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New compounds were prepared for evaluation as antidotal and/or prophylactic activity against toxic organophosphorus acetylcholinesterase inhibitors. One series of compounds consists of the 5-, 6-, 7-, and 8-(N,N-dimethylcarbamoyloxy) derivatives of 1-methylimidazo[1,2-a]pyridinium ion with varying C2 substituents. Fifteen new compounds were prepared. These compounds show substantial activity as inhibitors of acetylcholinesterase (electric eel) but no data are available on in vivo protective activity. A second series of compounds included thirteen new α-carbamoyloxyalkylimidazolium salts. Some of these compounds show marginal activity as acetylcholinesterase inhibitors. The two lead compounds in this series had shown in vivo activity, but no in vivo data has been obtained for the new compounds. Five additional compounds including two phenols and three enol carbamates were prepared. The report includes synthetic methods, spectroscopic data and elemental analysis for all new compounds prepared.
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Introduction

The purpose of this work was to prepare a number of quaternary heteroaromatic salts for evaluation as antidotal and/or prophylactic activity against organophosphorus inhibitors of acetylcholinesterase. The initial impetus for work in this particular type of compounds came from recognition of both antidotal and prophylactic activity in several compounds prepared in an earlier antiparasitic program. Specifically, compounds BL08205 and BL09042 showed antidotal activity and BL55142 showed prophylactic activity.

\[
\text{BL08205} \quad \begin{array}{c}
\text{n=2} \\
70-90\% \text{ survival of } 2 \text{ LD}_{50} \text{ GD}
\end{array}
\]

\[
\text{BL09042} \quad \begin{array}{c}
\text{n=3} \\
70\% \text{ survival of } 2 \text{LD}_{50} \text{ GD}
\end{array}
\]

\[
\text{BL55142} \quad 100\% \text{ survival of } 2 \text{LD}_{50} \text{ GD at 15 min pretreatment}
\]

During the period January 1, 1989 - June 30, 1991 these leads were pursued under the auspices of contract DAMD-17-89-C-9014. A total of 75 new compounds were prepared. These included various substituted 2-aryloxymethylpyridinium and imidazolium salts. These compounds indicated relatively little activity. Also prepared were a number of 2-[2-, 3-, and 4-carbamoyloxophenyl]imidazo[1,2-a]pyridinium salts and 2-(carbamoyloxophenoxy)methyl) derivatives of imidazole, pyridine, quinoline, benzimidazole and imidazo[1,2-a]pyridine. Many of these compounds were active. Results were published in two papers in 1993 (1). A number of these compounds show inhibition of acetylcholinesterase (electric eel) with compound
BM01738 being most active (IC$_{50}$ = 10 nM). Although this compound was not particularly promising in vivo, the pyridinium salt BM01265 showed substantial prophylactic activity.

![Chemical structures of BM01265 and BM01738]

BM01265

80-100% Survival of 2 LD$_{50}$ GD at 60 min. pretreatment 0.9-62.5 mg/kg

In the course of that work a single example having a carbamoyloxy substituent on the heterocyclic ring was prepared. This compound BM08648 showed some prophylactic activity and a principle emphasis of the current work was to systematically vary the position of substitution and the nature of the 2-substituent for the imidazo[1,2-a]pyridine series.

![Chemical structure of BM08648]

BM08648

80% Survival of 2 LD$_{50}$ GD of 60 min. pretreatment at 35.6 mg/kg

The prophylactic activity of several heterocyclic carbamates is well known with pyridostigmine and physostigmine having been well-studied. The positive charge on such compounds presumably makes them particularly good substrates for acetylcholinesterase (2, 3).
We successfully prepared a series of 16 compounds (including the previously prepared BM08648) representing the 2-H, 2-methyl, 2-isopropyl, and 2-phenyl compounds with N, N-dimethylcarbamoyloxy substituents at each of the other ring positions.

In addition, thirteen carbamoyloxyalkylimidazolium salts which were part of the series begun under the auspices of DAMD-17-89-C-9014 were prepared. We also prepared a few enol carbamates from aminketoncs having structure similarity to acetycholine or acetycholine mimics. In all 33 new compounds were prepared. They are listed in Table I in chronological order of submission.
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Synthetic Methods

A. Carbamoyloxyalkylimidazolium Salts

1-Substituted carbamoyloxyimidazolium salts were prepared by N-alkylation of the imidazole using BuLi, CH₂=O (n=1), BuLi, oxirane (n=2), and NaH, CH₂=CHCO₂C₂H₅ then LiAlH₄, respectively. The 1-(ω-hydroxyalkyl)imidazoles were then carbamoylated and quaternized. The methods are summarized in Scheme I and details are given in the Experimental Section.

**Scheme I**

\[ \text{N\textsubscript{2} (PN-II-32)} \]

\[ \text{N\textsubscript{2} (PN-II-112)} \]

\[ \text{N\textsubscript{2} (PN-II-184)} \]

\[ \text{N\textsubscript{2} (PN-II-108)} \]

\[ \text{N\textsubscript{2} (PN-II-178)} \]

a) BuLi; (CH₂O)n; Me₂NCOCl. b) BuLi; ethylene oxide; Me₂NCOCl.
c) CH₃N=C=O; d) Ethyl acrylate, cat. NaH. e) LiAlH₄. f) NaH; Me₂NCOCl.; g) Mel.
Scheme II depicts the synthesis of 2-(N,N-dimethylcarbamoyloxymethyl), 2-[2-(N,N-dimethylcarbamoyloxy)ethyl] and 2-[3-(N,N-dimethylcarbamoyloxy)propyl] imidazolium salts. Chain introduction or extension was accomplished by alkylation of lithium intermediates with formaldehyde or oxirane. The hydroxyl group was then carbamoylated and the heterocyclic molecule was quaternized. Details are given in the Experimental Section.

Scheme II

4a 4c (KC005)

5b  R₂ = CH₃, CH₃
5d  R₂ = H, CH₃
5c (PN68)  R₂ = CH₃, CH₃
5e (PN-II-68)  R₂ = H, CH₃

6b  R₂ = CH₃, CH₃
6d  R₂ = H, CH₃
6c (PN38)  R₂ = CH₃, CH₃
6e (PN-II-62)  R₂ = H, CH₃

a) CH₂O. b) Me₂NCOCl. c) HCl. d) BuLi. e) Oxirane. f) MeOsT.
Alkyl groups were introduced at the 4-position of the imidazole ring using a phenylthio substituent to block the 2-position. (4) Hydroxymethyl, 2-hydroxyethyl and 3-hydroxypropyl groups were then introduced using formaldehyde, oxirane and oxetane/BF₃, respectively. The alcohols were then carbamoylated. Desulfurization was accomplished with Raney nickel prior to Quaternization. These methods are outlined in Scheme III and described in Experimental Section.

Scheme III

\[ \text{Scheme III} \]

\[ \text{SPh} \]

\[ \text{Me}_2\text{NCO}_2 \]

\[ \text{BuLi} \quad -78^\circ \text{C} \]

\[ \text{Li} \]

\[ \text{c, d, e, f} \]

\[ \text{Me}_2\text{NCO}_2 \]

\[ 9d \text{ (PN-I-292)} \]

\[ \text{Me}_2\text{NCO}_2 \]

\[ 7c \text{ (PN-177)} \]

\[ \text{Me}_2\text{NCO}_2 \]

\[ 8c \text{ (PN-294)} \]

\[ \text{a) (CH}_2\text{O)}_n; \text{Me}_2\text{NCOCl.} \quad \text{b) Oxirane; Me}_2\text{NCOCl.} \quad \text{c) Oxetane, BF}_3\cdot\text{Et}_2\text{O.} \quad \text{d) NaH, DMF; Me}_2\text{NCOCl.} \quad \text{e) Raney Ni desulfurization.} \quad \text{f) Mel.} \]

B. Carbamoyloxyimidazo[1,2-a]pyridinium Salts

5-Hydroxyimidazo[1,2-a]pyridine was prepared from 5-aminomidazo[1,2-a]pyridine by reacting with 70% aqueous H₂SO₄. (5) This reaction was also applicable to the 2-methyl and 2-phenyl derivatives. The 2-(2-propyl) derivative was prepared from 2-amino-6-hydroxypyridine (5) and 1-bromo-3-methylbutan-2-one. (6) The 5-hydroxyimidazo[1,2-a]pyridines are in tautomeric equilibria with the 5-keto tautomers and are very weakly acidic. For this reason, carbamoylation was carried out on the sodium salts prepared with NaH. Quaternization could then be done with
methyl iodide (Scheme IV). In the case of 10a the N-methylation was done first (Scheme V).

