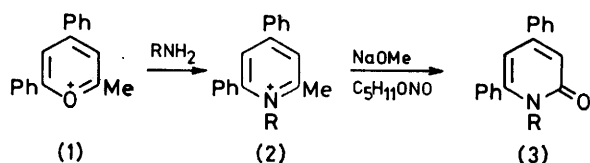


## 2- and 4-Pyridones by Oxidative Demethylation of 2- and 4-Methylpyridinium Cations <sup>1</sup>

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1-Substituted 2- and -4-methylpyridinium cations are converted by pentyl or ethyl nitrite and sodium methoxide into 1-substituted-2- and -4-pyridones respectively.

We required 1-substituted 4,6-diphenyl-2-pyridones (3) for other work <sup>2</sup> and now report that they can be obtained by oxidative demethylation of the 2-methylpyridinium cations (2), themselves readily available from the corresponding pyrylium salt (1).



The classical preparation of 2-pyridones from pyridinium salts suffers from lack of regioselectivity and is usually not applicable to preparation of 4-pyridones.<sup>3</sup> Most other methods from pyridinium compounds require amino or halogen groups for displacement,<sup>4</sup>

given oximes in yields of *ca.* 50%. We reasoned that dehydration of an oxime should give the nucleophilically displaceable cyano-group.

The 2-methyl-4,6-diphenylpyridinium salts (2) were conveniently prepared (Table 1) from 2-methyl-4,6-diphenylpyrylium tetrafluoroborate (1)<sup>11</sup> in yields averaging 76%. These compounds reacted with pentyl nitrite and sodium methoxide to form the corresponding 1-substituted 2-pyridones (3) (Table 2). The chief difficulty with the reaction lies in the purification of the product pyridone from tarry by-products. The use of an excess of ethyl nitrite in place of the pentyl nitrite led to easier work-ups. Elution down an alumina (UG-01) column with ethyl acetate also conveniently purified the pyridones.

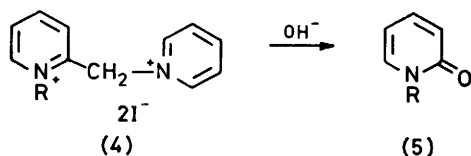
The reaction is believed to involve the intermediate formation of the oxime (6) and cyano-compound (7). In

TABLE I  
1-Substituted 2-methyl-4,6-diphenylpyridinium tetrafluoroborates

N-Subst.	Crystal form <sup>a</sup>	M.p. (°C)	Yield (%)	Found (%)			Formula	Required (%)		
				C	H	N		C	H	N
PhCH <sub>3</sub>	Needles	227—229	80	71.0	5.5	3.2	C <sub>26</sub> H <sub>22</sub> BF <sub>4</sub> N	70.9	5.3	3.3
<i>p</i> -MeC <sub>6</sub> H <sub>4</sub> CH <sub>3</sub>	Needles	232—235	90	71.2	5.6	3.1	C <sub>28</sub> H <sub>24</sub> BF <sub>4</sub> N	71.4	5.5	3.2
<i>o</i> -ClC <sub>6</sub> H <sub>4</sub> CH <sub>3</sub>	Needles	226—227	75	65.3	4.9	3.1	C <sub>26</sub> H <sub>21</sub> BF <sub>4</sub> ClN	65.6	4.6	3.1
Ph	Flakes	214—215	63	70.4	5.2	3.3	C <sub>24</sub> H <sub>20</sub> BF <sub>4</sub> N	70.4	4.9	3.4
Bu <sup>n</sup>	Needles	145—148	70	67.9	6.2	3.8	C <sub>28</sub> H <sub>34</sub> BF <sub>4</sub> N	67.9	6.2	3.6
<i>n</i> -C <sub>8</sub> H <sub>13</sub>	Needles	123—125	74	69.0	6.8	3.2	C <sub>24</sub> H <sub>28</sub> BF <sub>4</sub> N	69.1	6.8	3.4
<i>n</i> -C <sub>8</sub> H <sub>17</sub>	Needles	125—126	75	70.0	7.4	3.0	C <sub>28</sub> H <sub>32</sub> BF <sub>4</sub> N	70.1	7.5	3.2

<sup>a</sup> All compounds were crystallised from ethanol.

however Berson and Cohen <sup>5</sup> have described the conversion of 2- and 4-methylpyridinium cations into 2- and 4-pyridones (5) *via* the King reaction intermediates (4). Unfortunately the yield is rather low over the two

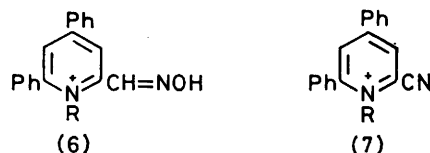


steps required <sup>6</sup> and some reactions fail completely.<sup>7</sup> We therefore sought alternatives to this reaction.

