

## Quaternisation of 1,4-Diazabicyclo[2,2,2]octane and of Hexamethylenetetramine by N-Substituted Pyridiniums, and Oxidation of N-Substituents

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(Received 7th April 1980)

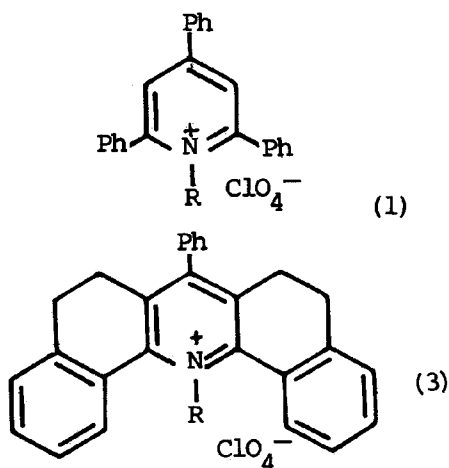
**Summary:** N-Substituents of pyridiniums undergo nucleophilic displacements to give quaternary derivatives and (with dichromate) carbonyl compounds.

Although N-Substituted pyridiniums are good alkylating agents for heteroaromatic tertiary amines such as pyridine,<sup>1</sup> similar quaternisations of aliphatic tertiary amines have not yet been reported. Indeed, the reactions of morpholine and piperidine with 1-substituted-2,4,6-triphenyl-pyridiniums (1) afforded selectively the tertiary amines, and the absence of quaternary salt was attributed to steric hindrance.<sup>1</sup> We now find that although 1-benzyl-2,4,6-triphenylpyridinium (1c) did not react smoothly with triethylamine or dimethylaniline, the less hindered 1,4-diazabicyclo [2,2,2] octane (DBCO) (5) readily gave the quaternary derivative (4c).

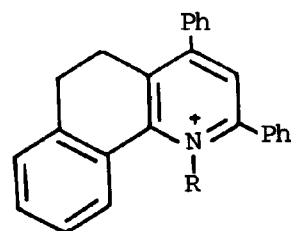
A series of these salts (4) was prepared (Table 1): the benzyl and substituted benzyl derivatives (4c-f) were all prepared using the corresponding monocyclic pyridinium (1c-f) in refluxing chlorobenzene. For N-methyl compound (4a) it was necessary either to re-

flux in dimethylformamide or to use the more reactive<sup>2</sup> tricyclic pyridinium (2a). For the N-ethyl analogue this did not suffice, but a good yield was obtained with the still more reactive<sup>3</sup> pentacyclic (3b).

Hexamethylenetetramine quaternary salts are useful in that they can be transformed into either amines or carbonyl compounds under hydrolytic conditions, depending on the pH.<sup>4</sup> We have therefore studied the reaction of hexamethylenetetramine with pyridiniums as a potential route to isotopically labelled amines and carbonyl compounds. The tricyclic pyridiniums (2) readily afforded a series of hexaminiums (6) (Table 2). For the N-methyl derivative (2a) reflux in chlorobenzene was required, but benzyl derivatives reacted in refluxing chloroform. Attempts to use the monocyclic pyridiniums in this reaction failed for (1a) and gave incomplete reaction for (1c).



- a, R = Me; b, R = Et;  
 c, R = PhCH<sub>2</sub>; d, R = ClC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub> (o);  
 e, R = ClC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub> (p);  
 f, R = MeC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub> (p);  
 g, R = 3-Pyridyl-CH<sub>2</sub>-;  
 h, R = Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub> (o,p); j, R = 4-Pyridyl-CH<sub>2</sub>; k, R = Cyclohexyl.



- i, X = ClO<sub>4</sub><sup>-</sup>  
 ii, X = CF<sub>3</sub>SO<sub>3</sub><sup>-</sup> (2)

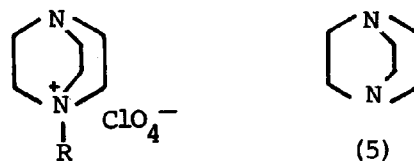


Table 1. 1-Substituted-1,4-diazoniabicyclo [2.2.2] octyl perchlorates (4)

Starting Pyridinium Perchlorate	1-Substituent	Yield (%)	Solvent for recryst.	M.p. (°C)	Crystal form	Found %			Formula	Required %		
						C	H	N		C	H	N
(1c)	PhCH <sub>2</sub>	92	EtOAc-EtOH	163	plates	51.9	6.4	9.1	C <sub>13</sub> H <sub>19</sub> ClN <sub>2</sub> O <sub>4</sub>	51.6	6.3	9.3
(1d)	Cl-C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> (o)	94	EtOAc-Et <sub>2</sub> O	207-209	prisms	46.2	5.4	8.3	C <sub>13</sub> H <sub>18</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>4</sub>	46.3	5.4	8.3
(1e)	Cl-C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> (p)	95	EtOAc-EtOH	191-193	Prisms	46.4	5.4	8.2	C <sub>13</sub> H <sub>18</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>4</sub>	46.3	5.4	8.3
(1f)	Me-C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> (p)	99	EtOH-Et <sub>2</sub> O	195-197	prisms	53.1	6.6	8.8	C <sub>14</sub> H <sub>21</sub> ClN <sub>2</sub> O <sub>4</sub>	53.1	6.7	8.8
(2a)	Me	98 <sup>d</sup>	EtOAc-EtOH	211-213	prisms	36.8	6.7	12.2	C <sub>7</sub> H <sub>15</sub> ClN <sub>2</sub> O <sub>4</sub>	37.1	6.7	12.4
(3b)	Et	70	EtOH-Et <sub>2</sub> O	138-139	prisms	39.8	7.1	11.8	C <sub>8</sub> H <sub>17</sub> ClN <sub>2</sub> O <sub>4</sub>	39.9	7.1	11.6