Scheme IV

\[
\begin{align*}
11b & \quad R = CH_3 \\
12b & \quad R = CH(CH_3)_2 \\
13b & \quad R = Ph \\
11c & \quad R = CH(CH_3)_2 \\
11d & \quad R = CH(CH_3)_2 \\
12c & \quad R = CH(CH_3)_2 \\
12d & \quad R = CH(CH_3)_2 \\
13c & \quad R = CH(CH_3)_2 \\
13d & \quad R = CH(CH_3)_2 \\
\end{align*}
\]

Scheme V

2-Amino-6-benzoyloxypyridine was prepared by an adaptation of the method of Moore and coworkers. Details are given in the Experimental Section. This compound was cyclized with an appropriate α-halocarbonyl compound, solvolyzed, carbamoylated and then quaternized with methyl iodide or methyl tosylate (Scheme VI).
An existing route to 2-amino-4-hydroxypyridine was substantially improved during the course of this work. (8) As with the 5-isomers the possibility of a tautomeric equilibrium exists and carbamoylation was best done with the sodium salt of 2-amino-4-hydroxypyridine. The product, 4-(N,N-dimethylcarbamoyloxy)-2-aminopyridine can rearrange by O-to-N acyl migration but it was possible to cyclize the compound directly with the various α-halomethyl reactants. This provided a more convergent route than was employed for the other series of compounds. Quaternization was then done with methyl iodide (Scheme VII).
The 8-substituted imidazo[1,2-a]pyridine derivatives were prepared beginning with commercially available 2-amino-3-hydroxypyridine. (9) Each of the 8-hydroxy intermediates was carbamoylated and then quaternized with methyl iodide or methyl tosylate (Scheme VIII).

Scheme VIII

C. Carbamoyl enolates of Choline Analogs

The enolates of 1-methyl-3-piperidone and 1-methyl-4-piperidone were prepared from 3-hydroxyl and 4-hydroxypyrindine, respectively. The piperidines were first carbamoylated with N,N-dimethylcarbamoyl chloride and then reduced with NaBH₄ to give the enol carbamates (tetrahydroxypyrindines). The enol carbamate were then quaternized. Compound BM34821, the N-methylcarbamate of the enol of 1-methyl-3-piperidone was prepared following the same route using methyl isocyanide for carbamoylation. The route is outlined in Scheme IX and details are given in the Experimental Section.
D. Miscellaneous Compounds

Two phenols, KC012/BM14306 and KC020/BM14324 which are precursors of active carbamates were submitted to determine if the uncarbamoylated compounds show any activity, since Gandour, Quinn and coworkers had demonstrated that the phenol precursor of neostigmine has activity as an AChE inhibitor (10). These compounds had been prepared earlier as intermediates and are described in the final report for project DAMD-17-89-C-9014.

Biological Results

All compounds were submitted to Walter Reed Army Institute of Research for evaluation of prophylactic and antidotal activity against organophosphorus inhibitors of AChE. In order to have preliminary and more rapid evidence of activity to guide synthetic efforts we also conducted in vitro assays using electric eel type AChE, following the method of Ellman (11). The available data are given in Tables 2 and 3.
Table 2. Activity of Carbamoyloxy Imidazo[1,2-a]pyridinium Salts as AChE Inhibitors

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a) Final report DAMD-17-89-C-9014
Table 3. Inhibition of Acetylcholinesterase by Carbamoyloxyalkylimidazolium Salts

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<td>9d</td>
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a. Prepared under contract DAMD-17-89-C-9014. Biological results obtained during current period.
Table 4. *In Vivo* Data for BM03698 and BM02646

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Experimental Section

A. Carbamoyloxyalkylimidazolium Salts

1-[(N,N-Dimethylcarbamoyloxy)methyl]-1H-imidazole (1a) To a cooled solution (-15 °C) of imidazole (6.81 g, 0.1 mol) in dry THF (130 mL) was added dropwise a solution of n-BuLi in hexane (44 mL, 0.11 mol). The mixture was stirred at -10 °C for 30 min then predried paraformaldehyde (4.5 g, 0.15 mol) was added in small portions. After being stirred at -5 °C for 10 min the cooled bath was removed and the reaction mixture was stirred at room temperature overnight. N,N-dimethyl-carbamoyl chloride (1.38 mL, 0.15 mol) was added and the reaction mixture was stirred at room temperature overnight. The mixture was quenched with dilute aqueous HCl solution then extracted with ether (3 x 50 mL). The aqueous layer was basified with 20% NaOH solution and extracted with CH₂Cl₂ (4 x 70 mL). The organic layers were washed with H₂O (30 mL), brine (30 mL) and dried (Na₂SO₄). Removal of solvent gave a crude product which was purified by column chromatography (silica gel, CHCl₃-MeOH, 9:1) to give 1a (12.4 g, 73%) as an off-white solid from EtOAc/hexane; mp 72-73 °C; Rf = 0.48 (CHCl₃-MeOH, 9:1); ¹H NMR (CDCl₃) δ 7.72 (s, 1 H), 7.14 (s, 1 H), 7.04 (s, 1 H), 5.86 (s, 2 H), 2.91 (s, 3 H), 2.88 (s, 3 H); ¹³C NMR (CDCl₃) δ 154.74, 138.09, 129.57, 119.51, 68.36, 36.36, 35.71. Anal. Calcd for C₇H₁₁N₃O₂: C, 49.69; H, 6.55; N, 24.92. Found: C, 49.72; H, 6.52; N, 24.92.

General Procedure for Quaternization of ω-Carbamoyloxylimidazoles A mixture of carbamate and methyl iodide or methyl p-toluenesulfonate (1.5 equiv) in dry THF (or acetonitrile) was maintained at 60 °C overnight. Ether was then added and the reaction mixture was cooled in ice. The precipitate was collected and purified by recrystallization.

3-Methyl-1-[(N,N-dimethylcarbamoyloxy)methyl]-1H-imidazolium Iodide (1b) (PN-II-32, BM18957) Following the general procedure for quaternization, the reaction of 1a (2.3 g, 13.6 mmol) with methyl iodide (1.69 mL, 27 mmol) in dry THF (10 mL) gave a crude white solid 1b (4.16 g, 98%) which was recrystallized in MeOH/Et₂O: mp 171-172 °C; IR (KBr)νmax 3155, 3102, 1701, 1180, 1147, 1054 cm⁻¹.
1H NMR (DMSO-d$_6$) δ 9.32 (s, 1 H), 7.85 (s, 1 H), 7.73 (s, 1 H), 6.05 (s, 2 H), 3.88 (s, 3 H), 2.86 (s, 3 H), 2.83 (s, 3 H); $^{13}$C NMR (DMSO-d$_6$) δ 153.86, 137.97, 123.75, 122.44, 36.19, 36.05, 35.60. Anal. Calcd for C$_8$H$_{14}$IN$_3$O$_2$: C, 30.88; H, 4.53; N, 13.50. Found: C, 30.94; H, 4.57; N, 13.50.

1-[2-(N,N-Dimethylcarbamoyloxy)ethyl]-1H-imidazole (2a) To a cooled solution (-40 °C) of imidazole (6.8 g, 0.1 mol) in dry THF (200 mL) was added slowly a solution of n-BuLi in hexane (45.8 mL, 0.11 mol). The mixture was stirred for 30 min and cooled ethylene oxide (10 mL, 0.2 mol) was added at once via canula. The reaction mixture was stirred at room temperature overnight and then N,N-dimethylcarbamoyl chloride (13.8 mL, 0.15 mol) was added. After being stirred at room temperature overnight the mixture was quenched with 100 mL of cold water. Organic solvent was removed under aspirator pressure. The aqueous mixture was saturated with NaCl, then extracted with CHCl$_3$ (5 x 100 mL). The organic layers were washed with brine, dried (Na$_2$SO$_4$) and filtered. Removal of solvent to dryness gave a yellow solid. Purification of the crude product by column chromatography (silica gel; CHCl$_3$-MeOH, 19:1) gave 2a (14.4 g, 79%) as a white solid from EtOAc/hexane: mp 80-81 °C; R$_f$ = 0.36 (CHCl$_3$-MeOH, 9:1); $^1$H NMR (CDCl$_3$) δ 7.51 (s, 1 H), 7.07 (s, q H), 6.96 (s, 1 H), 4.33 (t, 2 H, J = 5.2 Hz), 4.21 (t, 2 H, J = 5.2 Hz), 2.91 (s, 3 H), 2.86 (s, 3 H). Anal. Calcd for C$_8$H$_{14}$IN$_3$O$_2$: C, 52.45; H, 7.15; N, 22.94. Found: C, 52.38; H, 7.18; N, 22.83.

