# A NOVEL SYNTHESIS OF (±)-NORAPORPHINE ALKALOIDS, (±)-WILSONIRINE AND (±)-NORDOMESTICINE#

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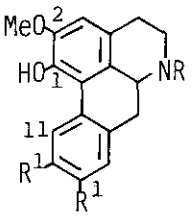
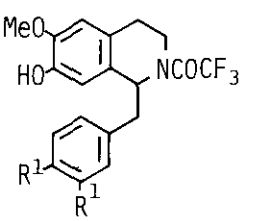
Abstract— (±)-Wilsonirine (1a) and (±)-nordomesticine (1b) were synthesized in moderate yields on acid treatment, followed by alkaline hydrolysis of o-quinol acetates (o-QAs)(3) readily obtained by lead tetraacetate oxidation of (±)-N-trifluoroacetyltetrahydroisoquinolin-7-ols (2).

Noraporphine alkaloids have been expected to be useful key compounds for synthesis of biologically active compounds[1]. However, only a few papers[2] have been published on their synthesis so far. In continuation of our studies[3] on application of lead tetraacetate [$Pb(OAc)_4$] oxidation to synthesis of isoquinoline alkaloids, we found that (±)-N-trifluoroacetyltetrahydroisoquinolin-7-ols (2) were readily oxidized with the oxidant in $CH_2Cl_2$ to give rise to the corresponding (±)-N-trifluoroacetyl-6-acetyl-6-methoxy-7-oxo-$\Delta^{4a,5,8,8a}$-hexahydroisoquinolines [o-quinol acetates (o-QAs)](3), which could be converted into (±)-noraporphines. We now wish to report a novel synthesis of (±)-wilsonirine (1a)[4] and (±)-nordomesticine (1b)[5].



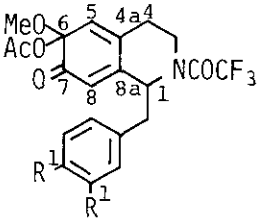

1 : $R^1$=H

4 : R=$COCF_3$




2

a : $R^1$=OMe b : $R^1+R^1$=$OCH_2O$




3

# Dedicated to Professor G. Stork on the occasion of his sixty-fifth birthday.

A typical example is as follows. $Pb(OAc)_4$ (127 mg) was added in one portion to an ice-cold, stirred solution of 2a[2b] (mp 149-151°C)(100 mg) in $CH_2Cl_2$ (1 ml) and stirring was continued at 0-5°C for 0.5 h. A careful work-up of the reaction mixture gave quantitatively a 1:1.2 diastereoisomeric mixture of 3a (oil)[IR[6] ν:1735, 1680 $cm^{-1}$; $^1$H-nmr[6] δ:2.10, 2.12 (1:1.2)(3H, each s, 6-OCOMe), 3.42, 3.43 (1.2:1)(3H, each s, 6-OMe)]. $CF_3COOH$ (5 ml) was added dropwise to an ice-cold, stirred solution of crude 3a in $CH_2Cl_2$ (5 ml) and the mixture was stirred at room temperature for 1 h. Usual work-up of the reaction mixture gave quantitatively a solid, which was purified on preparative thin-layer chromatography ($SiO_2$; developing solvent; $CHCl_3$) to give 4a[6] (61 mg, 61%), mp 190-191°C($CH_2Cl_2$-n-hexane)(lit.[2b], 196.5-197°C). $^1$H-Nmr spectra datum of 4a was identical with that noted in literature[2b].

From the above results, it was proved that $Pb(OAc)_4$ oxidation of 2a gave o-QA (3a), acid treatment of which afforded (±)-N-trifluoroacetylwilsonirine (4a) in a moderate yield.

Similarly, 2b (mp 137-138°C) gave o-QA (3b)[6], which was converted into 4b[6] in 21% overall yield.

Alkaline hydrolysis (aq.$K_2CO_3$-MeOH, reflux, 2 h) of 4a and 4b afforded 1a[6] (93%), mp 210-213°C($CH_2Cl_2$)(lit.[4], 211-213°C) and 1b[6] (98%), mp 205-207°C($CH_2Cl_2$-n-hexane), respectively.

Thus, a novel synthesis of (±)-noraporphine alkaloids was accomplished *via* o-QAs (3) of (±)-N-trifluoroacetyltetrahydroisoquinolin-7-ols (2). *Further development of the present method is in progress.*

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4. S.R.Johns, J.A.Lamberton, C.S.Li, and A.A.Sioumis, Aust. J. Chem., 1970, 23, 363.
5. As (+)-nordomesticine; S.R.Johns, J.A.Lamberton, and A.A.Sioumis, Aust. J. Chem., 1966, 19, 2331.
6. IR spectra were taken with a Hitachi 260-10 spectrophotometer in $CHCl_3$ solution. $^1$H-Nmr spectra were measured with a JEOL-JNM-FX-100(100MHz) instrument in $CDCl_3$ solution using TMS as internal standard. 3a; δ: 2.10, 2.12 (1:1.2)(3H, each s, 6-OCOMe), 3.42, 3.43 (1.2:1)(3H, each s, 6-OMe), 3.82, 3.83, 3.84 (9H, each s, 3xOMe), 5.15 (1H, dd, J=4.3, 8.5 Hz, 1-H), 5.14, 5.99 (2H, each br s, 2xolefinic H), 6.60-6.70 (3H, m, 3xAr-H). 4a; δ: 3.94 (3H, s, OMe), 3.96 (3H, s, 2xOMe), 5.08 (1H, dd, J=5.4, 12.9 Hz, 6a-H), 6.60, 6.80 (2H, each s, 2xAr-H), 8.15 (1H, s, 11-H). 1a; δ: 3.95 (9H, s, 3xOMe), 6.58, 6.77 (2H, each s, 2xAr-H), 8.10 (1H, s, 11-H). 3b (oil); ν: 1730, 1680 $cm^{-1}$; δ: 2.10, 2.12 (1:1.2)(3H, s, 6-OCOMe), 3.42 (3H, s, 6-OMe), 4.96-5.24 (1H, m, 1-H), 5.46, 5.57 (1:1.2)(1H, each s, olefinic H), 5.90 (2H, s, $OCH_2O$), 5.96-6.08 (1H, m, olefinic H), 6.44-6.78 (3H, m, 3xAr-H). 4b; δ: 3.97 (3H, s, 2-OMe), 5.05 (1H, dd, J=5.7, 12.8 Hz, 6a-H), 6.00 (2H, s, $OCH_2O$), 6.60, 6.78 (2H, each s, 2xAr-H), 8.04 (1H, s, 11-H). 1b; δ: 3.95 (3H, s, 2-OMe), 5.98 (2H, s, $OCH_2O$), 6.57, 6.76 (2H, each s, 2xAr-H), 8.00 (1H, s, 11-H).

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