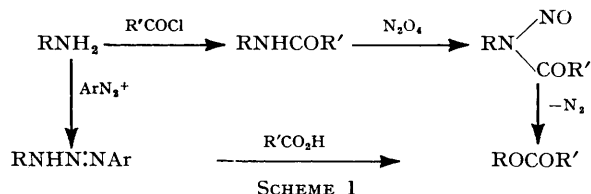


## Heterocycles in Organic Synthesis. Part 10.<sup>1</sup> Conversion of Amines into Esters

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Alkyl, benzyl, and aralkyl primary amines are converted into the corresponding acetates and benzoates *via* intermediate triphenylpyridinium tetrafluoroborates in good yield.

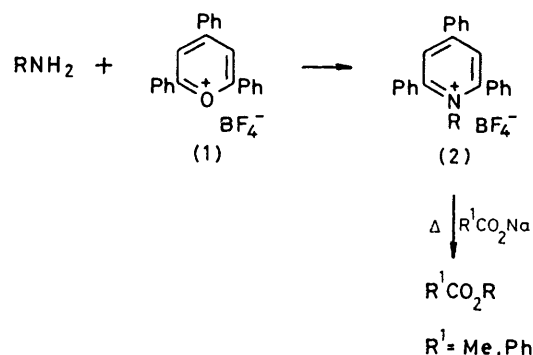
ONE of the apparently simplest reactions of organic chemistry is the conversion of an amino-compound  $\text{RNH}_2$  into the hydroxy-analogue  $\text{ROH}$ . Elementary texts often show this as being achieved by reaction with nitrous acid; in reality the products from the reaction of aliphatic amines with nitrous acid are usually complex.<sup>2</sup> For example 1-aminobutane with nitrous acid in acetic acid gives a mixture of *n*- and *s*-butyl acetates (ratio 2 : 1) and 1-, *cis*-2-, and *trans*-2-butenes (ratio 7 : 1 : 2);<sup>3</sup> preparatively *n*-butyl and *s*-butyl alcohols were obtained in 25 and 13% yield, respectively.<sup>4</sup> Although good yields have in some instances<sup>5</sup> been reported from the conversion of aliphatic amines into the corresponding alcohols, it is normally only with aromatic primary amines that satisfactory yields are obtained.<sup>6</sup> Another direct method for the conversion  $\text{RNH}_2 \rightarrow \text{ROH}$ , the Bucherer reaction, is restricted to the fused ring aromatic series.<sup>7</sup> Indirect methods involving esters as intermediates include the rearrangements of *N*-nitroso-amides<sup>8</sup> and triazenes<sup>9</sup> (Scheme 1).



SCHEME 1

The conversion of a primary amine ditosyl derivative into the corresponding acetate by potassium acetate in

placements on pyridinium cations (themselves formed from pyrylium salts and a primary amine) by amines,<sup>12</sup>



SCHEME 2

chloride,<sup>13</sup> iodide,<sup>14</sup>† and other nucleophiles.<sup>15</sup> We now show that esters (and thus alcohols) may be prepared in high yield from primary amines *via* suitable pyridinium salts in a new two-step process (Scheme 2).

**Preparation of Pyridinium Salts.**—2,4,6-Triphenylpyrylium tetrafluoroborate (1) is readily available<sup>16</sup> and has previously<sup>17</sup> been shown to react with primary amines to give *N*-substituted pyridinium tetrafluoroborates (2). We utilised tetrafluoroborates since the subsequent procedure involves a pyrolysis (indicating the unsuitability of perchlorates) and we encountered difficulties in the synthesis of tosylates,<sup>18</sup> although tetrafluoroborates give somewhat erratic combustion

