

Unexpected Course of the Reaction of  
Aromatic Aldehydes on Lithiated *N,N*-Dimethyl  
*O*-(3-Quinoly)carbamate

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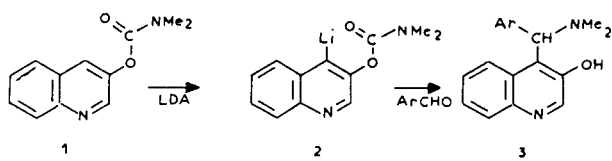
The reaction of aromatic aldehydes with *N,N*-dimethyl *O*-(3-lithioquinoly)carbamate produces 4-(dimethylaminomethyl)3-hydroxyquinolines *via* a new rearrangement.

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The metalation procedure recently published by Snieckus for phenyl and pyridine carbamates [1,2] was used in the quinoline series. This method appears to be a good technique to synthesize *ortho*-substituted hydroxyquinolines. This complete work will be published later [3].

This study enables us to observe unexpected reactions subsequent to the addition of the lithiated species **2** to the carbonyl of aromatic aldehydes: metalation of 3-quinoly dimethyl carbamate **1** under standard conditions (1.1 equivalent of LDA, THF,  $-78^{\circ}$ ) followed by an aromatic aldehyde quench resulted in the formation of *N,N*-dimethyl-4-(3-hydroxyquinoly)arylmethane **3** in good yields (50-95%); (**3a**, Ar =  $C_6H_5$ ; **3b**, Ar =  $2-CH_3O-C_6H_4$ ; **3c**, Ar =  $4-CH_3O-C_6H_4$ ; **3d**, Ar =  $3,4-(CH_3O)_2C_6H_3$ ; **3e**, Ar =  $2-Cl-C_6H_4$ ; **3f**, Ar = 2-thienyl; **3g**, Ar = 2-pyridyl).

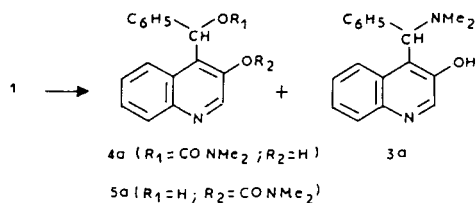
Scheme 1



We did not observe the formation of amines when *O*-quinoly carbamates of different structures were treated under similar conditions [3] and such results were not described in the benzene and in the pyridine series.

Some observations lead to the following mechanism proposal: When benzaldehyde was used as an electrophile, formation of two compounds **3a** and **4a** (or **5a**) was noted. Moreover **4a** or **5a** gave **3a** on moderate heating.

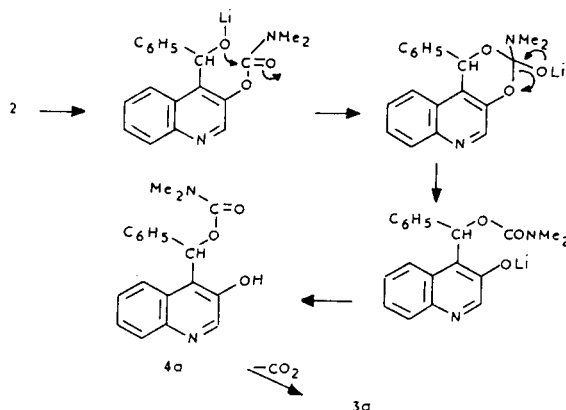
Scheme 2



In the  $^1H$  nmr spectrum of **4a** or **5a**, the signal attributed to CH-O appears at a low field: 7.65 ppm. This favoured the structure **4a** which is analogous to benzhydrol acetate [5] and not its isomer **5a**. Moreover compound **4a** is a phenol soluble in 5% sodium hydroxide solution.

This leads to the following scheme:

Scheme 3



This surprising reaction can be explained by a sequence of intramolecular reactions and decarboxylation. It allows an easy synthesis of *N,N*-dimethyl-4-quinolyarylmethanes.

## EXPERIMENTAL

Melting points were determined on a Kofler hot stage and are uncorrected. The  $^1H$  nmr spectra were recorded in deuteriochloroform at 60 MHz on a Varian EM-360 L instrument. Microanalyses were performed on a Carlo Erba CHNOS 1106 apparatus.

