A SYNTHESIS OF (±)-1- AND (±)-3-HYDROXY-(C)-HOMOAPORPHINES VIA META-BRIDGED AROMATIC LACTAMS#

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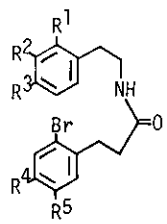
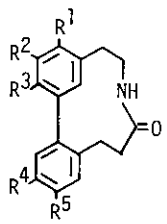
Abstract—— The title (C)-homoaporphines (4) were synthesized starting with meta-bridged aromatic lactams (2) readily obtained by photolysis of phenolic N-phenethylbromophenylpropionamides (1).

Previously, we have reported that photolysis[1] of phenolic N-phenethylbromophenylpropionamides (1) gives rise to meta-bridged aromatic lactams (2). The lactams (2) seemed to be useful key compounds for synthesis of (C)-homoaporphines.[2,3] The present paper deals with a synthesis of (C)-homoaporphines by a new synthetic route.



1



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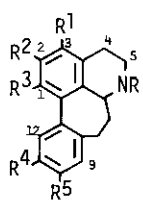

3 : R=H

4 : R=Me

	R^1	R^2	R^3	R^4	R^5
a	OH	OMe	H	OMe	OMe
b	OH	OMe	H	OCH_2O	
c	OH	OMe	H	H	H
d	H	OMe	OH	OMe	OMe

In a typical example, a mixture of 2a[1] (107.1 mg) and $POCl_3$ (0.75 ml) in CH_3CN (10 ml) was refluxed for 1 h. Usual work-up of the reaction mixture gave an oil, which was reduced with $NaBH_4$ (23 mg) in MeOH (10 ml) at room temperature for 30 min. Usual work-up of the reaction mixture gave an oil, which was crystallized on trituration in n-hexane to afford a solid (3a)[4] (99 mg, 97%), mp 215-217°C (MeOH). N-Methylation (1. 35%aq.HCHO; 2. $NaBH_4$) of 3a afforded an oil, which was purified on preparative thin-layer chromatography (SiO_2; developing solvent: $CHCl_3$:MeOH= 10 : 1) to afford 4a[4] (46 mg, 87%), mp 209-211°C (i-PrOH)(lit.[3], 199-200°C). It was identical with

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

an authentic sample[3] by comparison of their spectral data.

Similarly, reaction of 2b-d[1] afforded 4b-d[4] via 3b-d.[4]

Thus, a synthesis of (±)-1- and (±)-3-hydroxy-(C)-homoaporphines (4) was accomplished by a new synthetic route starting with meta-bridged aromatic lactams (2).

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4. ^{1}H-Nmr spectra were taken with a JEOL-JNM-FX-100 (100MHz) or Hitachi R24B (60MHz) instrument in $CDCl_3$ solution using TMS as internal standard. 3a; δ(60MHz):3.85 (9H, s, 3xOMe), 6.60, 6.62, 6.70 (3H, each s, 3xAr-H). 4a; δ(60MHz):2.31 (3H, s, NMe), 3.81 (9H, s, 3xOMe), 6.58, 6.60, 6.68 (3H, each s, 3xAr-H). 3b (90%), mp 216-218°C(dec.)(MeOH); δ(100MHz):3.88 (3H, s, 2-OMe), 5.92 (2H, s, OCH_2O), 6.67, 6.69, 6.78 (3H, each s, 3xAr-H). 4b (81%), mp 181-183°C(MeOH)(lit.[3], 188-190°C); δ(100MHz):2.40 (3H, s, NMe), 3.90 (3H, s, 2-OMe), 5.94 (2H, s, OCH_2O), 6.68, 6.70, 6.78 (3H, each s, 3xAr-H). 3c (94%), mp 198-199.5°C(dec.)(MeOH); δ(100MHz)($CDCl_3$-CD_3OD):3.91 (3H, s, 2-OMe), 6.78 (1H, s, 1-H), 7.10-7.30 (4H, m, 4xAr-H). 4c (82%), mp 200.5-201.5°C(dec.)(MeOH); δ(100MHz):2.46 (3H, s, NMe), 3.94 (3H, s, 2-OMe), 6.83 (1H, s, 1-H), 7.20-7.30 (4H, m, 4xAr-H). 3d (94%)(amorphous mass); δ(60MHz):3.76 (3H, s, OMe), 3.82 (6H, s, 2xOMe), 6.42, 6.59, 6.90 (3H, each s, 3xAr-H). 4d (96%), mp 199-200°C(i-PrOH)(lit.[5], 199-200° C); δ(60MHz):2.34 (3H, s, NMe), 3.79 (3H, OMe), 3.84 (6H, s, 2xOMe), 6.46, 6.60, 6.92 (3H, each s, 3xAr-H).

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