3-Methyl-1-[2-(N,N-dimethylcarbamoyloxy)ethyl]-1H-imidazolium Iodide (2b) (PN-II-112, BM19098) Following the general procedure for quaternization, the reaction of 2a (1.83 g, 10 mmol) with methyl iodide (2.5 mL, 40 mmol) in dry THF (10 mL) yielded 2b (2.85 g, 87%) as a white solid from acetone/ether: mp 87-88 °C; IR (KBr) $\nu_{max}$ 3146, 3084, 1701, 1192 cm$^{-1}$; $^1$H NMR (DMSO-d$_6$) δ 9.15 (s, 1 H), 7.77 (brs, 1 H), 7.72 (br s, 1 H), 4.45 (t, 2 H, J = 4.8 Hz), 4.29 (t, 2 H, J = 4.8 Hz), 3.86 (s, 3 H), 2.78 (s, 6 H); $^{13}$C NMR (DMSO-d$_6$) δ 154.89, 136.86, 123.59, 122.71, 63.03, 48.39, 36.08, 35.89, 35.56. Anal. Calcd for C$_9$H$_{16}$IN$_3$O$_2$: C, 33.24; H, 4.96; N, 12.92. Found: C, 33.32; H, 4.99; N, 12.87.

Ethyl 3-(Imidazol-1-yl)propionate (3a) A mixture of imidazole (6.8 g, 0.1 mol) and NaH (48 mg, 2 mmol) in dry THF (100 mL) was stirred for 15 min at room
temperature. Ethyl acrylate (13 mL, 0.12 mol) was then added at once. After being stirred at 60 °C for 2 days, the reaction mixture was cooled in an ice bath and quenched with water. The organic solvent was removed under aspirator pressure. The aqueous mixture was basified with aqueous 20% NaOH solution to pH=11, saturated with NaCl and then extracted with CH₂Cl₂. The organic layers were washed with brine, dried (Na₂SO₄) and filtered. Removal of the solvent to dryness gave a dark yellow liquid. Purification of the crude product by column chromatography on silica gel (CHCl₃-MeOH, 9:1) gave 3a (14.7 g, 87%), a very pale yellow liquid: Rₚ = 0.39 (CHCl₃-MeOH, 9:1); ¹H NMR (CDCl₃) δ 7.51 (s, 1 H), 7.04 (s, 1 H), 6.94 (s, 1 H), 4.27 (t, 2 H, J = 6.6 Hz), 4.14 (q, 2 H, J = 7.2 Hz), 2.77 (t, 2 H, J = 6.6 Hz), 1.24 (t, 3 H, J = 7.2 Hz); ¹³C NMR (CDCl₃) δ 170.34, 137.12, 129.50, 118.68, 60.96, 42.14, 35.87, 13.94.

1-(3-Hydroxypropyl)-1H-imidazole (3b) To an ice-cooled mixture of LiAlH₄ (0.9 g, 23.8 mmol) in THF (30 mL) was added dropwise a solution of 3a (2 g, 11.88 mmol) in THF (5 mL). After 10 min the ice-bath was removed and the mixture was stirred at room temperature for 2 h. The reaction mixture was then cooled in an ice bath and sequentially quenched with water (0.9 mL), 20% NaOH solution (0.8 mL) and water (2.7 mL). The mixture was filtered with the aid of Celite. The filtered cake was washed thoroughly with hot THF. Evaporation of the solvent to dryness gave 3b (1.5 g, 100%) as a colorless liquid: Rₚ = 0.12 (CHCl₃-MeOH, 9:1); ¹H NMR (CDCl₃) δ 7.46 (s, 1 H), 7.04 (s, 1 H), 6.93 (s, 1 H), 4.12 (t, 2 H, J = 6.7 Hz), 3.60 (t, 2 H, J = 5.7 Hz), 1.99 (m, 2 H); ¹³C NMR (CDCl₃) δ 137.39, 129.12, 118.91, 57.99, 43.35, 33.28.

1-[3-(N,N-Dimethylcarbamoyloxy)propyl]-1H-imidazole (3c) A solution of N,N-dimethylcarbamoyl chloride (0.71 mL, 7.72 mmol) in THF (3 mL) was added dropwise to a slurry mixture of 3b (0.65 g, 5.15 mmol) and NaH (0.17 g, 7.0 mmol) in THF (12 mL) at reflux temperature. The reaction mixture stirred at that temperature for 6 h, and was then cooled to room temperature, quenched with water (15 mL), basified to pH=10, saturated with NaCl and extracted with CHCl₃ (4 x 30 mL). The organic layers were washed with brine (30 mL), dried (Na₂SO₄) and filtered. Removal of the solvent gave a brown liquid. Column chromatography (silica gel,
CHCl₃-MeOH, 9:1) of the crude product gave 3c (0.71 g, 69%) as a colorless liquid: 

\[ R_f = 0.40 \text{ (CHCl₃-MeOH, 9:1); } \]

\[ ^1H \text{ NMR (CDCl}_3\text{)} \delta 7.48 \text{ (s, 1 H), 7.05 (s, 1 H), 6.94 (s, 1 H), 4.03-4.10 (m, 4 H), 2.90 (s, 6 H), 2.07-2.16 (m, 2 H); } \]

\[ ^13C \text{ NMR (CDCl}_3\text{)} \delta 155.85, 136.81, 129.24, 118.51, 61.52, 43.50, 36.12, 35.54, 30.38. \]


3-Methyl-1-[3-(N,N-dimethylcarbamoyloxy)propyl]-1H-imidazolium Iodide (3d) (PN-II-108, BM19089) Following the general procedure for quaternization, the reaction of 3c (0.513 g, 2.5 mmol) with methyl iodide (0.32 mL, 5.2 mmol) in THF (5 mL) yielded a thick, pale yellow oil which gave a white solid 3d (0.85 g, 96%) on standing in the freezer. Analytical sample was recrystallized from acetone: mp 117.5-118 °C; IR (KBr) \( \nu_{max} \) 3142, 3067, 1703, 1197 cm\(^{-1}\); \(^1H\) NMR (DMSO-d\(_6\)) \( \delta \) 9.13 (s, 1 H), 7.78 (d, 1 H, J = 1.5 Hz), 7.71 (d, 1 H, J = 1.5 Hz), 4.24 (t, 2 H, J = 7.1 Hz), 4.00 (t, 2 H, J = 6.0 Hz), 3.84 (s, 3 H), 2.79 (s, 6 H), 2.07-2.16 (m, 2 H). Anal. Calcd for C\(_{10}\)H\(_{18}\)N\(_3\)O\(_2\): C, 35.39; H, 5.35; N, 12.39. Found: C, 35.46; H, 5.37; N, 12.33.

1-[2-(N-Methylcarbamoyloxy)ethyl]-1H-imidazole (2c) To an ice-cooled solution of 1-(2-hydroxyethyl)-1H-imidazole (3.48 g, 31 mmol) and methyl isocyanate (5.5 mL, 93 mmol) in dry CH₂Cl₂ (10 mL) were added a few drops of Bu₂Sn(OAc)₂. The mixture was stirred at room temperature for 2 h and the solvent was evaporated to dryness to give a crude yellow solid. Purification of the crude product by flash column chromatography on silica gel (CHCl₃-MeOH, 9:1) afforded 2c (4.48 g, 85%) as a white solid from EtOAc: mp 121.5-122.5 °C; IR (KBr) \( \nu_{max} \) 3115, 1722 cm\(^{-1}\); \(^1H\) NMR (CDCl₃) \( \delta \) 7.47 (s, 1 H), 7.04 (s, 1 H), 5.68 (br s, 1 H), 4.31 (t, 2 H, J = 5.1 Hz), 4.17 (t, 2 H, J = 5.1 Hz), 2.77 (d, 3 H, J = 4.8 Hz); \(^13C\) NMR (CDCl₃) \( \delta \) 156.35, 137.34, 129.30, 118.97, 63.30, 46.21, 27.30. Anal. Calcd for C\(_{7}\)H\(_{11}\)N\(_3\)O\(_2\): C, 49.70; H, 6.55; N, 24.84. Found: C, 49.79; H, 6.59; N, 24.88.

