

THE SYNTHESIS OF CONDENSED QUINOLIZINIUM SYSTEMS<sup>‡</sup>

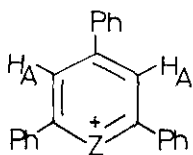
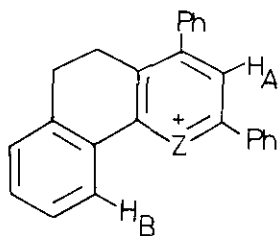
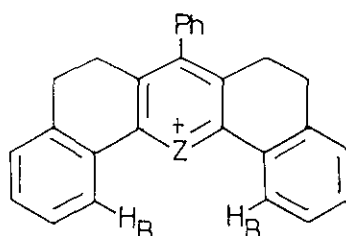
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**Abstract** - Dimethyl  $\beta$ -aminoethylacetal reacts with pyryliums (1-3a) to yield pyridiniums (1-3b) which are cyclised to fused benzoquinoliziniums (4-6).

Bradsher and Beavers<sup>1</sup> prepared the first fully aromatic benzoquinolizinium derivatives by cyclodehydration of 1-acetonil- and 1-phenacyl-2-phenylpyridiniums. Reactions of this general type have been reviewed.<sup>2,3</sup> Chloroacetaldoxime was previously used as a quaternising agent to give the equivalent of 1- $\beta$ -oxyethyl substituent.<sup>4</sup> We now find that dimethyl  $\beta$ -aminoethylacetal can be used as an alternative route to such compounds. This acetal reacts with pyryliums to yield 1- $\beta$ , $\beta$ -dimethoxyethyl derivatives which have led to syntheses of the condensed ring systems 4, 5 and 6. Ring systems 5 and 6 were previously unreported.

Dimethyl  $\beta$ -aminoethylacetal condensed with pyryliums 1a, 2a and 3a to give the expected pyridiniums 1b, 2b and 3b (Table 1) by the usual method.<sup>5</sup> On treatment with strong acid, each of the N-( $\beta$ , $\beta$ -dimethoxyethyl)pyridiniums cyclised to form quinolizinium salts (4-6) (Table 2), presumably via the carbonium ion intermediates (1c-3c).

123a Z = Ob Z = NCH<sub>2</sub>CH(OMe)<sub>2</sub>c Z = NCHCHOMe

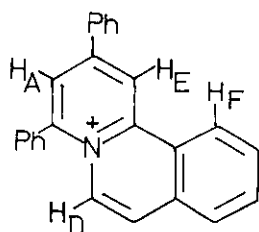
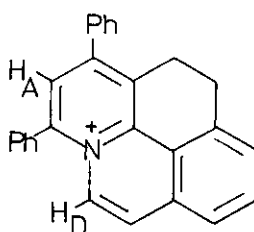
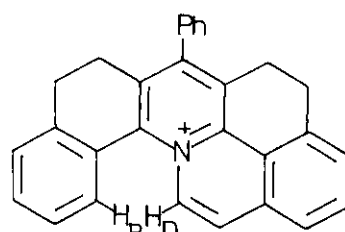
<sup>‡</sup>Submitted in honour of the retirement of Dr. Tetsuji Kametani, Founder and Chief Editor of "Heterocycles" with profound good wishes.

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Table 1: Preparation of pyridiniums (1b-3b), and quinoliziniums (4-6)

| Compound no.          | Yield % | Mp (°C) | Crystal form <sup>a</sup> | Found % |     |     | Formula                                                          | Required % |     |     |
|-----------------------|---------|---------|---------------------------|---------|-----|-----|------------------------------------------------------------------|------------|-----|-----|
|                       |         |         |                           | C       | H   | N   |                                                                  | C          | H   | N   |
| <u>1b</u>             | 54      | 178-179 | plates                    | 67.0    | 5.3 | 2.9 | C <sub>27</sub> H <sub>26</sub> BF <sub>4</sub> NO <sub>2</sub>  | 67.1       | 5.4 | 2.9 |
| <u>2b</u>             | 57      | 154-155 | plates                    | 62.6    | 4.8 | 2.4 | C <sub>30</sub> H <sub>28</sub> F <sub>3</sub> NO <sub>5</sub> S | 63.0       | 4.9 | 2.4 |
| <u>3b</u>             | 78      | 256-257 | plates                    | 69.4    | 5.5 | 2.5 | C <sub>31</sub> H <sub>30</sub> BF <sub>4</sub> NO <sub>2</sub>  | 69.6       | 5.6 | 2.6 |
| <u>4</u> <sup>b</sup> | 76      | 231-232 | needles <sup>c</sup>      | 68.2    | 4.3 | 3.2 | C <sub>25</sub> H <sub>20</sub> BF <sub>4</sub> NO               | 68.6       | 4.6 | 3.2 |
| <u>5</u>              | 86      | 196-197 | prisms                    | 66.1    | 3.9 | 2.7 | C <sub>28</sub> H <sub>20</sub> F <sub>3</sub> NO <sub>3</sub> S | 66.3       | 3.9 | 2.8 |
| <u>6</u>              | 64      | 254-256 | needles                   | 74.2    | 4.5 | 3.0 | C <sub>29</sub> H <sub>22</sub> BF <sub>4</sub> N                | 73.9       | 4.7 | 3.0 |

a) From MeOH unless otherwise indicated. b) Monohydrate. c) From 80% aqueous EtOH.