<sup>d</sup> Using (1a) as starting material and 2 h reflux in HCONMe<sub>2</sub> as solvent gave a yield of 65%.

Table 2. Synthesis of hexaminium perchlorates (6)

Pyridinium perchlorate <sup>a</sup>	N-Subst.	Method	Crystal form <sup>b</sup>	M.p. (°C)	Yield (%)	Found			Formula	Required		
						C	H	N		C	H	N
(2ai)	Me	B	prisms	211-213	75	33.2	6.0	21.9	C <sub>7</sub> H <sub>15</sub> ClN <sub>4</sub> O <sub>4</sub>	33.0	6.0	22.0
(2ci)	PhCH <sub>2</sub>	A	prisms	153-158	95	—	—	16.6	C <sub>13</sub> H <sub>19</sub> ClN <sub>4</sub> O <sub>4</sub>	—	—	16.9
(2ei)	ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> (p)	A	needles	172-174	94	42.6	4.9	15.3	C <sub>13</sub> H <sub>18</sub> Cl <sub>2</sub> N <sub>4</sub> O <sub>4</sub>	42.8	5.0	15.3
(2fi)	MeC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> (p)	A	prisms	165	92	48.6	6.1	16.3	C <sub>14</sub> H <sub>21</sub> ClN <sub>4</sub> O <sub>4</sub>	48.8	6.2	16.3
(2gi)	3-Pyridyl CH <sub>2</sub>	B	prisms	208-209	77	—	—	21.1	C <sub>12</sub> H <sub>18</sub> ClN <sub>5</sub> O <sub>4</sub>	—	—	21.1

<sup>a</sup> Previously reported ref. 1. <sup>b</sup> From CHCl<sub>3</sub>.

A recent report<sup>5</sup> of the conversion of alkyl halides into aldehydes by tetrabutylammonium dichromate prompted us to modify our previously reported<sup>6</sup> conversion of 1-substituted-2,4,6-triphenyl-pyridiniums by pyrolysis with the sodium salt of 1-hydroxy-4,6-diphenyl-2-pyridone (7).

1-Benzyl-2,4,6-triphenylpyridinium perchlorate (5) indeed gave benzaldehyde (65%) on refluxing with bis-tetrabutylammonium dichromate 1-cyclohexyl-2,4,6-triphenylpyridinium tetrafluoroborate (1k) gave cyclohexanone (44%).

However, the use of the more reactive<sup>2,7</sup> 1-benzyl- and their soluble trifluoromethanesulphonate salts gave good results with potassium dichromate and n-tetrabutylammonium tetrafluoroborate (Bu<sub>4</sub><sup>n</sup>NBF<sub>4</sub>) (Table 3).

### Experimental

Bis-tetra-n-butylammonium Dichromate [(Bu<sub>4</sub><sup>n</sup>N)<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>] was prepared as reported, m.p. 130-134°C (lit.,<sup>5</sup> m.p. 129-133°C).

The preparation of the following compounds has already been reported: 1-benzyl-(1c),<sup>1</sup> 1-(p-chlorobenzyl)-(1e),<sup>1</sup> and 1-(p-methylbenzyl)-2,4,6-triphenylpyridinium perchlorate (1f),<sup>1</sup> 5,6-dihydro-1-methyl-2,4-diphenyl-naphtho [1,2-b] pyridinium perchlorate (2ai),<sup>2</sup>

1-(2,4-dichlorobenzyl)-2,4,6-triphenylpyridinium perchlorate (1h)<sup>8</sup>.

1-(o-Chlorobenzyl)-2,4,6-triphenylpyridinium Perchlorate (1d).-2,4,6-Triphenylpyridinium perchlorate was reacted with o-chlorobenzylamine using the procedure described previously.<sup>2</sup> The pyridinium perchlorate (1d) (87%) had m.p. 203-205; prisms (EtOH) (Found: N, 2.6. C<sub>30</sub>H<sub>23</sub>Cl<sub>2</sub>NO<sub>4</sub> requires N, 2.6%);  $\nu_{\max}$  (CHBr<sub>3</sub>) 1620, 1604, 1580, and 1150 vs cm<sup>-1</sup> (ClO<sub>4</sub><sup>-</sup>);  $\delta$ (CF<sub>3</sub>-CO<sub>2</sub>H) 8.2 (2 H,s), 8.1-7.5 (15 H,m), 7.3-6.7 (4 H,m), and 5.82 (2 H,s).