Ethyl nitrite and HCl react with alkylpyrimidines to yield the corresponding oximes.<sup>8</sup> Similar reactions have been performed under basic conditions: thus 2- and 4-alkylpyridines <sup>9</sup> or their methohalides <sup>10</sup> with Na, <sup>9a</sup> alkali amide, <sup>9b,9c</sup> or NaOH <sup>10</sup> and alkyl nitrite have

support we isolated in one case the oxime (6; R = *p*-tolyl). The conversion of 1-methyl-2-oximinomethylpyridinium iodide into 1-methyl-2-pyridone has been briefly reported.<sup>12</sup>

The reaction appears to be general: 1-benzyl-2-methyl- and 1-benzyl-4-methyl-pyridinium cations are converted into 1-benzyl-2- and 1-benzyl-4-pyridone



respectively (Table 2), and it should be applicable to other ring systems. This reaction could be of considerable general utility in heterocyclic chemistry.

## EXPERIMENTAL

*N*-Substituted 2-Methyl-4,6-diphenylpyridinium Tetrafluoroborates.—The appropriate amine (20 mmol) was added dropwise to a stirred suspension of 2-methyl-4,6-diphenylpyrylium tetrafluoroborate (10 mmol) in ether (50 ml) at 20 °C. The mixture was stirred for 3 h and then kept 12 h. The product was collected by filtration and crystallised from ethanol.

The 1-phenylpyridinium salt was prepared by adding

under reflux for 3 h. The mixture was filtered and the solvent evaporated. The residue was dissolved in water (50 ml), filtered, the filtrate extracted with ether (3 × 50 ml), and the extracts discarded. The aqueous layer was then saturated with sodium carbonate and extracted with chloroform (3 × 30 ml). The dried (Na<sub>2</sub>CO<sub>3</sub>) chloroform extracts were evaporated to afford the corresponding pyridone.

Essentially the same procedure was followed for pre-

TABLE 2  
Preparation of pyridones

2- or 4-Pyridone	<i>N</i> -subst.	C-substs.	Yield	Cryst. solvent	Cryst. form	M.p. (°C)	Lit. m.p. (°C)	Ref.
2	Bu <sup>a</sup>	4,6-Ph <sub>2</sub>	63	EtOAc-light petroleum	Needles	95—98	98—99	a
2	<i>n</i> -C <sub>6</sub> H <sub>13</sub>	4,6-Ph <sub>2</sub>	63		Oil			b, c
2	<i>n</i> -C <sub>8</sub> H <sub>17</sub>	4,6-Ph <sub>2</sub>	70		Oil			b, d
2	PhCH <sub>2</sub>	4,6-Ph <sub>2</sub>	60	EtOH	Prisms	140—142	133—134	a
2	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub>	4,6-Ph <sub>2</sub>	75	EtOH	Yellow needles	176—177		e
2	<i>o</i> -ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub>	4,6-Ph <sub>2</sub>	52	EtOH	Needles	163—165		f
2	Ph	4,6-Ph <sub>2</sub>	65	EtOH	Prisms	170—172		g
2	Me		65		Oil			h, i
2	PhCH <sub>2</sub>		72	Light petroleum (60—80 °C)	Pale brown flakes	70—73	75	i, j
4	Me		60	Benzene-light petroleum (60—80 °C)	Pale yellow needles <sup>k</sup>	89—93	94.5—96.5	i, l
4	PhCH <sub>2</sub>		63	Benzene	Pale yellow needles	105—108	109—111	i, m