3-Methyl-1-[2-(N-methylcarbamoyloxy)ethyl]-1H-imidazolium Iodide (2d) (PN-II-184, BN 34812) Following the general procedure for quaternization, the reaction of 2c (1.44 g, 8.5 mmol) and methyl iodide (1.64 mL, 25.5 mmol) in THF
(10 mL) and CH₃CN (4 mL) at room temperature gave 2d (2.15 g, 81%) as white needles from acetone/ether: mp 104-105 °C; IR (KBr) νmax 3248, 3145, 3115, 1710 cm⁻¹; ¹H NMR (DMSO-d₆ + CDCl₃) δ 9.63 (s, 1 H), 7.79 (s, 1 H), 7.61 (s, 1 H), 6.70 (br s, 1 H), 4.59 (dd, 2 H, J = 4.5, 5.1 Hz), 4.37 (dd, 2 H, J = 4.5, 5.1 Hz), 4.10 (s, 3 H), 2.70 (d, 3 H, J = 8.1 Hz); ¹³C NMR (DMSO-d₆ + CDCl₃) δ 155.11, 136.26, 122.56, 122.30, 61.09, 48.42, 35.89, 26.15. Anal. Calcd for C₈H₁₄N₃O₂: C, 30.88; H, 4.54; N, 13.51. Found: C, 30.95; H, 4.55; N, 13.52.

1-[3-(N-Methylcarbamoyloxy)propyl]-1H-imidazole (3e) Carbamoylation of 3b (2.16 g, 16.64 mmol) with methyl isocyanate (2.97 mL, 50 mmol) as described for 2c gave a thick oil. Purification of the crude product by column chromatography on silica gel (CHCl₃-MeOH, 9:1) gave 3e (3.07 g, 98%), as white crystals from EtOAc/hexane: mp 61-62.5 °C; Rf = 0.24 (CHCl₃-MeOH, 9:1); IR (KBr) νmax 1079 cm⁻¹; ¹H NMR (CDCl₃) δ 7.48 (s, 1 H), 7.05 (s, 1 H), 6.93 (s, 1 H), 5.39 (br s, 1 H), 4.02-4.08 (m, 4 H), 2.78 (d, 3 H, J = 5.1 Hz), 2.04-2.12 (m, 2 H); ¹³C NMR (CDCl₃) δ 156.74, 136.95, 129.25, 118.67, 60.93, 43.49, 30.48, 27.24. Anal. Calcd for C₈H₁₃N₃O₂: C, 52.45; H, 7.15; N, 22.93. Found: C, 52.29; H, 7.17; N, 22.77.

3-Methyl-1-[3-(N-methylcarbamoyloxy)propyl]-1H-imidazolium Iodide (3f) (PN-II-178, BN34803) Following the general procedure for quaternization, the reaction of 3e (1.83 g, 10 mmol) with methyl iodide in dry THF (15 mL) gave 3f (2.86 g, 88%) as white needles from acetone/ether: mp 82-82.5 °C; IR (KBr) νmax 3076, 1709 cm⁻¹; ¹H NMR (DMSO-d₆) δ 9.11 (s, 1 H), 7.76 (s, 1 H), 7.70 (s, 1 H), 6.91 (br s, 1 H), 4.21 (t, 2 H, J = 6.4 Hz), 3.95 (t, 2 H, J = 6.1 Hz), 3.84 (s, 3 H), 2.54 (d, 3 H, J = 4.8 Hz), 2.05-2.12 (m, 2 H); ¹³C NMR (DMSO-d₆) δ 156.45, 136.64, 123.60, 122.26, 60.54, 46.16, 35.81, 29.08, 26.91. Anal. Calcd for C₉H₁₆I₃N₂O₂: C, 33.25; H, 4.96; N, 12.92. Found: C, 33.25; H, 4.94; N, 12.87.

1-Methyl-2-hydroxymethyl-1H-imidazole (4a) (12) 1-Methyl-1H-imidazole (10.9 mL, 0.136 mol) and formaldehyde (37% in water, 18.4 mL, 1.5 equiv) were heated in a pressure bottle for 5 h at 140 °C. The excess water and formaldehyde was removed under reduced pressure and the crude product 4a obtained as a yellowish oil was used for next reaction without further purification.
1-Methyl-2-(N,N-dimethylcarbamoyloxy)methyl-1H-imidazole (4b) To a solution of 4a in THF were added N,N-dimethylcarbamoyl chloride (6.3 mL, 0.68 mol) and triethylamine (9.5 mL, 0.68 mol). The mixture was refluxed for 16 h. The solvent was removed and the residue was partitioned between water and methylene chloride. The aqueous layer was washed with methylene chloride and the combined organic layer was evaporated to give the crude product 4b as a thick oil.

1-Methyl-2-(N,N-dimethylcarbamoyloxy)methyl-1H-imidazole Hydrochloride (4c) (KC005, BM14299) 4b was dissolved in ether and HCl gas was introduced. After reflux for 1 h a solid precipitate was obtained. The hydrochloride was recrystallized from ethanol/ether to give 4c as white needle crystals: mp 161-3 °C; IR (KBr) v max 3405, 3141, 3066, 2935, 1712, 1534, 1400, 1185 cm⁻¹; ¹H NM (D₂O) δ 7.41 (s, 2 H), 5.34 (s, 2 H), 3.88 (s, 3 H), 2.92 (s, 3 H), 2.85 (s, 3 H). Anal. Calcd for C₈H₁₄C₁N₃O₂: C, 43.74; H, 6.42; N, 19.13; Cl, 16.10. Found: C, 43.60; H, 6.40; N,19.04; Cl, 16.03.

1-Methyl-2-(2-hydroxyethyl)-1H-imidazole (5a) A solution of n-BuLi in hexane (44 mL, 0.11 mol) was added dropwise via a canula to an ice-cooled (-5 °C) solution of 1-methylimidazole (8.21 g, 0.1 mol, colorless liquid, bp 47°C/0.3mmHg) in dry THF (200 mL). The mixture was stirred at 0 °C for 1 h, then ethylene oxide (6.61 g) was slowly added. The mixture was allowed to gradually warm to room temperature and was stirred overnight. The reaction mixture was quenched with cold 10% HCl solution (200 mL). The organic layer was washed with 10% HCl solution (2 x 30 mL). The combined aqueous layers were basified with K₂CO₃, saturated with NaCl and then extracted with CHCl₃ (6 x 50 mL). The combined organic layers were washed with brine and dried (MgSO₄). Evaporation of the solvent gave a thick yellow oil. Removal of unreacted starting material (2.9 g) by vacuum distillation (Kugelrohr) afforded 5a as a yellow solid (4.68 g, 57% conversion): ¹H NMR (CDCl₃) δ 6.89 (s, 1 H), 6.80 (s, 1 H), 4.00 (t, 2 H, J = 5.6 Hz), 3.57 (s, 3 H), 2.84 (t, 2 H, J = 5.6 Hz); ¹³C NMR (CDCl₃) δ 146.7, 126.6, 120.3, 59.7, 32.4, 28.9.

1-Methyl-2-(2-N,N-dimethylcarbamoyloxyethyl)-1H-imidazole (5b) NaH (1.1 g, 36.6 mmol, 80% dispersion in mineral oil) was carefully added to a mixture of 5a (4.2 g, 33.3 mmol) in dry DMF (50 mL) at 0 °C. After being stirred for 10 min in an ice-
bath, then 30 min at room temperature, the mixture was cooled to 0 °C and N,N-
dimethylcarbamoyl chloride (4.65 g, 43 mmol) was slowly added by syringe. The ice-
bath was removed and the reaction mixture was stirred at room temperature
overnight. The mixture was quenched with 1% KOH solution, saturated with NaCl
and then extracted with CHCl₃ (5 x 50 mL). The organic extract was washed with 5%
HCl solution (2 x 150 mL). The cooled combined aqueous layers were basified with
10% KOH solution, saturated with NaCl and then extracted with CHCl₃ (6 x 50 mL).
The organic phase was dried (MgSO₄) and evaporated to dryness to give a thick oil
5b (3.76 g, 57%): ¹H NMR (CDCl₃) δ 6.89 (s, 1 H), 6.77 (s, 1 H), 4.36 (t, 2 H, J =
7.2 Hz), 3.58 (s, 3 H), 2.99 (t, 2 H, J = 7.2 Hz), 2.84 (br s, 6 H).