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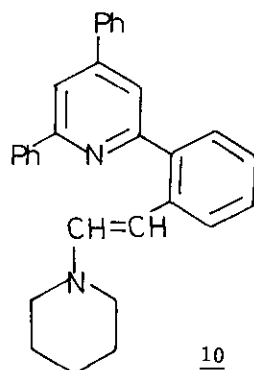
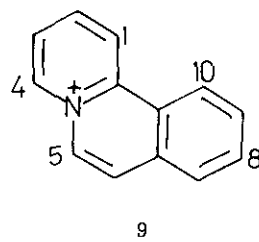
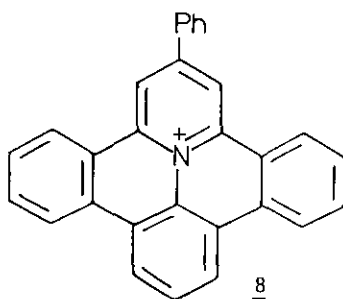
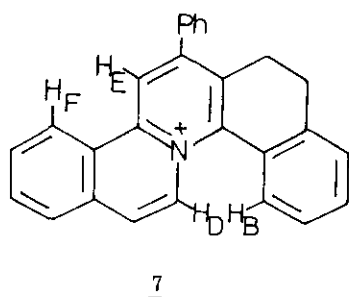
The structures of the cyclised products 4-6 are supported by the <sup>1</sup>H nmr data (Table 2). In the case of 1b and 3b the direction of cyclisation is unambiguous, and the spectra are satisfactorily interpreted on the basis of structures 4 and 6. However, 2b could cyclise to yield either 5 or 7; a distinction between these two structures is achieved by comparison of the spectra with those of the products 4 and 6.

The <sup>1</sup>H nmr of 7 would be expected to have at least four deshielded ( $\delta$  8.5-9.5) resonances as found in 4: most downfield being H<sub>D</sub> doublet and H<sub>E</sub> singlet (ca  $\delta$  9), with H<sub>F</sub> and H<sub>B</sub> (ca  $\delta$  8.5) multiplets (1,2 and 1,3 coupling) next most downfield due to steric polarisation; and H<sub>A</sub> should be absent. Similar downfield shifts are observed in photocyclised heterocycle 8.<sup>6</sup> In fact we find only one deshielded proton at 8.4 for H<sub>D</sub>. In other respects, the product from 2b has a spectrum similar to that of 6 (cf CH<sub>2</sub>CH<sub>2</sub> at  $\delta$  3.2 and 2.9 in 6 and at  $\delta$  3.4 in 5) and therefore it is assigned structure 5. Further evidence for structure 5 comes from uv:  $\lambda_{\text{max}}$  for 4 and 6 are respectively 376 and 400 nm. The product from 2b has  $\lambda_{\text{max}}$  = 376 nm, consistent with structure 5; 7 should have  $\lambda_{\text{max}}$  similar to that of 6.

Nucleophilic attack on the benzo[a]quinolizinium ring (cf 9) has previously<sup>7</sup> occurred at the 4-position, with ring-opening to an isoquinoline. When piperidine is reacted with 4, pyridine 10 is obtained. Presumably the phenyl at position-4 in quinolizinium 4 hinders approach of piperidine: hence ring opening preferentially to pyridine 10 occurs.

