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Received February 5, 1991

3-(Arylamino)-2-(4-pyridinyl)acroleins **3** prepared by reacting anilines **1** with 3-(dimethylamino)-2-(4-pyridinyl)acrolein (**2**) were cyclized with phosphorus oxychloride or acetic acid to give 3-(4-pyridinyl)quinolines **4**.

*J. Heterocyclic Chem.*, **28**, 1453 (1991).

3-(4-Pyridinyl)quinolines were needed in our laboratory for cardiovascular testing. A literature search revealed only a few examples of 3-arylquinolines. In 1943, Coates *et al.* [2] reported the coupling of 3-quinolinediazonium chloride with pyridine and isolation of two (2-pyridinyl and 3-pyridinyl) of the three possible isomeric 3-(pyridinyl)quinolines. Later, in 1972, Jutz and Wagner [3] published the synthesis of 3-phenylquinoline and 6-methoxy-3-phenylquinoline by the thermal cyclization of Schiff bases [prepared by reacting the adduct obtained from 3-(dimethylamino)-2-phenylacrolein and dimethyl sulphate with aniline or *p*-anisidine] at high temperature (180-200°). We report here a convenient synthesis of 3-(4-pyridinyl)quinolines by the cyclization of 3-(arylamino)-2-(4-pyridinyl)acrolein (**3**) under mild conditions.

Michael reaction of anilines **1** with 3-(dimethylamino)-2-(4-pyridinyl)acrolein (**2**) [4] followed by the elimination of

dimethylamine resulted in the formation of 3-arylamino-2-(4-pyridinyl)acroleins **3** which were used in the next step without isolation.

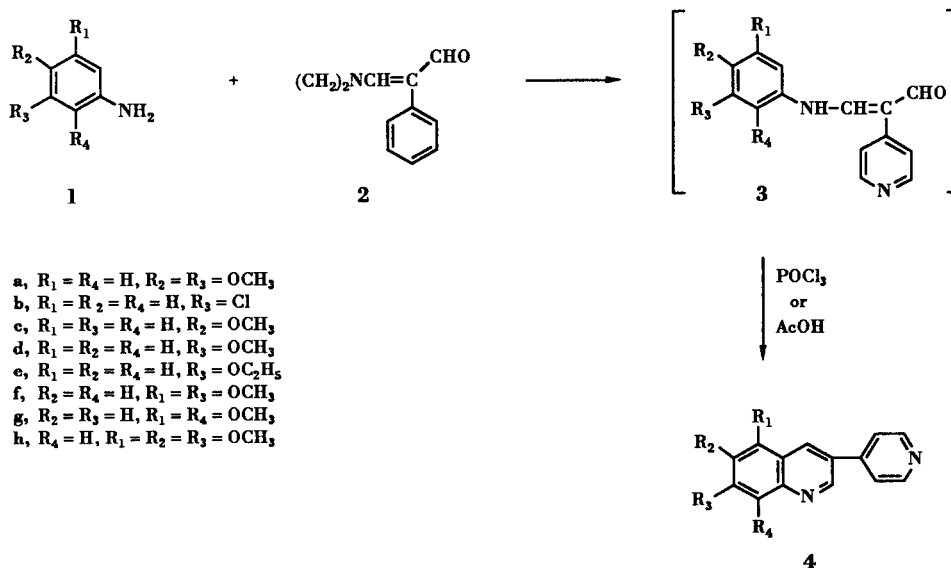
When 3-(3,4-dimethoxyphenylamino)-2-(4-pyridinyl)acrolein (**3a**) [prepared by reacting 3,4-dimethoxyaniline (**1a**) with 3-(dimethylamino)-2-(4-pyridinyl)acrolein (**2**) [4]] was treated with phosphorus oxychloride, 6,7-dimethoxy-3-(4-pyridinyl)quinoline (**4a**) was obtained in 34% yield (procedure A). Later, it was discovered that acroleins **3** which have activating groups in positions 3 or 5 or both positions of the phenyl ring undergo cyclization readily in acetic acid (procedure B). The lack of an activating group in these positions has a detrimental effect on the yield. For example, **3c** failed to cyclize in acetic acid and gave quinoline **4c** in 20% yield on cyclization in phosphorus oxychloride.