1,3-Dimethyl-2-(2-N,N-dimethylcarbamoyloxyethyl)-1H-imidazolium Tosylate
(5c) (PN68, BM16186) A mixture of 5b (0.3 g, 1.57 mmol) and methyl p-
toluenesulfonate (0.44 g, 2.35 mmol) in dry CH₃CN (10 mL) was stirred at 60 °C
(bath temperature) for 14 h. The reaction mixture was diluted with CH₃CN and
decolorized with charcoal. The volume of organic solvent was reduced under
aspirator pressure then ether was added. The resulting mixture was cooled in the
freezer to give a crude solid 5c (0.48 g, 67%) as white crystals from CH₃CN/ether:
mp 145 - 145.5 °C; IR (KBr) v_max 3173, 3088, 1695, 1207 cm⁻¹; ¹H NMR (CDCl₃) δ
7.67 (d, 2 H, J = 8.0 Hz), 7.53 (s, 2 H.), 7.11 (s, 2 H, J = 8.0 Hz), 4.26 (t, 2 H, J = 6.3
Hz), 3.82 (s, 6 H), 3.42 (t, 2 H, J = 6.3 Hz), 2.81 (s, 3 H), 2.76 (s, 3 H), 2.32 (s, 3 H);
¹³C NMR (CDCl₃) δ 155.25, 144.06, 143.89, 138.75, 128.30, 125.48, 122.89, 60.47,
N, 10.96. Found: C, 53.16; H, 6.59; N, 10.94.

1-Methyl-2-[2-(N-methylcarbamoyloxy)ethyl]-1H-imidazole (5d) 1-Methyl-2-
(2-hydroxyethyl)-1H-imidazole (13) (3.4 g, 26.9 mmol) was carboxamoylated with
methyl isocyanate (8 mL, 134 mmol) as described for 2c gave a dark yellow oil.
Purification of the crude product by column chromatography on silica gel (CHCl₃-
MeOH, 9:1) yielded 5d (2.526 g, 51%) as white needles from CH₂Cl₂/hexane: mp
125 - 125.5 °C; Rᶠ = 0.32 (CHCl₃-MeOH, 9:1); ¹H NMR (CDCl₃) δ 6.83 (s, 1 H),
6.72 (s, 1 H), 5.39 (br s, 1 H), 4.31 (t, 2 H, J = 7.0 Hz), 3.53 (s, 3 H), 2.93 (t, 2 H, J =
7.0 Hz), 2.69 (d, 3 H, J = 4.8 Hz); ¹³C NMR (CDCl₃) δ 156.93, 144.70, 127.09,
120.61, 62.32, 32.46, 27.19, 26.77. Anal. Calcd for C$_8$H$_{13}$N$_3$O$_2$: C, 52.45; H, 7.15; N, 22.93. Found: C, 52.47; H, 7.17; N, 23.01.

1,3-Dimethyl-2-[2-((N-methylcarbamoyloxy)ethyl]-1H-imidazolium Iodide (5e) (PN-II-68, BM18975) Following the general procedure for Quaternization, the reaction of 5d (0.46 g, 2.5 mmol) with methyl iodide (0.3 mL, 5 mmol) gave a white solid 5e (0.76 g, 93%): mp 142-143 °C from MeOH/Et$_2$O; IR (KBr)$_{v_{max}}$ 3315, 3117, 3090, 1724 cm$^{-1}$; $^1$H NMR (DMSO-d$_6$) $\delta$ 7.65 (s, 2 H), 7.06 (br m, 1 H), 4.19 (t, 2 H, J = 5.9 Hz), 3.79 (s, 6 H), 3.34 (t, 2 H, J = 5.9 Hz), 2.46 (d, 3 H, J = 5.1 Hz); $^{13}$C NMR (DMSO-d$_6$) $\delta$ 155.84, 144.24, 122.59, 59.92, 35.03, 26.79, 23.29. Anal. Calcd for C$_9$H$_{16}$N$_3$O$_2$: C, 33.25; H, 4.96; N, 12.92. Found: C, 33.33; H, 4.96; N, 12.98.

1-Methyl-2-(3-hydroxypropyl)-1H-imidazole (6a) To a cooled (-5 °C) solution of 1,2-dimethylimidazole (10.48 g, 0.109 mol) in dry THF (250 mL) was added dropwise a solution of n-BuLi in hexane (48 mL, 0.12 mol). The rate of addition was such that the temperature of the mixture remained <0 °C. The mixture was stirred at this temperature for 30 min, then ethylene oxide (6 mL, 0.12 mol) was added at such a rate that the temperature of the mixture was below 10 °C. After being stirred at this temperature for an additional 1 h, then at room temperature overnight, the reaction mixture was quenched with 10% HCl solution (300 mL). The organic layer was washed with 10% HCl solution (2 x 50 mL). The combined aqueous layers were basified with K$_2$CO$_3$, then extracted with CHCl$_3$ (8 x 50 mL). The organic phase was dried (MgSO$_4$) and evaporated to dryness to give a thick yellow oil 6a (13 g, 85%): $^1$H NMR (CDCl$_3$) $\delta$ 6.9 (s, 1 H), 6.76 (s, 1 H), 4.14 (t, 2 H, J = 6.3 Hz), 3.55 (s, 3 H), 2.87 (s, 3 H), 2.72 (t, 2 H, J = 7.6 Hz), 2.06-2.16 (m, 2 H).

1-Methyl-2-(3-N,N-dimethylcarbamoyloxypropyl)-1H-imidazole (6b) N,N-Dimethylcarbamoyl chloride (3.68 g, 34.2 mmol) was added via a syringe to a solution of 6a (3.2 g, 22.8 mmol) in dry pyridine (20 mL). The reaction mixture was heated to gentle reflux for 30 h, then cooled to room temperature. Water (30 mL) was added and the mixture was stirred for 10 min. The aqueous phase was basified with K$_2$CO$_3$, saturated with NaCl, then extracted with CHCl$_3$ (6 x 25 mL). The combined organic layers were washed with brine, dried (MgSO$_4$) and decolorized with charcoal. Removal of the solvent gave a brown oil 6b (3.5 g, 73%): $^1$H NMR (CDCl$_3$) $\delta$ 6.9
1,3-Dimethyl-2-(3-N,N-dimethylcarbamoyloxypropyl)-1H-imidazolium Tosylate (6c) (PN38, BM16177) Quaternization of 6b (2.03 g, 9.6 mmol) was carried out with MeOTs (2.68 g, 14.4 mmol) in CH₃CN (25 mL) to give 6c (1.75 g, 46%) as colorless needles from CH₃CN/ether: mp 124.5-125.5 °C; IR (KBr) vmax 3115, 3082, 1709, 1215, 1182 cm⁻¹; ¹H NMR (CDCl₃) δ 7.67 (d, 2 H, J = 8.1 Hz), 7.54 (s, 2 H), 7.11 (d, 2 H, J = 8.1 Hz), 4.04 (t, 2 H, J = 5.8 Hz), 3.82 (s, 6 H), 3.11 (t, 2 H, J = 7.6 Hz), 2.86 (s, 3H), 2.79 (s, 3 H), 2.32 (s, 3 H), 1.93 (m, 2H); ¹³C NMR (CDCl₃) δ 155.76, 146.17, 144.18, 138.80, 128.35, 125.59, 122.81, 63.41, 36.29, 35.72, 35.11, 25.83, 21.07, 20.12. Anal. Calcd for C₁₈H₂₇N₃O₅S: C, 54.39; H, 6.85; N, 10.57; S, 8.06. Found: C, 54.21; H, 6.92; N, 10.52; S, 7.99.

1-Methyl-2-[3-(N-methylcarbamoyloxy)propyl]-1H-imidazole (6d) 1-Methyl-2-(3-hydroxypropyl)-1H-imidazole (14) (3.67 g, 26.2 mmol) was carbamoylated as described for 2c with methyl isocyanate (7.8 mL, 131 mmol) in the presence of a catalytic amount of Bu₂Sn(OAc)₂ in dry CH₂Cl₂ (25 mL) to give 6d as a dark brown oil (4.68 g, 91%): ¹H NMR (CDCl₃) δ 6.92 (s, 1 H), 6.79 (s, 1 H), 4.63 (br s, 1 H), 4.15 (t, 2 H, J = 6.2 Hz), 3.57 (s, 3 H), 2.79 (d, 3 H, J = 4.5 Hz), 1.83-1.90 (m, 2 H); ¹³C NMR (CDCl₃) δ 156.38, 146.16, 122.33, 62.34, 34.82, 26.82, 25.19, 19.38. Anal. Calcd for C₁₀H₁₈N₃O₅S: C, 35.41; H, 5.35; N, 12.39. Found: C, 35.25; H, 5.42; N, 12.32.

