

## Convenient Synthesis of 3-(2-Pyridyl)- and 8-(2-Pyridyl) Carbostryrils

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3-( $\omega$ -Bromoacetyl) carbostryril (1) and 4-methyl-7-methoxy-8-( $\omega$ -bromoacetyl) carbostryril (5) on reaction with pyridine in refluxing toluene provide the pyridinium salts 2 and 6 respectively. Condensation of salts 2 and 6 with chalcones in acetic acid in the presence of ammonium acetate gives 3-(2-pyridyl) and 8-(2-pyridyl) carbostryrils in high yield.

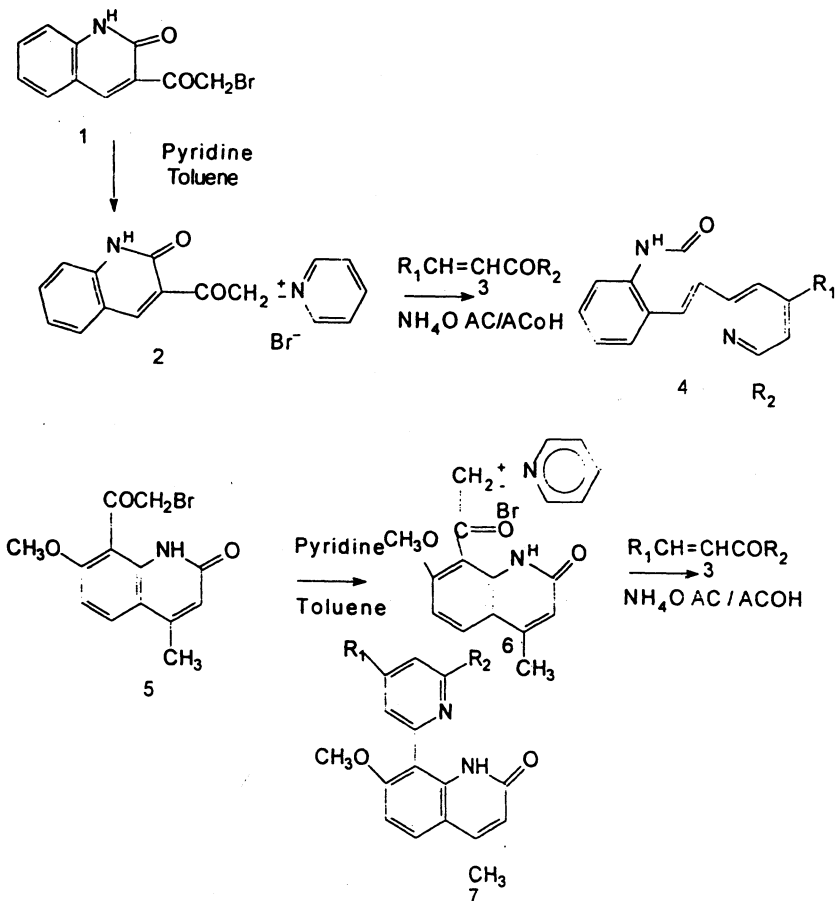
**Key Words:** 3-(2-Pyridyl)/8-(2-Pyridyl) carbostryrils, Synthesis.

### INTRODUCTION

Several carbostryrils containing heterocyclic moieties like pyridine, indole, triazole and oxazine possess important biological activities<sup>1-3</sup>, CNS depressant and antifungal activities<sup>3</sup>. Though a few methods are reported for the synthesis of 3- and 4-pyridyl carbostryrils, those approaches do not provide various substitutions in pyridine nucleus. In view of this it was planned to synthesise 3- and 8-pyridyl carbostryrils, having various substituents in pyridine part. We report here a convenient method for the synthesis of these carbostryrils (4a-f) and (7a-f) from the early accessible  $\omega$ -bromoacetyl carbostryril (1). Salt (1) was first converted into salt (2) by reacting with pyridine in refluxing toluene. The salt (2) was then reacted with chalcones (3a-f) in acetic acid solution in the presence of ammonium acetate to provide 3-(2-pyridyl) carbostryril (4a-f) in 46–60% yield. The 8-( $\omega$ -bromoacetyl) carbostryril (5) on similar reaction with pyridine followed by the treatment with chalcones (3a-f) furnished 8-(2-pyridyl) carbostryrils (7a-f) in 42.55% yield. The formation of pyridine nucleus in these compounds involves the Kroehnke's mechanism in which the aroyl pyridinium salt reacts with  $\alpha$ ,  $\beta$  unsaturated ketone system resulting in a 1,5-dionyl pyridinium derivative which subsequently undergoes cyclization in the presence of  $\text{NH}_4\text{OAc}/\text{AcOH}$  to afford a pyridine ring.

