

A SYNTHESIS OF ( $\pm$ )-1- AND ( $\pm$ )-3-HYDROXY-(C)-HOMOAPORPHINES VIA  
META-BRIDGED AROMATIC LACTAMS<sup>#</sup>

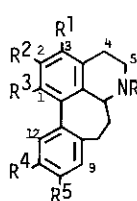
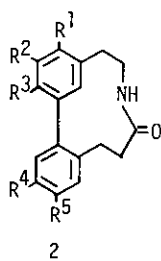
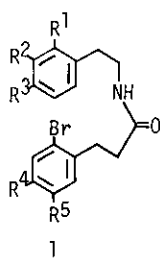
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**Abstract**— The title (C)-homoaporphines (4) were synthesized starting with meta-bridged aromatic lactams (2) readily obtained by photolysis of phenolic N-phenethylbromophenylpropionamides (1).

Previously, we have reported that photolysis<sup>1</sup> 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.<sup>2,3</sup> The present paper deals with a synthesis of (C)-homoaporphines by a new synthetic route.



4 : R=Me

	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	R <sup>5</sup>
a	OH	OMe	H	OMe	OMe
b	OH	OMe	H	OCH <sub>2</sub> O	
c	OH	OMe	H	H	H
d	H	OMe	OH	OMe	OMe

In a typical example, a mixture of 2a<sup>1</sup> (107.1 mg) and POCl<sub>3</sub> (0.75 ml) in CH<sub>3</sub>CN (10 ml) was refluxed for 1 h. Usual work-up of the reaction mixture gave an oil, which was reduced with NaBH<sub>4</sub> (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)<sup>4</sup> (99 mg, 97%), mp 215–217°C (MeOH). N-Methylation (1. 35%aq.HCHO; 2. NaBH<sub>4</sub>) of 3a afforded an oil, which was purified on preparative thin-layer chromatography (SiO<sub>2</sub>; developing solvent: CHCl<sub>3</sub>:MeOH=10:1) to afford 4a<sup>4</sup> (46 mg, 87%), mp 209–211°C (i-PrOH) (lit.<sup>3</sup>, 199–200°C). It was identical with

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

an authentic sample<sup>3</sup> by comparison of their spectral data.

Similarly, reaction of 2b-d<sup>1</sup> afforded 4b-d<sup>4</sup> via 3b-d.<sup>4</sup>

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

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4. <sup>1</sup>H-Nmr spectra were taken with a JEOL-JNM-FX-100 (100MHz) or Hitachi R24B (60MHz) instrument in CDCl<sub>3</sub> solution using TMS as internal standard. 3a;  $\delta$  (60MHz): 3.85 (9H, s, 3xOMe), 6.60, 6.62, 6.70 (3H, each s, 3xAr-H). 4a;  $\delta$  (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);  $\delta$  (100MHz): 3.88 (3H, s, 2-OMe), 5.92 (2H, s, OCH<sub>2</sub>O), 6.67, 6.69, 6.78 (3H, each s, 3xAr-H). 4b (81%), mp 181-183°C(MeOH) (lit.<sup>3</sup>, 188-190°C);  $\delta$  (100MHz): 2.40 (3H, s, NMe), 3.90 (3H, s, 2-OMe), 5.94 (2H, s, OCH<sub>2</sub>O), 6.68, 6.70, 6.78 (3H, each s, 3xAr-H). 3c (94%), mp 198-199.5°C(dec.) (MeOH);  $\delta$  (100MHz) (CDCl<sub>3</sub>-CD<sub>3</sub>OD): 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);  $\delta$  (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);  $\delta$  (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.<sup>5</sup>, 199-200°C);  $\delta$  (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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