### General Procedure.

A solution of 0.97 g (0.0045 mole) of *N,N*-dimethyl *O*-(3-quinoly)carbamate in anhydrous THF (8 ml) was added to LDA (0.005 mole) in anhydrous THF (30 ml) at  $-78^{\circ}$ . After stirring for 1 hour, the lithiated carbamate was quenched by aromatic aldehydes (0.025 mole) at the same temperature during 30 minutes. After hydrolysis and extraction at neutral pH by dichloromethane, the crude products were purified by liquid chromatography (silica gel).

Compound **3a** (Ar = 2-C<sub>6</sub>H<sub>5</sub>).

This compound was obtained in a yield of 90%, mp 135-136°; <sup>1</sup>H nmr (deuteriochloroform): δ 8.75 (s, H<sub>2</sub>), 7.95 (m, H<sub>5</sub> and H<sub>6</sub>), 7.40 (m, H<sub>6</sub> and H<sub>7</sub>), 4.95 (s, CH-N), 2.35 (s, N(CH<sub>3</sub>)<sub>2</sub>), 7.40 (m, H'<sub>2</sub>, H'<sub>3</sub>, H'<sub>4</sub>, H'<sub>5</sub> and H'<sub>6</sub>).

*Anal.* Calcd. for C<sub>18</sub>H<sub>18</sub>N<sub>2</sub>O: C, 77.67; H, 6.52; N, 10.06. Found: C, 77.55; H, 6.54; N, 10.02.

Compound **3b** (Ar = 2-CH<sub>3</sub>O-C<sub>6</sub>H<sub>4</sub>-).

This compound was obtained in a yield of 90%, mp 160°; <sup>1</sup>H nmr (deuteriochloroform): δ 8.73 (s, H<sub>2</sub>), 7.9 (m, H<sub>5</sub> and H<sub>6</sub>), 7.35 (m, H<sub>6</sub> and H<sub>7</sub>), 5.75 (s, CH-N), 2.35 (s broad, N(CH<sub>3</sub>)<sub>2</sub>), 4.05 (s, OCH<sub>3</sub>), 6.8 and 7.35 (m, H<sub>3</sub>, H'<sub>3</sub>, H'<sub>4</sub>, H'<sub>5</sub> and H'<sub>6</sub>).

*Anal.* Calcd. for C<sub>19</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>: C, 74.00; H, 6.53; N, 9.08. Found: C, 73.78; H, 6.65; N, 9.00.

Compound **3c** (Ar = 4-OCH<sub>3</sub>-C<sub>6</sub>H<sub>4</sub>).

This compound was obtained in a yield of 63%, mp 144°; <sup>1</sup>H nmr (deuteriochloroform): δ 8.65 (s, H<sub>2</sub>), 7.90 (m, H<sub>5</sub> and H<sub>6</sub>), 7.4 (m, H<sub>6</sub> and H<sub>7</sub>), 4.90 (s, CH-N), 2.3 (s, N(CH<sub>3</sub>)<sub>2</sub>), 6.75 (d, H'<sub>3</sub> and H'<sub>5</sub>), 7.46 (d, H'<sub>2</sub> and H'<sub>6</sub>), 3.7 (s, OCH<sub>3</sub>).

*Anal.* Calcd. for C<sub>19</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>: C, 74.00; H, 6.53; N, 9.08. Found: C, 74.1; H, 6.6; N, 9.0.

Compound **3d** (Ar = 3,4-(CH<sub>3</sub>O)<sub>2</sub>-C<sub>6</sub>H<sub>3</sub>).

This compound was obtained in a yield of 78% mp 170°; <sup>1</sup>H nmr (deuteriochloroform): δ 8.75 (s, H<sub>2</sub>), 8.00 (m, H<sub>5</sub> and H<sub>6</sub>), 7.50 (m, H<sub>6</sub> and H<sub>7</sub>), 4.95 (s, CH-N), 2.35 (s, N(CH<sub>3</sub>)<sub>2</sub>), 6.75 (d, J = 9 Hz, H'<sub>2</sub>), 7.15 (m, H'<sub>5</sub> and H'<sub>6</sub>), 3.85 (s, OCH<sub>3</sub>).