N-Ethyl-5,6,8,0-tetrahydro-7-phenyldibenzo [c,h] acridinium Perchlorate (3b).-5,6,8,9-Tetrahydro-7-phenyldibenzo [c,h] xanthylum perchlorate<sup>2</sup> (1.5 g, 0.003 mol) was stirred overnight with EtNH<sub>2</sub> (2.0 g, 0.004 mol) in Et<sub>2</sub>O. The product was filtered and recrystallised from abs. EtOH giving the perchlorate (1.5 g, 95%) as prisms, m.p. 257-258°C (Found: C, 71.1; H,

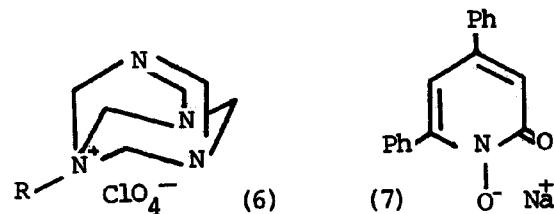


Table 3. Synthesis of carbonyl compounds by oxidation of pyridinium salts

Pyridinium salt	Method	Reaction time (h)	Product	Yield %
(1c)	B	4.0	PhCHO <sup>d</sup>	67
(1j) <sup>b</sup>	B	5.0	Cyclohexanone <sup>a,c</sup>	44
(2cii) <sup>d</sup>	AB	3.0	PhCHO <sup>a,c</sup>	70
(2eii) <sup>d</sup>	A	2.0	ClC <sub>6</sub> H <sub>4</sub> CHO (p) <sup>a,c</sup>	62
(2fii) <sup>d</sup>	A	2.5	MeC <sub>6</sub> H <sub>4</sub> CHO (p) <sup>a,c</sup>	88
(2hii) <sup>d</sup>	A	2.0	Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub> CHO (o,p) <sup>a,c</sup>	56
(2jii) <sup>d</sup>	A	2.0	4-Pyridyl CHO <sup>d</sup>	55

<sup>a</sup>l.r. identical with that of authentic sample. <sup>b</sup>Pyridinium tetrafluoroborate used m.p. 164-165°C lit., m.p. 163-164°C (R. Lombard and A. Kress, *Bull. Soc. chim. France*, 1528 (1960)). <sup>c</sup><sup>1</sup>H n.m.r. identical with that of authentic sample. <sup>d</sup>A.R. Katritzky, A.M. El-Mowafy, L. Marzorati, R.C. Patel, and S.S. Thind, in preparation.

5.5; N, 2.8. C<sub>29</sub>H<sub>26</sub>ClNO<sub>4</sub> requires C, 71.4; H, 5.4; N, 2.9%;  $\nu_{\max}$  (CHBr<sub>3</sub>) 1605s and 1090 vs cm<sup>-1</sup> (ClO<sub>4</sub><sup>-</sup>);  $\delta$ (CF<sub>3</sub>CO<sub>2</sub>H) 8.3-7.1 (13 H,m), 4.7 (2 H,q), 2.7 (8 H,m), and 1.6 (3 H,t).

**General Procedure for Oxidation of Pyridinium Salts (Table 3).-Method A.** The pyridinium (3 g, 0.005 mol) tetra-n-butylammonium tetrafluoroborate (1.6 g, 0.005 mol), potassium dichromate (3.0 g, 0.01 mol), and 1,2-dichloroethane (20 ml) was refluxed until reaction was complete (t.l.c.). The solution was cooled to 20°C and passed through silica gel (30 g). The silica was washed with Et<sub>2</sub>O (100 ml). Solvents were removed at 50°C (20 mmHg) and the aldehyde was obtained by distillation (2 mmHg) as a colourless oil. **Method B.** The same procedure as before, but using bis-n-tetrabutylammonium dichromate (in place of K<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub> and Bu<sub>4</sub><sup>+</sup>NBF<sub>4</sub><sup>-</sup>) with two mole equivalents.

**General Procedure for Synthesis of 1-Substituted 1,4-diazoniabicyclo [2.2.2] octyl Perchlorates (4).** The pyridinium perchlorates (0.003 mol) and diazabicyclo [2.2.2] octane (0.0032 mol) were refluxed in chlorobenzene (20 ml) for 2 h. The quaternary ammonium salts separated partially on cooling. After dilution with Et<sub>2</sub>O (50 ml), the products were recrystallised from the solvent indicated (Table 1).

**General Procedure for Synthesis of Hexaminium Perchlorates (6) (Table 3).** The 1-substituted 5,6-dihydro-2,4-diphenylbenzo [h] quinolinium perchlorate

(3a) (0.005 mol) and hexamine (1) (1.4 g, 0.01 mol) were refluxed in CHCl<sub>3</sub> (20 ml) for 12 h. On cooling, the pure hexaminium perchlorate (2) crystallised (Table 2).

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