMR spectral measurements and elemental analyses.

REFERENCES

1. O. Hoshino, M. Ohtani, and B. Umezawa, Chem. Pharm. Bull. (Tokyo), 1979, 27, 3101.
2. Satisfactory analytical data were obtained for all new compounds described.
3. Cf. H. Bredreck, R. Sieber, and L. Kamphenkel, Chem. Ber., 1956, 89, 1169.
4. B. Gregso-Allcott and J. M. Osbond, Tetrahedron Letters, 1969, 1771.
5. S. M. Kupchan and C.-K. Kim, J. Am. Chem. Soc., 1975, 97, 5623.
6. The formation of B was implicitly indicated by the appearance of a red coloration during the reaction.
7. Spectral data; IR $\nu(CHCl_3)$: 1770 cm^{-1}; NMR $\delta(CDCl_3)$: 2.29, 2.30 (each 3H, s, 2 x CH_3COO), 2.54 (3H, s, NCH_3), 5.96 (2H, s, OCH_2O), 6.76, 6.88, 7.41 (each 1H, s, 3 x arom. H).

Received, 26th January, 1981