<sup>a</sup> J. Faust, G. Speier, and R. Mayer, *J. prakt. Chem.*, 1969, **311**, 61. <sup>b</sup> Characterised by i.r. and n.m.r. spectroscopy and purity verified by t.l.c. (CHCl<sub>3</sub>). <sup>c</sup> <sup>1</sup>H N.m.r. data: δ(CDCl<sub>3</sub>) 7.48 (10 H, bs), 6.84 (1 H, d), 6.34 (1 H, d), 3.92 (2 H, bt), and 2.0—0.70 (11 H, m). <sup>d</sup> <sup>1</sup>H N.m.r. data: δ(CDCl<sub>3</sub>) 7.48 (10 H, bs), 6.84 (1 H, d), 6.34 (1 H, d), 3.90 (2 H, bt), and 2.10—0.85 (15 H, m). <sup>e</sup> Found: C, 85.8; H, 6.2; N, 4.0%. C<sub>25</sub>H<sub>21</sub>NO requires C, 85.4; H, 6.0; N, 4.0%. <sup>f</sup> Found: C, 77.6; H, 5.0; N, 3.7%. C<sub>24</sub>H<sub>18</sub>CINO requires C, 77.5; H, 4.9; N, 3.8%. <sup>g</sup> Found: C, 85.9; H, 5.4; N, 4.4%. C<sub>23</sub>H<sub>17</sub>NO requires C, 85.4; H, 5.3; N, 4.3%. <sup>h</sup> Ref. 5. <sup>i</sup> Further characterised by i.r. and n.m.r. spectroscopy. <sup>j</sup> C. Rāth, *Annalen*, 1931, **489**, 107. <sup>k</sup> Hygroscopic. <sup>l</sup> E. M. Kosower and J. W. Patton, *Tetrahedron*, 1966, **22**, 2081. <sup>m</sup> A. R. Katritzky and R. A. Jones, *J. Chem. Soc.*, 1960, 2947.

aniline (20 mmol) dropwise to a stirred suspension of the pyrylium salt (10 mmol) in ethanol (40 ml). The mixture was heated under reflux for 6 h and kept 12 h at 20 °C. The crystalline product was filtered off and recrystallised from ethanol. Details are given in Table 1.

*N*-Substituted 4,6-Diphenyl-2-pyridones.—Sodium ethoxide (10 mmol) in ethanol (10 ml) was added dropwise to a stirred mixture of the pyridinium tetrafluoroborate (10 mmol) and pentyl nitrite (10 mmol) at 0—5 °C. The reaction mixture was stirred for 3 h and kept 12 h at 5 °C. Inorganic salts were filtered off and the solvent was removed at 80 °C/20 mmHg. The residue was repeatedly extracted with ether (100 ml) and the extracts evaporated to give the pyridone. The ether-insoluble gummy material was boiled in ethanol for 90 min, evaporated, and ether-extracted to give more of the pyridone. Details are given in Table 2.

1-(*p*-Methylbenzyl)-2-(oximinomethyl)-4,6-diphenylpyridinium Tetrafluoroborate.—The gummy material mentioned above from the reaction of 2-methyl-4,6-diphenyl-1-*p*-tolylpyridinium tetrafluoroborate was dissolved in ethanol, cooled, and acidified with fluoroboric acid to give the tetrafluoroborate which was filtered off, washed with water, and the oxime crystallised from ethanol as yellowish white needles, m.p. 177—180 °C (Found: C, 67.3; H, 5.3; N, 6.2. C<sub>26</sub>H<sub>23</sub>BF<sub>4</sub>N<sub>2</sub>O requires C, 67.0; H, 5.0; N, 6.0%).

1-Methyl- and 1-Benzyl-2- and -4-pyridone.—Methyl iodide or benzyl chloride was treated with 2- or 4-picoline and the crude pyridinium salts used directly.

Sodium ethoxide (0.01 mol) in ethanol (10 ml) was added dropwise to a stirred mixture of *N*-methyl-2- or -4-picolinium iodide (0.011 mol) and pentyl nitrite (0.011 mol) at 0—5 °C. The mixture was stirred for 2 h, then heated

preparation of *N*-benzyl-2- and -4-pyridone but the residue, after evaporating the ethanol, was dissolved in chloroform (50 ml), filtered, and the dried (Na<sub>2</sub>CO<sub>3</sub>) chloroform solution evaporated off.

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