### EXPERIMENTAL

IR spectra were recorded in KBr Perkin-Elmer 983 spectrophotometer and PMR spectra in  $\text{CDCl}_3$  on a Perkin-Elmer Em-390 90 MHz spectrometer using TMS as internal standard.



- (a)  $R_1 = R_2 = -C_6H_5$   
 (b)  $R_1 = -C_6H_5$ ,  $R_2 = 4$ -methoxy phenyl  
 (c)  $R_1 = 3,4$ -methylene dioxy phenyl- $R_2 = C_6H_5$   
 (d)  $R_1 = 3,4$ -methylene dioxy phenyl,  $R_2 = 4$ -methoxy phenyl  
 (e)  $R_1 = 3,4,5$ -trimethoxy phenyl,  $R_2 = 4$ -methoxy phenyl  
 (f)  $R_1 = 3,4,5$ -trimethoxy phenyl,  $R_2 = -C_6H_5$

### 3-( $\omega$ -Bromoacetyl) carbostyril (1) and 4-methyl-7-methoxy/8-( $\omega$ -bromoacetyl) carbostyril (5)

To a solution of 3-acetyl carbostyril or 4-methyl-7-methoxy 8-acetyl carbostyril (0.1 mole) in glacial acetic acid (150 mL) was added bromine (0.1 mole) in glacial acetic acid (20 mL) with stirring for 30 min at room temperature. The mixture was stirred at room temperature for 3 h, poured into ice-cold water and the solid obtained was filtered out. It was washed with water and dried. The required product was recrystallized from chloroform.

Compound 1: yield 60%, m.p. 158°C; compound 5: yield 62%, m.p. 160°C, IR: 750 (C—Br), 1680 (C=O of —CO—CH<sub>2</sub>Br) and 1740 cm<sup>-1</sup> (lactone carbonyl of carbostyril).

### 3-Carbostyryl methyl pyridinium (2) and 4-methyl-7-methoxy-8-carbostyryl methyl pyridinium (6)

To a solution of  $\omega$ -bromoacetyl carbostyryl (1) or (5) 0.03 mole in dry toluene (100 mL) was added pyridine (2.5 g, 0.031 mole) and the mixture was heated at reflux temperature for 2 h. The solution was allowed to cool to room temperature for 4 to 5 h. The resultant salt was filtered out and washed with hot toluene. It was dried and crystallized from acetic acid.

Salt 2: yield 80%, m.p. 190–198°C; salt 6: yield 80%, m.p. 210–215°C; IR: 3400 (N—CH<sub>2</sub>), 1690 (C=O) and 1730 cm<sup>-1</sup> (lactone carbonyl of carbostyryl).