Table 2:  $^1\text{H}$  Nmr data<sup>a</sup>

| Cpd.<br>no.          | Aromatic                 |                 |                       |  |                       |                     | Aliphatic             |                                       |                                                           |                       |                      |                     |                               |                                            |
|----------------------|--------------------------|-----------------|-----------------------|--|-----------------------|---------------------|-----------------------|---------------------------------------|-----------------------------------------------------------|-----------------------|----------------------|---------------------|-------------------------------|--------------------------------------------|
|                      | A                        | B               | D                     |  | E                     |                     | F                     | Residual<br>aromatics<br>(m) $\delta$ | N <sup>+</sup> -CH <sub>2</sub> <sup>-</sup> <sub>2</sub> |                       | CH(OMe) <sub>2</sub> |                     | OCH <sub>3</sub> <sub>3</sub> | C <sub>2</sub> H <sub>4</sub> <sub>4</sub> |
|                      | (s)<br>$\delta$          | (m)<br>$\delta$ | (1H, d)<br>$\delta$ J |  | (1H, m)<br>$\delta$ J | (1H, m)<br>$\delta$ | (2H, d)<br>$\delta$ J |                                       |                                                           | (1H, t)<br>$\delta$ J |                      | (6H, s)<br>$\delta$ | (m)<br>$\delta$               |                                            |
| <u>1b</u>            | 7.9<br>(2H)              | -               | -                     |  | -                     | -                   | 7.5-8.0<br>(15H)      | 4.7 6                                 |                                                           | 3.9 6                 |                      | 2.9                 | -                             |                                            |
| <u>2b</u>            | 7.8<br>(1H)              | 8.2<br>(1H)     | -                     |  | -                     | -                   | 7.3-7.6<br>(13H)      | 5.2 4                                 |                                                           | 3.9 4                 |                      | 2.9                 | 2.7<br>(4H)                   |                                            |
| <u>3b</u>            | -                        | 8.1<br>(2H)     | -                     |  | -                     | -                   | 7.4-7.7<br>(11H)      | 5.5 <sup>b</sup> 4                    |                                                           | 4.0 <sup>b</sup> 4    |                      | 2.9                 | 2.9<br>(8H)                   |                                            |
| <u>4<sup>c</sup></u> | 8.2<br>(1H) <sup>d</sup> | -               | 8.5 8                 |  | 9.4 3                 | 9.0                 | 7.5-8.1<br>(14H)      | -                                     |                                                           | -                     |                      | -                   | -                             |                                            |
| <u>5</u>             | 8.0<br>(1H)              | -               | 8.4 8                 |  | -                     | -                   | 7.5-7.8<br>(14H)      | -                                     |                                                           | -                     |                      | -                   | 3.4<br>(4H)                   |                                            |
| <u>6<sup>e</sup></u> | -                        | 8.0<br>(1H)     | 9.2 7                 |  | -                     | -                   | 7.4-7.7<br>(12H)      | -                                     |                                                           | -                     |                      | -                   | 3.2<br>(4H)<br>2.9<br>(4H)    |                                            |

a) In  $\text{CDCl}_3$  unless otherwise indicated. b) Broadened. c) In  $\text{CF}_3\text{CO}_2\text{H}$ . d)  $\delta$ , J 3 Hz.e) In  $(\text{CD}_3)_2\text{SO}$ .

## EXPERIMENTAL

Ir and  $^1\text{H}$  nmr spectra were recorded on Perkin-Elmer 257 and Perkin-Elmer R12 instruments respectively. Mps are uncorrected and were obtained on a Kofler hot stage apparatus.

Preparation of Acetals (1b, 2b and 3b). The pyrylium salt (10 mmol) was suspended in  $\text{CH}_2\text{Cl}_2$  (5 ml);  $\beta,\beta$ -dimethoxyethylamine (10 mmol) and triethylamine (5 mmol) were added and the mixture was stirred for 40 min. Acetic acid (0.1 ml) was added and the mixture stirred for a further 12 min. After pouring into ether (200 ml), the resulting crystals were removed by filtration and washed with water, then with ether.

Preparation of Quinoliziniums (4, 5 and 6). Acetal (1b, 2b or 3b, 5 mmol) was heated at  $100^\circ\text{C}$  in water (25 ml) and the appropriate acid (fluoroboric for 1b and 3b; trifluoromethanesulphonic for 2b, 25 ml) for 1.5 h. The mixture was allowed to cool to ca  $25^\circ\text{C}$  and then the product was extracted into  $\text{CH}_2\text{Cl}_2$  (50 ml), poured into ether (200 ml), and stirred. Crystals were isolated by filtration, washed with water, and then with ether (Table 1).

2-(2-Piperidinioethenyl)-4,6-diphenylpyridine (10). Compound 4 (1 g, 2.4 mmol) was maintained at ca  $108^\circ\text{C}$  in piperidine (20 ml) for 5 days. Water (50 ml) was added and the product was extracted into ether (10 x 15 ml). The ethereal layer was washed with water (3 x 20 ml), dried over  $\text{MgSO}_4$ , and removal of the solvent at ca  $20^\circ\text{C}/25\text{ mmHg}$  gave the pyridine 10 (0.72 g, 76%), prisms from n-hexane, m.p.  $143\text{--}145^\circ\text{C}$  (Found: C, 86.2; H, 6.7; N, 6.4.  $\text{C}_{30}\text{H}_{28}\text{N}_2$  requires C, 86.5; H, 6.8; N, 6.7%);  $\delta$  ( $\text{CCl}_4$ ) 8.2 (2 H, m), 7.0-7.8 (14 H, m), 6.4 (1 H, d, J 13 Hz), 5.6 (1 H, d, J 13 Hz) 2 R (A H m) 1 A (B H m)

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