TABLE 1

*N*-Substituted 2,4,6-triphenylpyridinium tetrafluoroborates (2)<sup>a</sup>

No.	<i>N</i> -Substituent	Yield (%)	M.p. (°C)	Solvent	Found			Formula	Requires		
					C	H	N		C	H	N
(2a)	Methyl	87	217—218 <sup>b</sup>	Abs. EtOH							
(2b)	Ethyl	73	164—165 <sup>c</sup>	Abs. EtOH							
(2c)	<i>n</i> -Butyl	67	201—202	Abs. EtOH	72.0	5.6	3.2	C <sub>27</sub> H <sub>26</sub> BF <sub>4</sub> N	71.8	5.8	3.1
(2d)	2-Phenylethyl <sup>d</sup>	77	274	Abs. EtOH	74.6	5.5	2.8	C <sub>31</sub> H <sub>26</sub> BF <sub>4</sub> N	74.6	5.2	2.8
(2e)	2-Picolyl	65	218—219	Abs. EtOH	71.7	4.9	5.7	C <sub>29</sub> H <sub>23</sub> BF <sub>4</sub> N <sub>2</sub>	71.6	4.7	5.8
(2f)	3-Picolyl	76	166—168	Abs. EtOH	71.6	5.0	5.9	C <sub>29</sub> H <sub>23</sub> BF <sub>4</sub> N <sub>2</sub>	71.6	4.7	5.8
(2g)	Benzyl <sup>e</sup>	85	196—197	EtOH	71.8	5.4	2.9	C <sub>30</sub> H <sub>24</sub> BF <sub>4</sub> N <sub>2</sub> H <sub>2</sub> O	71.8	5.2	2.8
(2h)	2-Methylbenzyl	94	178	Me <sub>2</sub> CO-Et <sub>2</sub> O			2.8	C <sub>31</sub> H <sub>26</sub> BF <sub>4</sub> N			2.8

<sup>a</sup> All the tetrafluoroborates crystallised as needles. <sup>b</sup> Lit. m.p. 215—216 °C (ref. 17). <sup>c</sup> Lit. m.p. 164—165 °C (ref. 17). <sup>d</sup> B. P. Leddy, M.Sc. Thesis, University of East Anglia, 1975. <sup>e</sup> The presence of water of crystallisation is indicated by an i.r. band at 3 490 cm<sup>-1</sup>.

hexamethylphosphoramide<sup>10</sup> is useful for unhindered amines. The hydrolysis of esters to alcohols is well documented and usually proceeds in high yield.<sup>11</sup>

We have previously demonstrated the utility of dis-

† An early example of this reaction was reported by A. B. Susan and A. T. Balaban, *Rev. Roumaine Chim.*, 1969, **14**, 111.

analysis data.‡ Pyridinium salt formation proceeded (Table 1) in EtOH in 65—94% yield. Characteristic

‡ Use of silver oxide, tungstate, and vanadate on MgO, Chromosorb P, and pumice has now enabled us to analyse tetrafluoroborate salts satisfactorily. (We thank Dr. E. Lunt, May and Baker, Dagenham, for help on this point.)

spectral details (Table 2) include in the  $^1\text{H}$  n.m.r. spectra a deshielded singlet for the 3- and 5-protons of the pyridinium ring; chemical shifts for other protons are

suspended 2,4,6-triphenylpyrylium tetrafluoroborate  $^{16}$  (2 g, 15 mmol) in EtOH (50 ml) were stirred at 20 °C for 12 h. The solution became deep red and after 0.5 h all the solid

TABLE 2

I.r.<sup>a</sup> and  $^1\text{H}$  n.m.r. spectra of *N*-substituted 2,4,6-triphenylpyridinium tetrafluoroborates (2)

No.	$\nu_{\text{max.}}/\text{cm}^{-1}$	N.m.r. solvent	Chemical shift ( $\delta$ )
(2c)	1 620s, 1 600w, 1 580w, 1 560w, 1 490w, 1 410w, 1 375w, 1 160w, 1 050s,br, 890s, 765s, 760s, 690s	$\text{CDCl}_3$	0.9—2.4 (7 H, m), 4.9 (2 H, t), 7.9—8.2 (15 H, m), 8.3 (2 H, s)
(2d)	1 625s, 1 600w, 1 585w, 1 570w, 1 250w, 1 180w, 1 160m, 1 050s,br, 895s, 770s, 765s, 700s	$\text{CF}_3\text{CO}_2\text{H}$	2.72 (2 H, t), 4.81 (2 H, t), 6.45 (2 H, m), 7.15 (3 H, m), 7.66 (15 H, m), 8.06 (2 H, s)
(2e)	1 620s, 1 590w, 1 560w, 1 490w, 1 410w, 1 370w, 1 340w, 1 170w, 1 050s,br, 990w, 880s, 760s, 700s, 680s	$\text{CDCl}_3$	6.2 (2 H, s), 6.9 (1 H, m), 7.6—8.2 (15 H, m), 8.35 (2 H, s), 8.9 (1 H, m)
(2f)	1 630s, 1 590w, 1 570w, 1 380w, 1 190w, 1 160w, 1 060s,br, 1 000w, 775s, 700s	$\text{CDCl}_3$	6.2 (2 H, s), 7.5 (1 H, m), 7.8—8.2 (17 H, m), 8.35 (2 H, s), 8.8 (1 H, m)
(2g)	3 490w, 1 622s, 1 598w, 1 050s,br, 719s, 690s	$\text{CF}_3\text{CO}_2\text{H}$	5.25 (2 H, s), 7.2—7.4 (2 H, m), 7.6—7.75 (2 H, m), 7.30 (15 H, m), 7.85 (2 H, s)

<sup>a</sup> In Nujol.

as expected. The i.r. spectra show the typical tetrafluoroborate peak and characteristic ring-stretching bands at 1 630—1 620 and 1 600—1 570  $\text{cm}^{-1}$ .