1-Methyl-2-phenylthio-5-[(N,N-dimethylcarbamoyloxy)methyl]-1H-imidazole (7a) To a cooled solution (-78 °C) of 1-methyl-2-phenylthio-1H-imidazole (4) (1.9 g,
10 mmol) in dry THF (40 mL) was added dropwise a solution of n-BuLi in hexane (4 mL, 10 mmol). The mixture was stirred for 30 min, then predried paraformaldehyde (0.45 g, 15 mmol) was added. The mixture was stirred at -78 °C for 15 min and allowed to warm up slowly. The temperature of the reaction mixture was maintained at 10-15 °C using an ice bath until the color of the mixture changed from orange to milky white (about 30 min). The reaction mixture was then cooled to 0 °C and N,N-dimethylcarbamoyl chloride (1.6 g, 15 mmol) was added dropwise. The mixture was stirred at room temperature for 1 h then quenched with cold aqueous solution of 10% HCl (40 mL) and extracted with ether (2 x 15 mL). The aqueous phase was basified with 20% KOH solution, saturated with NaCl and extracted with EtOAc (6 x 50 mL). The organic layers were washed with brine and dried (Na₂SO₄). Removal of solvent gave 7a (2.5 g, 86%) as a thick oil: ¹H NMR (CDCl₃) δ 7.18-7.30 (m, 6 H), 5.10 (s, 2 H), 3.63 (s, 3 H), 2.93 (s, 3 H), 2.86 (s, 3 H).

1-Methyl-5-[(N,N-dimethylcarbamoyloxy)methyl]-1H-imidazole (7b) A mixture of 7a (1.17 g, 4 mmol) and Raney Nickel (ca. 4.7 g, W-2 in ethanol) in ethanol/acetone was stirred at room temperature for 15 min. The solvent was carefully decanted and the solid nickel residue was washed with EtOH (2x50 mL), then CH₂Cl₂ (2 x 50 mL). The combined organic phase was evaporated to dryness to give a residue which was redissolved in CHCl₃. The mixture was dried (MgSO₄) and filtered (Celite). Removal of solvent gave 7b (0.414 g, 56%) as colorless solid: ¹H NMR (CDCl₃) δ 7.45 (s, 1 H), 7.10 (s, 1 H), 5.10 (s, 2 H), 3.67 (s, 3 H), 2.93 (s, 3 H), 2.87 (s, 3 H).

1,3-Dimethyl-4-[(N,N-dimethylcarbamoyloxy)methyl]-1H-imidazolium Iodide (7c) (PN-177, BM17816) A mixture of 7b (0.36 g, 1.96 mmol) and methyl iodide (0.97 mL, 15 mmol) in dry THF (8 mL) was stirred at 60 °C for 2 h. The solvent was then removed under reduced pressure. The resulting yellow oil was dissolved in H₂O (5 mL). The aqueous solution was then washed with CHCl₃ (3 x 4 mL), ether (4 mL) and evaporated to dryness to afford a thick, yellow oil 7c (0.8 g, 82%) which gave a white solid on crystallization with acetone/ether: mp 105.5 - 6.5 °C; IR (KBr) v_max 3109, 3061, 1709, 1188 cm⁻¹: ¹H NMR (DMSO) δ 9.14 (s, 1 H), 7.80 (s, 1 H), 5.14 (s, 2 H), 3.84 (s, 3 H), 3.83 (s, 3 H), 2.83 (s, 3 H), 2.81 (s, 3 H); ¹³C NMR (DMSO) δ
154.60, 137.81, 129.82, 123.29, 54.68, 36.16, 35.89, 35.60, 33.79. Anal. Calcd for C₉H₁₆O₂N₃I: C, 33.25; H, 4.96; N, 12.92. Found: C, 33.31; H, 4.94; N, 12.83.

1-Methyl-2-phenylthio-5-[2-(N,N-dimethylcarbamoyloxy)ethyl]-1H-imidazole (8a) n-BuLi in hexane (4.4 mL, 11 mmol) was added to a solution of 1-methyl-2-phenylthio-1H-imidazole (1.9 g, 10 mmol) in dry THF (50 mL) at -78 °C. The mixture was stirred for 30 min, then pre-cooled ethylene oxide (0.9 g, 20 mmol) was added. After being allowed to warm to room temperature overnight the reaction mixture was cooled in an ice-bath, then N,N-dimethylcarbamoyl chloride (1.61 g, 15 mmol) was added via a syringe. The mixture was stirred at room temperature for 14 h, then diluted with ether (20 mL) and quenched with cold 10% HCl solution. The organic phase was separated and washed with 10% HCl solution (2 x 15 mL). The combined aqueous layers were basified with cold 20% KOH solution to pH = 10, and extracted with EtOAc (4 x 50 mL). The combined organic layers were washed with brine and dried (Na₂SO₄). Removal of solvent gave 8a (2.9 g, 95%) as a thick oil: ¹H NMR (CDCl₃) δ 7.11-7.28 (m, 5 H), 7.04 (s, 1 H), 4.29 (t, 2 H, J = 6.9 Hz), 3.56 (s, 3 H), 2.8-2.95 (overlapped m, 8 H).

1-Methyl-5-[2-(N,N-dimethylcarbamoyloxy)ethyl]-1H-imidazole (8b) Desulfurization of 8a (1.5 g, 5 mmol) with Raney Ni (ca. 5.8 g, W-2 in ethanol) in absolute EtOH (30 mL) following the procedure described for 7a gave 8b (0.84 g, 85%) as an oil: ¹H NMR (CDCl₃) δ 7.39 (s, 1 H), 6.87 (s, 1 H), 4.27 (t, 2 H, J = 6.9 Hz), 3.60 (s, 3 H), 2.84-2.93 (overlapped m, 8 H); ¹³C NMR (CDCl₃) δ 156.27, 137.77, 128.04, 127.26, 63.29, 36.34, 35.81, 31.21, 24.06.

1,3-Dimethyl-4-[2-(N,N-dimethylcarbamoyloxy)ethyl]-1H-imidazolium Iodide (8c) (PN-294, BM17843) Quaternization of 8b (0.33 g, 1.67 mmol) was carried out with methyl iodide (0.83 mL, 13.4 mmol) in THF (5 mL) to give 8c as a thick, pale yellow oil: ¹H NMR (DMSO-d₆) δ 8.98 (s, 1 H), 7.54 (s, 1 H), 4.20 (t, 2 H, J = 6.4 Hz), 3.81 (s, 3 H), 3.77 (s, 3 H), 2.99 (t, 2 H, J = 6.4 Hz), 2.81 (s, 6 H); ¹³C NMR (DMSO-d₆) δ 155.27, 136.63, 131.89, 120.68, 61.86, 36.00, 35.70, 35.55, 33.31. Anal. Calcd for C₁₀H₁₈O₂N₃I-1/2H₂O: C, 34.49; H, 5.50; N, 12.06. Found: C, 34.48; H, 5.51; N, 11.97.
1-Methyl-2-phenylthio-5-(3-hydroxypropyl)-1H-imidazole (9a) To a solution of 1-methyl-2-phenylthio-1H-imidazole (4.1 g, 21.54 mmol) in dry THF (45 mL) at -78 °C was added dropwise a solution of n-BuLi in hexane (9.05 mL, 22.62 mmol). After being stirred at -78 °C for 30 min, the mixture was added via canula to a precooled (-78 °C) solution of oxetane (1.25 g, 21.5 mmol) and BF₃-OF₃ (3.97 mL, 32.3 mmol) in dry THF (50 mL). The reaction mixture was stirred at -78 °C for 2 h and warmed up to room temperature overnight. Work up as usual gave a crude product 9a (2.37 g, 44%) as a dark yellow oil: ¹H NMR (CDCl₃) δ 7.01-7.28 (m, 5 H), 6.93 (s, 1 H), 3.71 (t, 2 H, J = 6.2 Hz), 3.49 (s, 3 H), 2.65 (t, 2 H, J = 7.9 Hz), 1.89 (m, 2 H); ¹³C NMR (CDCl₃) δ 129.16, 127.48, 127.01, 125.94, 61.17, 31.02, 30.63, 21.48.

1-Methyl-2-phenylthio-5-[3-(N,N-dimethylcarbamoyloxy)propyl]-1H-imidazole. (9b) To a cooled (-78 °C) solution of 9a (1.66 g, 6.71 mmol) in dry THF (40 mL) was added dropwise 2.95 mL (7.4 mmol) of n-BuLi in hexane. The mixture was stirred at -78 °C for 30 min. Then 0.82 mL (8.7 mmol) of N,N-dimethylcarbamoyl chloride in THF (10 mL) was added slowly. After 15 min the reaction mixture was allowed to warm to room temperature and was heated to gentle reflux for 30 min. The mixture was cooled to room temperature, carefully basified to pH=10 using aqueous 20% NaOH solution, saturated with NaCl and extracted with CHCl₃ (5 x 30 mL). The combined organic layers were washed with brine (50 mL), dried (Na₂SO₄) and filtered. The brown filtrate was evaporated to dryness to give a brown oil. Purification of the crude product by column chromatography on silica gel (CHCl₃-MeOH, 9:1) afforded 9b (1.12 g, 52%) as an oil: Rf = 0.6 (CHCl₃-MeOH); ¹H NMR (CDCl₃) δ 7.11-7.27 (m, 5 H), 6.98 (s, 1 H), 4.16 (t, 2 H, J = 6.3 Hz), 3.52 (s, 3 H), 2.97 (br s, 6 H), 2.64 (t, 2 H, J = 7.7 Hz), 1.96-2.05 (m, 2 H); ¹³C NMR (CDCl₃) δ 156.00, 136.52, 134.91, 134.51, 128.78, 127.20, 126.99, 125.95, 63.88, 38.16, 35.97, 35.45, 30.66, 27.04, 21.43.