TABLE-1  
ANALYTICAL AND SPECTRAL DATA OF 4a-f AND 7a-f

Compd.	m.p. (°C)	Yield (%)	m.f.	PMR ( $\delta$ ppm)
4a	186	60	C <sub>26</sub> H <sub>18</sub> N <sub>2</sub> O	7.2–9.0 (m, 17H, C <sub>4</sub> H + 16 aromatic protons) and 8.85 (broad s & —NH)
4b	173	50	C <sub>27</sub> H <sub>20</sub> N <sub>2</sub> O <sub>2</sub>	3.9 (S, OCH <sub>3</sub> ), 7.0–8.96 m (m, 15H, C <sub>4</sub> H + 14 aromatic protons) and 8.55 (broad s & —NH)
4c	182	48	C <sub>27</sub> H <sub>18</sub> N <sub>2</sub> O <sub>3</sub>	6.05 (S, 2H, O—CH <sub>2</sub> —O), 6.9–9.0 (m, 15H, C <sub>4</sub> H + 14 aromatic proton) and broad s & —NH
4d	152	52	C <sub>28</sub> H <sub>20</sub> N <sub>2</sub> O <sub>4</sub>	3.85 (S, OCH <sub>3</sub> ), 6.05 (S, —O—CH <sub>2</sub> O—), 6.8–8.9 (m, 14H, C <sub>4</sub> H + 13 aromatic proton) and broad s & —NH
4e	212	46	C <sub>30</sub> H <sub>26</sub> N <sub>2</sub> O <sub>5</sub>	3.95 {three singlets, 12H (OCH <sub>3</sub> ) <sub>4</sub> }, 6.95–8.97 (m, 13H C <sub>4</sub> H-12 aromatic Proton) and broad s & —NH
4f	183	49	C <sub>29</sub> H <sub>24</sub> N <sub>2</sub> O <sub>4</sub>	3.89 {two singlets, 9H (OCH <sub>3</sub> ) <sub>3</sub> }, 6.9–8.9 (m 14H, C <sub>4</sub> H + 13 aromatic proton) and broad s & —NH
7a	193	55	C <sub>28</sub> H <sub>27</sub> N <sub>2</sub> O <sub>2</sub>	2.27 (S, —CH <sub>3</sub> ), 3.74 (S, 3H, —OCH <sub>3</sub> ), 6.85–8.1 (M, 14H, aromatic proton) and broad s & —NH
7b	208	48	C <sub>29</sub> H <sub>24</sub> N <sub>2</sub> O <sub>3</sub>	2.4 (S, 3H —CH <sub>3</sub> ), 4.0 (two singlets, 6H, two —OCH <sub>3</sub> ), 6.89–8.4 (m, 13H, aromatic proton) and broad s & —NH
7c	240	43	C <sub>29</sub> H <sub>22</sub> N <sub>2</sub> O <sub>4</sub>	2.4 (S, 3H, —CH <sub>3</sub> ), 3.85 (S, 3H, —OCH <sub>3</sub> ), 6.0 (S, 2H, —O—CH <sub>2</sub> —O—), 6.1 (S, 1H, C <sub>5</sub> H), 6.84–8.0 (m, 12H, aromatic proton) and broad s & —NH
7d	216	45	C <sub>30</sub> H <sub>23</sub> N <sub>2</sub> O <sub>5</sub>	2.45 (S, 3H, —CH <sub>3</sub> ), 3.85–3.93 (two singlets, 6H, two —OCH <sub>3</sub> ), 6.89–8.7 (m, 11H, aromatic proton) and broad s & —NH
7e	110	44	C <sub>32</sub> H <sub>30</sub> N <sub>2</sub> O <sub>6</sub>	2.44 (S, 3H, —CH <sub>2</sub> ), 3.9 [two singlets, 15H, (CH <sub>3</sub> ) <sub>5</sub> ], 6.95–8.15 (m 1.0H, aromatic proton) and broad s & —NH
7f	190	44	C <sub>31</sub> H <sub>28</sub> N <sub>2</sub> O <sub>5</sub>	2.45 (S, 3H —CH <sub>3</sub> ), 3.94 [two singlets, 12H (OCH <sub>3</sub> ) <sub>4</sub> ], 6.15 (S, 1H, C <sub>3</sub> —H), 6.93–8.03 (m, 11H, aromatic proton) and broad s & —NH

### 3-(2-pyridyl) carbostyrils (4a-f) and 4-methyl-7-methoxy-8-(2-pyridyl) carbostyrils

#### General Procedure

To a well stirred solution of above pyridinium salt (2) or (6) 0.003 mole in glacial acetic acid (15 mL) was added ammonium acetate (3 g) and then a solution of chalcone in glacial acetic acid (10 mL) at room temperature for 1 h and then refluxed for 6 h at 130°C. The reaction mixture was allowed to cool to room temperature and was left overnight. It was poured into ice-cold water and the solid contained was filtered, washed with cold water and dried.

The product thus obtained was purified by column chromatography using silica gel and benzene-ethyl acetate (10 : 1) as an eluent and recrystallized from CHCl<sub>3</sub>.

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