Table I

Compound	Method	Mp (°C)	Yield (%)	Molecular Formula	Analysis			<sup>1</sup> H NMR [a,b,c] δ
					Calcd.	Found		
					C	H	N	
<b>4a</b>								4.02 (s, 6H, 2 x OCH <sub>3</sub> ), 7.02 (d, 1H), 7.41 (d, 1H), 7.54 (d, 2H, pyrimidine H-3, H-5), 8.1 (d, 1H, H-4), 8.68 (d, 2H, pyridine H-2, H-6), 8.93 (d, 1H, H-2)
<b>4b</b>	A	136-138	53	C <sub>14</sub> H <sub>9</sub> ClN <sub>2</sub>	69.86	3.77	11.64	7.6-8.04 (m, 7H, 3ArH + C <sub>5</sub> H <sub>4</sub> N), 8.69 (d, 1H, H-4), 9.26 (d, 1H, H-2)
<b>4c</b>	A	145-147	20	C <sub>15</sub> H <sub>12</sub> N <sub>2</sub> O	76.25	5.12	11.86	3.97 (s, 3H, OCH <sub>3</sub> ), 7.46-7.98 (m, 5H, 3ArH + pyridine H-3, H-5), 8.68 (d, 1H, H-4), 8.75 (d, 2H, pyridine H-2, H-6), 9.15 (d, 1H, H-2)
<b>4d</b>								4.0 (s, 3H, OCH <sub>3</sub> ), 7.35-8.0 (m, 5H, 3ArH + pyridine H-3, H-5), 8.69 (d, 2H, pyridine H-2, H-6), 8.75 (d, 1H, H-4), 9.28 (d, 1H, H-2)
<b>4e</b>	B	122-125	51	C <sub>16</sub> H <sub>14</sub> N <sub>2</sub> O	76.78	5.64	11.19	1.43 (t, 3H, OCH <sub>2</sub> CH <sub>3</sub> ), 4.23 (q, 2H, OCH <sub>2</sub> CH <sub>3</sub> ), 7.43-7.99 (m, 5H, 3ArH + pyridine H-3, H-5), 8.72 (d, 2H, pyridine H-2, H-6), 8.74 (d, 1H, H-4), 9.28 (d, 1H, H-2)
<b>4f</b>	B	173-175	55	C <sub>16</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub>	72.17	5.30	10.52	3.96 (s, 3H, OCH <sub>3</sub> ), 4.03 (s, 3H, OCH <sub>3</sub> ), 6.57 (d, 1H), 7.07 (d, 1H), 7.65 (d, 2H, pyridine H-3, H-5), 8.71 (m, 3H, H-4, pyridine H-2, H-6), 9.12 (d, 1H, H-2)
<b>4g</b>	B	175-177	42	C <sub>16</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub>	72.17	5.30	10.52	4.03 (s, 3H, OCH <sub>3</sub> ), 4.11 (s, 3H, OCH <sub>3</sub> ), 6.82 (d, 1H), 7.1 (d, 1H), 7.67, 8.75 (A <sub>2</sub> B <sub>2</sub> , 4H, C <sub>5</sub> H <sub>4</sub> N), 8.81 (d, 1H, H-4), 9.22 (d, 1H, H-2)
<b>4h</b>	B	127-129	58	C <sub>17</sub> H <sub>16</sub> N <sub>2</sub> O <sub>3</sub>	68.91	5.44	9.45	4.02 (s, 3H, OCH <sub>3</sub> ), 4.04 (s, 3H, OCH <sub>3</sub> ), 4.14 (s, 3H, OCH <sub>3</sub> ), 7.28 (s, 1H, 8-H), 7.60, 8.71 (A <sub>2</sub> B <sub>2</sub> , 4H, C <sub>5</sub> H <sub>4</sub> N), 8.57 (d, 1H, H-4), 9.01 (d, 1H, H-2)
					68.69	5.42	9.41	

[a] The <sup>1</sup>H nmr spectra were recorded on Varian HA-100 spectrometer using tetramethylsilane as an internal standard. [b] The <sup>1</sup>H nmr spectra of **4a**, **4f**, **4g**, and **4h** were recorded in deuteriochloroform. [c] The <sup>1</sup>H nmr spectra of **4b**, **4c**, **4d**, and **4e** were recorded in DMSO-d<sub>6</sub>.

## Scheme



## EXPERIMENTAL

## Typical Procedure A.

6,7-Dimethoxy-3-(4-pyridinyl)quinoline (**4a**).

A mixture of 3-(dimethylamino)-2-(4-pyridinyl)acrolein (**2**) [4] (30 g, 0.17 mole) and 3,4-dimethoxyaniline (**1a**) (25 g, 0.16 mole) was heated in an oil bath at 120-130° for 3 hours and then cooled in an ice bath. To the resulting yellow solid was added phosphorus oxychloride (75 ml). This mixture was heated under reflux for 3 hours and then poured over ice to give a brown solution which was neutralized by treating with concentrated aqueous ammonia. The resulting dark oil was extracted with chloroform (2 x 400 ml). Removal of chloroform gave 37 g of a dark oil which was crystallized from 2-propanol after decolorizing with charcoal to give yellow needles of **4a**, yield 14 g (34%), mp 136-138°.

*Anal.* Calcd. for  $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}_2$ : C, 72.12; H, 5.30; N, 10.52. Found: C, 71.88; H, 5.35; N, 10.45.

## Typical Procedure B.

7-Methoxy-3-(4-pyridinyl)quinoline (**4d**).

A mixture of **2** (17.2 g, 0.1 mole) and *m*-anisidine (**1d**) (13 g, 0.1

mole) was heated in an oil bath at 120-130° for 4 hours and then cooled to room temperature. After adding acetic acid (50 ml), the resulting mixture was heated on a steam bath for 7 hours and then poured into water (300 ml). The resulting mixture was made basic by treating with concentrated aqueous ammonia. The yellow precipitate was collected and recrystallized from 2-propanol to afford **4d** as a pale yellow solid, yield 11.5 g (51%), mp 160-163°.

*Anal.* Calcd. for  $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}$ : C, 76.25; H, 5.12; N, 11.86. Found: C, 76.14; H, 5.11; N, 11.70.

## Acknowledgement.

The authors are thankful to the Department of Molecular Characterization for the  $^1\text{H}$  nmr spectra.

## REFERENCES AND NOTES

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