*Preparation of Esters.*—The pyridinium salts (2) on

had dissolved. The solvent was removed at 60 °C and 20 mmHg and residual salt washed with ether and crystallised from absolute EtOH; yield 4.2 g, 85%; m.p. 196—197 °C.

TABLE 3

*N*-Substituted 2,4,6-triphenylpyridinium tetrafluoroborates (2) and their conversion into acetates and benzoates

No.	<i>N</i> -Substituent	Preparation of acetate $\text{MeCO}_2\text{R}$			Preparation of benzoate $\text{PhCO}_2\text{R}$		
		Pyrolysis Temp. (°C)	Yield (%)	Characterisation	Pyrolysis Temp. (°C)	Yield (%)	Characterisation
(2a)	Methyl	175	65	<i>a</i>	180	70	<i>a</i>
(2b)	Ethyl	180	79	<i>a</i>	180	60	<i>a</i>
(2c)	<i>n</i> -Butyl	185	75	<i>a</i>	190	85	<i>a</i>
(2d)	2-Phenylethyl	220	70	<i>a</i>	<i>b</i>		
(2e)	2-Picolyl	180	60	<i>c</i>	200	68	<i>d</i>
(2f)	3-Picolyl	185	78	<i>e</i>	200	75	<i>f</i>
(2g)	Benzyl	210	70	<i>a</i>	180	85	<i>a</i>
(2h)	2-Methylbenzyl	210	70	<i>a</i>	<i>b</i>		

<sup>a</sup> Identified by comparison with i.r. spectrum of an authentic sample. <sup>b</sup> Not attempted. <sup>c</sup> As the hydrochloride, m.p. 92—93 °C [lit., m.p. 94—95 °C (K.-B. Augustinsson and H. Hasselquist, *Acta Chem. Scand.*, 1964, **18**, 1006)]. <sup>d</sup> As the picrate, m.p. 159—160 °C [lit., m.p. 161—162 °C (J. H. Boyer and L. T. Wolford, *J. Amer. Chem. Soc.*, 1958, **80**, 2741)]. <sup>e</sup> As the hydrochloride, m.p. 95 °C [lit., m.p. 96—98 °C; see ref. in *c*]. <sup>f</sup> As the methiodide, m.p. 158—159 °C [lit., m.p. 159 °C (L. Panizzon, *Helv. Chim. Acta*, 1941, **24**, 24 E)].

pyrolysis at 180—220 °C with sodium acetate gave the acetate esters in yields of 60—79% (Table 3). The compounds were identified by comparison of i.r. spectra with those of authentic samples and/or the preparation of a derivative.

The reaction appears to be general: a series of benzoates were prepared analogously (Table 3), and a single butyrate (see Experimental section). The overall yields of the esters from the primary amines average 50%, and the procedure thus represents a feasible synthetic route for the conversion  $\text{RNH}_2 \rightarrow \text{R}'\text{CO}_2\text{R}$  (and hence ROH). The detailed mechanism of the reaction is unknown; it may proceed either by direct nucleophilic displacement or through an intermediate ring-addition product: we favour the former alternatives.

#### EXPERIMENTAL

I.r. spectra were measured with a Perkin-Elmer 237 instrument and n.m.r. spectra with a Perkin-Elmer R12 instrument ( $\text{Me}_4\text{Si}$  as internal standard). M.p.s were determined with a Reichert microscope.

*Preparation of Pyridinium Tetrafluoroborates (2).*—In a typical experiment, benzylamine (2 g, 18.7 mmol) and

*Preparation of Acetates.*—The appropriate *N*-substituted pyridinium tetrafluoroborate (*ca.* 5 mmol), anhydrous NaOAc (*ca.* 10 mmol), and 2,4,6-triphenylpyridine (*ca.* 1.5 mmol) were heated in a distillation apparatus first at 100 °C and 0.1—0.2 mmHg for 4 h to remove water and then at *ca.* 200 °C (the precise temperature is given in Table 3). The acetate smoothly distilled out of the reaction mixture and was collected in a receiver cooled with liquid nitrogen.

*Preparation of Benzoates.*—The preceding method was used with the substitution of NaOBz for NaOAc.

Benzyl butyrate (60%) was prepared from *N*-benzyl-2,4,6-triphenylpyridinium tetrafluoroborate (5 mmol) and sodium butyrate (10 mmol) by a similar procedure at 190 °C and 0.2 mmHg.

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