1-Methyl-5-[3-(N,N-dimethylcarbamoyloxy)propyl]-1H-imidazole (9c) Desulfurization of 9b (0.85 g, 2.68 mmol) with Raney Nickel (3.15 g, 53.6 mmol) in EtOH as described previously gave 9c (0.214 g, 37.8%) as a pale yellow oil: ¹H NMR (CDCl₃) δ 7.37 (s, 1 H), 6.79 (s, 1 H), 4.15 (t, 2 H, J = 6.3 Hz), 3.56 (s, 3 H), 2.91 (s, 3 H).
6 H), 2.63 (t, 2 H, J = 7.6 Hz), 1.93-2.02 (m, 2 H); $^{13}$C NMR (CDCl$_3$) $\delta$
156.19, 137.28, 130.82, 125.90, 64.08, 36.07, 35.52, 30.85, 27.59, 20.22.

1,3-Dimethyl-4-[3-(N,N-dimethylcarbamoyloxy)propyl]-1H-imidazolium Iodide (9d) (PN-I-292, BM19070) Quaternization of 9c (95 mg, 0.45 mmol) with methyl iodide (0.14 mL, 2.25 mmol) in THF (3 mL) gave a white solid 9d (134 mg, 85%): mp 115-6 °C from acetone/ether; IR (KBr) $\nu_{\text{max}}$ 3172, 1701, 1188 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$
10.00 (s, 1 H), 7.22 (s, 1 H), 4.18 (t, 2 H, J = 6.2 Hz), 4.04 (s, 3 H), 3.96 (s, 3 H), 2.74 (t, 2 H, J = 7.5 Hz), 1.99-2.09 (m, 2 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 137.30, 135.06, 119.86, 63.28, 36.83, 36.45, 36.01, 34.21, 28.82, 20.23. Anal. Calcd for C$_{11}$H$_{20}$O$_2$N$_3$I: C, 37.40; H, 5.70; N, 11.89. Found: C, 37.45; H, 5.74; N, 11.81.

Imidazo[1,2-a]pyridin-5-ol (10a) A mixture of 2,6-diaminopyridine (10.9 g, 0.1 mol) and chloroacetaldehyde (17.5 g, 45% w/w in water, 0.1 mol) in acetone (200 mL) was refluxed overnight. The reaction mixture was cooled and filtered to give a solid, which was washed with several portions of fresh acetone and dried under vacuum to afford 5-aminoimidazo[1,2-a]pyridine hydrochloride (16.9 g, 100%) as tan solid: $^1$H NMR (DMSO-d$_6$) $\delta$ 8.45 (d, 1 H, J = 2.4 Hz), 8.08 (d, 1 H, J = 2.4 Hz), 7.99 (br s, 2 H), 7.69 (dd, 1 H, J = 7.8, 8.4 Hz), 7.00 (d, 1 H, J = 8.4 Hz), 6.49 (d, 1 H, J = 7.8 Hz). A mixture of 5-aminoimidazo[1,2-a]pyridine hydrochloride (16.6 g, 97.8 mmol) in 70% H$_2$SO$_4$ solution was stirred at 120 °C (oil bath temperature) for 10 h. The reaction mixture was cooled and carefully neutralized with an aqueous 20% NaOH solution. Filtration of the mixture gave 10a (10.93 g, 75.4%) as an olive green solid: $R_f$ = 0.53 (CHCl$_3$-MeOH, 9:1); $^1$H NMR (DMSO-d$_6$) $\delta$ 7.64 (d, 1 H, J = 2.1 Hz), 7.53 (d, 1 H, J = 2.1 Hz), 7.34 (dd, 1 H, J = 8.1, 8.4 Hz), 6.15 (d, 1 H, J = 8.1 Hz), 5.63 (d, 1 H, J = 8.4 Hz), 1.82 (br s, 1 H).

1-Methylimidazo[1,2-a]pyridin-5-one (10b) A mixture of 10a (2.68 g, 20 mmol) and sodium amide (1.09 g, 28 mmol) in dry DMF (30 mL) was stirred at room temperature for 30 min. Methyl iodide (1.62 mL, 26 mmol) was added dropwise by syringe and the mixture was stirred at room temperature for 2 h. Solvent was evaporated to dryness under vacuum and the resulting residue was partitioned between a sat’d NaHCO$_3$ solution and CHCl$_3$. Insoluble material was removed by
filtration. The aqueous phase was extracted with CHCl₃ (5 x 50 mL). The organic layers were washed with brine (2 x 50 mL), dried (anhydrous Na₂SO₄) and filtered. Removal of solvent yielded a crude product which was purified by column chromatography (silica gel, 5% of MeOH in CHCl₃) to afford 10b (1.44 g, 48.6%) as an off-white solid from acetone/hexane: mp 70-72 °C; Rᵣ = 0.38 (CHCl₃-MeOH, 19:1); ¹H NMR (CDCl₃) δ 7.74 (d, 1 H, J = 2.4 Hz), 7.44 (t, 1 H, J = 8.4 Hz), 6.97 (d, 1 H, J = 2.4 Hz), 6.01 (d, 2 H, J = 8.4 Hz), 3.68 (s, 3 H); ¹³C NMR (CDCl₃) δ 156.97, 142.44, 136.98, 120.24, 108.46, 99.41, 83.47, 32.85.

1-Methyl-5-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridinium Chloride (10c) (PN-III-220, BN38865) To a mixture of 10b (1.0 g, 6.8 mmol) in dry THF (15 mL) and HMPT (2.35 mL, 13.5 mmol) was added slowly N,N-dimethylcarbamoyl chloride (1.24 mL, 13.5 mmol). The reaction mixture was stirred at 60 °C overnight, then cooled in an ice bath. Solvent was carefully removed by pipette and the solid was washed with ether and dried. Recrystallization of the crude in CH₃CN/ether gave 10c (1.38 g, 80%) as a gray solid: mp 149-151 °C; ¹H NMR (CDCl₃) δ 8.90 (d, 1 H, J = 2.0 Hz), 8.12 (d, 1 H, J = 2.0 Hz), 8.07 (d, 1 H, J = 9.0 Hz), 8.00 (dd, 1 H, J = 7.7, 9.0 Hz), 7.32 (d, 1 H, J = 7.7 Hz), 4.42 (s, 3 H), 3.29 (s, 3 H), 3.12 (s, 3 H). Anal. Calcd for C₁₁H₁₄ClN₃O₂: C, 51.67; H, 5.52; Cl, 13.86; N, 16.43. Found: C, 51.43; H, 5.59; Cl, 13.73; N, 16.34.

2-Methyl-5-aminoimidazo[1,2-a]pyridine (11a) To a mixture of 2,6-diaminopyridine (10.9 g, 0.1 mol) in absolute ethanol (100 mL) at 70 °C was added dropwise a solution of chloroacetone (7.96 mL, 0.1 mol) in absolute ethanol (30 mL). The mixture was gently refluxed overnight. Additional chloroacetone (2 mL) was added and the mixture was refluxed for 5 h. The solvent was reduced to 1/3 of its original volume and Et₂O was added. The mixture was cooled in an ice bath to give a solid which was dissolved in water and neutralized with a saturated NaHCO₃ solution. The volume of water was reduced to give 11a (7.2 g, 48.6%) as black solid: mp 155-156.5 °C; Rᵣ = 0.17 (CHCl₃-MeOH, 9:1); ¹H NMR (DMSO-d₆) δ 7.52 (s, 1 H), 7.02 (dd, 1 H, J = 7.4, 8.7 Hz), 6.68 (d, 1 H, J = 8.7 Hz), 6.45 (br s, 2 H), 5.89 (dd, 1 H, J = 0.8, 7.4 Hz), 2.29 (d, 3 H, J = 0.8 Hz); ¹³C NMR (DMSO-d₆) δ 145.79, 142.00.

