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Facile Preparation of Pyrylium and Pyridinium Bromides Under Neutral Conditions

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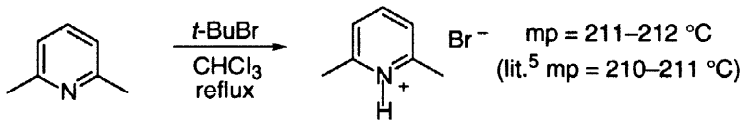
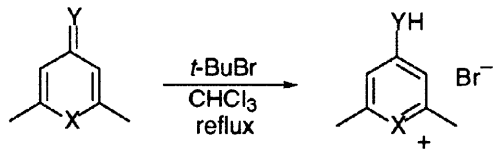
Abstract: Pyrylium and pyridinium bromides may be prepared in virtually quantitative yield by reaction of the corresponding base with an excess of *tert*-butyl bromide under reflux in chloroform solution.

Pyrylium,[1] pyridinium,[2] and related aromatic salts are generally prepared by protonation of the appropriate base with a strong Brønsted acid.[1-3] In light of the well-studied dehydrobromination that results when *tert*-alkyl bromides are treated with amine bases,[4] it is somewhat surprising that this elimination reaction has apparently not been exploited as a route to pyridinium bromides.[2,3] Thus, as might be anticipated,[4] treatment of 2,6-dimethylpyridine with an excess of *tert*-butyl bromide in chloroform solution at reflux delivers the pure hydrobromide salt in virtually quantitative yield. It occurred to us that *tert*-butyl bromide might also serve as an in situ equivalent of anhydrous HBr for the protonation of even weakly basic substrates such as γ-pyrones, 4-pyridones, and their thia-analogs. Indeed, as illustrated by the results presented below, treatment of such weak bases with an excess of *tert*-butyl bromide in chloroform solution at reflux delivers the corresponding pyrylium or pyridinium salts in excellent yield (Table 1); isobutylene is generated as a by-product in these presumably bimolecular dehydrobromination reactions.



95 %

The conversion of heterocycles **1–5**, prepared by standard methods,[6] to their hydrobromide salts is easily accomplished in high yield (Table 1) by simply heating a chloroform solution of the base and an excess (typically 5 molar equivalents) of freshly distilled *tert*-butyl bromide at gentle reflux overnight. The pyrylium (**1a–2a**) and pyridinium salts (**3a–5a**) may be isolated by simple filtration (in the case of relatively insoluble salts) or, more generally, by concentration of the reaction mixture under reduced pressure; recrystallization affords analytically pure material.[7]



1, X = Y =O — **1a**
2, X = O, Y = S — **2a**
3, X = NH, Y = O — **3a**
4, X = NMe, Y = O — **4a**
5, X = NMe, Y = S — **5a**

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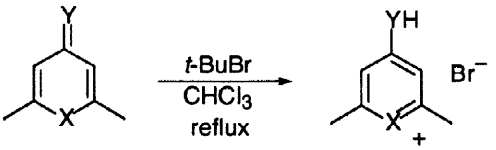
Table 1. Preparation of Pyrylium and Pyridinium Bromides[a]



entry	base	salt	mp, °C	yield,[b] %
1	**1**, X = Y = O	**1a**	194-195[c]	95
2	**2**, X = O, Y = S	**2a**	143-144 (dec)	93
3	**3**, X = NH, Y = O	**3a**	> 260 (dec)	94
4	**4**, X = NMe, Y = O	**4a**	280-281 (dec)	95
5	**5**, X = NMe, Y = S	**5a**	228-229 (subl)	94

[a] Bromide salts were prepared by heating a solution of the base (10 mmol) and *tert*-butyl bromide (50 mmol) in dry chloroform (15 mL) at gentle reflux overnight. [b] Isolated yield of analytically pure product. [c] Lit.(ref. 8) mp = 192-193 °C.

While the dehydrobromination of tertiary alkyl bromides upon treatment with relatively strong bases such as substituted pyridines finds ample literature precedent,[2,4] the reaction seems not to have been recognized as a convenient route to hydrobromide salts of either pyridines or more weakly basic heterocycles such as γ-pyrones and 4-pyridones (it might be noted that the pK_a of **1a** is a mere 0.30).[9] As demonstrated by the results presented above, the ability of *tert*-butyl bromide to function as a surrogate for anhydrous HBr allows for the preparation of a variety of heterocyclic hydrobromide salts in high yield under essentially neutral conditions.

References and Notes

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6. Literature procedures were followed for the preparation of the parent heterocycles: (a) **1** and **2**, King, L.C.; Ozog, F.J.; Moffat, J. *J. Am. Chem. Soc.* **1951**, *73*, 300. (b) **3**, Iguchi, S.; Inoue, A. *Chem. Pharm. Bull.* **1963**, *11*, 390. (c) **4**, Cook, D. *Can. J. Chem.* **1963**, *41*, 1435. (d) **5**, Elkaschef, M.; Nosseir, M. *J. Am. Chem. Soc.* **1960**, *82*, 4344.
7. Satisfactory C/H/N/Br analyses have been determined for all previously unreported bromide salts (**2a–5a**) and their IR, ^1H NMR and ^{13}C NMR spectra are fully in accord with the assigned structures.
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