*Anal.* Calcd. for C<sub>20</sub>H<sub>22</sub>N<sub>2</sub>O<sub>3</sub>: C, 70.98; H, 6.55; N, 8.28. Found: C, 70.98; H, 6.60; N, 8.30.

Compound **3e** (Ar = 2-Cl-C<sub>6</sub>H<sub>4</sub>-).

This compound was obtained in a yield of 65% mp 147-148°; <sup>1</sup>H nmr (deuteriochloroform): δ 8.76 (s, H<sub>2</sub>), 7.80 (m, H<sub>5</sub> and H<sub>6</sub>), 7.4 (m, H<sub>6</sub> and H<sub>7</sub>), 5.78 (s, CH-N), 2.35 (s, N(CH<sub>3</sub>)<sub>2</sub>), 7.4 and 7.1 (m, H'<sub>3</sub>, H'<sub>4</sub>, H'<sub>5</sub> and H'<sub>6</sub>).

*Anal.* Calcd. for C<sub>18</sub>H<sub>17</sub>ClN<sub>2</sub>O: C, 69.12; H, 5.48; N, 8.96. Found: C, 69.36; H, 5.54; N, 8.94.

Compound **3f** (Ar = 2-thienyl).

This compound was obtained in a yield of 55% mp 133°; <sup>1</sup>H nmr (deuteriochloroform): δ 8.75 (s, H<sub>2</sub>), 8.00 (m, H<sub>5</sub> and H<sub>6</sub>), 7.45 (m, H<sub>6</sub> and H<sub>7</sub>), 5.26 (s, CH-N), 2.35 (s, N(CH<sub>3</sub>)<sub>2</sub>), 6.85 (dd, H'<sub>3</sub>), 7.15 (m, H'<sub>4</sub> and H'<sub>5</sub>).

*Anal.* Calcd. for C<sub>16</sub>H<sub>16</sub>N<sub>2</sub>OS: C, 67.57; H, 5.67; N, 9.85. Found: C, 67.37; H, 5.71; N, 9.75.

Compound **3g** (Ar = 2-pyridyl).

This compound was obtained in a yield of 60%, mp 100°; <sup>1</sup>H nmr (deuteriochloroform): δ 8.75 (s, H<sub>2</sub>), 8.10 (m, H<sub>5</sub> and H<sub>6</sub>), 7.5 (m, H<sub>6</sub> and H<sub>7</sub>), 5.25 (s, CH-N), 2.35 (s, N(CH<sub>3</sub>)<sub>2</sub>), 8.66 (dd, H'<sub>6</sub>), 7.5 (m, H'<sub>3</sub> and H'<sub>4</sub>), 7.13 (m, H'<sub>5</sub>).

*Anal.* Calcd. for C<sub>17</sub>H<sub>17</sub>N<sub>3</sub>O: C, 73.09; H, 6.13; N, 15.04. Found: C, 73.17; H, 5.95; N, 14.91.

Compound **4a** (R<sub>1</sub> = CONMe<sub>2</sub>, R<sub>2</sub> = H).

This compound had mp 132-134°; <sup>1</sup>H nmr (DMSO): δ 8.75 (s, H<sub>2</sub>), 7.75 (m, H<sub>5</sub> and H<sub>6</sub>), 7.30 (m, H<sub>6</sub> and H<sub>7</sub>), 7.25 (m, H'<sub>2</sub>, H'<sub>3</sub>, H'<sub>4</sub>, H'<sub>5</sub> and H'<sub>6</sub>), 2.8 (s broad, N(CH<sub>3</sub>)<sub>2</sub>), 7.65 (s, CH-OCO).

*Anal.* Calcd. for C<sub>19</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub>: C, 70.79; H, 5.63; N, 8.68. Found: C, 70.60; H, 5.81; N, 8.70.

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- [5] The <sup>1</sup>H nmr signal of CH-O appears at 5.8 ppm in benzhydrol and at 6.8 ppm in benzhydrol acetate.