2-Methyl-5-hydroxyimidazo[1,2-a]pyridine (11b) Following the general procedure for preparation of 5-hydroxyimidazo[1,2-a]pyridine, 11a (3.4 g, 23.1 mmol) gave 11b (2.64 g, 77.2%): Rf = 0.39 (CHCl₃-MeOH, 9:1); ¹H NMR (DMSO-d₆) δ 7.38 (s, 1 H), 7.28 (dd, 1 H, J = 7.8, 8.4 Hz), 6.08 (d, 1 H, J = 7.8 Hz), 5.60 (d, 1 H, J = 8.4 Hz); ¹³C NMR (DMSO-d₆) δ 155.55, 142.21, 135.89, 127.85, 105.04, 97.00, 84.52, 10.25.

General Procedure for Carbamoylation of 5-Hydroxyimidazo[1,2-a]pyridine Derivatives A mixture of 5-hydroxyimidazo[1,2-a]pyridine derivative (1 equiv) and sodium hydride (1.5 equiv) in dry DMF was stirred at room temperature for 30 min, then at 50 °C for 30 min. N,N-dimethylcarbamoyl chloride (1.5 equiv) was added slowly by syringe and the reaction mixture was stirred at 80 °C for 10 h. Solvent was evaporated under vacuum. The resulting residue was partitioned between an aqueous NaHCO₃ solution and CHCl₃. Insoluble material was removed by filtration. The aqueous phase was extracted with CHCl₃. The organic layers were washed with brine, dried (Na₂SO₄) and filtered. Removal of solvent gave a crude product which was purified by column chromatography.

General Procedure for Quaternization of Carbamoyloxyimidazo[1,2-a]pyridine Derivatives A mixture of carbamate and methyl iodide or methyl p-toluene sulfonate (1.5 equiv) in dry THF (or acetonitrile) was maintained at 60 °C overnight. Ether was then added and the reaction mixture was cooled in ice. The precipitate was collected and purified by recrystallization.

2-Methyl-5-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridine (11c) Following the general procedure for carbamoylation of 5-hydroxyimidazo[1,2-a]pyridine, 11b (1.1 g, 7.4 mmol) gave a crude product which was purified by column chromatography (silica gel; gradient elution, 4 to 8% of MeOH in CHCl₃) to give 11c (1.09 g, 67.3%) as an off-white solid from EtOAc/hexane: mp 110-111 °C; Rf = 0.59 (CHCl₃-MeOH, 24:1); ¹H NMR (CDCl₃) δ 7.38 (d, 1 H, J = 8.7 Hz), 7.27 (s, 1 H),
7.16 (dd, 1 H, J = 7.5, 8.7 Hz), 6.59 (d, 1 H, J = 7.5 Hz), 3.20 (s, 3 H), 3.06 (s, 3 H),
2.46 (s, 3 H); 13C NMR (CDCl3) δ 151.58, 146.43, 143.31, 140.14, 112.92, 104.83,
101.29, 36.90, 36.52, 14.27. Anal. Calcd for C11H13N3O2: C, 60.26; H, 5.98; N,
19.17. Found: C, 60.25; H, 5.99; N, 19.06.

1,2-Dimethyl-5-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridinium
p-Toluenesulfonate (11d) (PN-III-190, BN38856) Following the general
procedure for Quaternization, 11c (1.2 g, 5.5 mmol) was reacted with methyl
p-toluenesulfonate (1.52 g, 8.2 mmol) in dry THF (10 mL) to give 11d (2.15 g, 96.8
%) as a white solid from CH3CN/ether: mp 162-162.5 °C; IR (KBr) vmax 3094, 1755,
1205, 1190, 1141 cm⁻¹; 1H NMR (CDCl3) δ 8.03 (s, 1H), 7.98 (d, 1 H, J = 9.0 Hz),
7.84 (dd, 1 H, J = 7.8, 9.0 Hz), 7.68 (d, 2 H, J = 8.3 Hz), 7.19 (d, 1 H, J = 7.8 Hz),
7.03 (d, 2 H, J = 8.3 Hz), 4.00 (s, 3H), 3.23 (s, 3 H), 3.04 (s, 3 H), 2.54 (s, 3 H), 2.13
(s, 3 H); 13C NMR (CDCl3) δ 150.23, 144.44, 141.63, 140.30, 138.49, 135.99, 134.23,
for C19H23N3O5S: C, 56.28; H, 5.72; N, 10.36. Found: C, 56.40; H, 5.67; N, 10.44.

2-(2-Propyl)imidazo[1,2-a]pyridin-5-ol (12b) To a cooled mixture of sodium
hydride (1.46 g, 61.0 mmol, washed with pentane twice) in dry DMF (30 mL) was
added slowly a solution of 2-amino-6-hydroxypyridine (5) (4.77 g, 40 mmol) in dry
DMF (30 mL). The mixture was stirred in the cooling bath for 15 min then warmed
and stirred at room temperature for 3 h. A solution of 1-bromo-3-methylbutan-2-one
(7.26 g, 44 mmol) in dry THF (20 mL) was added at once. The reaction mixture was
stirred at 80 °C (oil bath temperature) overnight. Solvent was removed to dryness
under reduced pressure. The resulting residue was partitioned between water and
CHCl₃. The aqueous phase was extracted with CHCl₃ (4 x 40 mL). The organic layers
were washed with water, brine and dried (anhydrous Na₂SO₄). Removal of solvent
gave a crude, which was purified by column chromatography (silica gel, CHCl₃-
MeOH, 9:1) to give 12b (3.32 g, 47.1%) as a tan solid: mp 163-165 °C; Rₖ = 0.5
(CHCl₃-MeOH, 9:1); 1H NMR (CDCl₃) δ 7.51 (s, 1 H), 7.37 (t, 1 H, J = 8.4 Hz), 6.41
(d, 1 H, J = 8.4 Hz), 5.98 (d, 1 H, J = 8.4 Hz), 3.13 (septet, 1 H, J = 6.9 Hz), 1.39 (d, 6
H, J = 6.9 Hz); 13C NMR (CDCl₃) δ 156.84, 142.73, 139.94, 136.05, 103.39, 97.32,
89.31, 25.90, 21.62. Anal. Calcd for C_{10}H_{12}N_{2}O: C, 68.16; H, 6.86; N, 15.90. Found: C, 67.87; H, 6.88; N, 15.65.

2-(2-Propyl)-5-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridine (12c) To an ice-cooled mixture of sodium hydride (0.5 g, 20.8 mmol, washed with pentane twice and dried under Ar) in dry THF (20 mL) was added via canula a solution of 12b (2.64 g, 15 mmol) in dry THF (15 mL). The mixture was warmed up and stirred at 50 °C for 3 h. N,N-dimethylcarbamoyl chloride (2.07 mL, 22.5 mmol) was then added by syringe. After being stirred at 50 °C for 5 h, the reaction mixture was evaporated to dryness and the resulting residue was partitioned between water and CHCl₃. The aqueous phase was extracted with CHCl₃ (4 x 30 mL). The organic layers were washed with brine (2 x 30 mL), dried (anhydrous Na₂SO₄) and filtered. Evaporation of the solvent gave a crude which was purified by column chromatography (silica gel, 20% of hexane in EtOAc) to give 12c (2.83 g, 76.3 %) as colorless needles from EtOAc/hexane: mp 91-92 °C; Rf = 0.5 (EtOAc-hexane, 9:1); ¹H NMR (CDCl₃) δ 7.42 (dd, 1 H, J = 0.6, 9.0 Hz), 7.24 (s, 1 H), 7.17 (dd, 1 H, J = 7.5, 9.0 Hz), 6.58 (dd, 1 H, J = 0.6, 7.5 Hz), 3.23 (s, 3 H), 3.07-3.16 (overlapped m, 1 H), 3.08 (overlapped s, 3 H), 1.38 (d, 6 H, J = 6.9 Hz); ¹³C NMR (CDCl₃) δ 154.21, 151.81, 146.57, 140.48, 124.34, 113.36, 102.77, 101.28, 37.09, 36.72, 28.47, 22.41. Anal. Calcd for C_{13}H_{17}N_{3}O_{2}: C, 63.14; H, 6.93; N, 16.99. Found: C, 63.24; H, 6.97; N, 16.92.

1-Methyl-2-(2-propyl)-5-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridinium Iodide (12d) (PN-IV-36, BN40490) Following the general procedure for Quaternization, 12c (70 mg, 0.28 mmol) was treated with methyl iodide (excess) in THF (2 mL) to give 12d (99 mg, 96 %) as white needles from CH₃CN/Et₂O: mp 155-6 °C; IR (KBr) νmax 3103, 3053, 1749, 1141 cm⁻¹; ¹H NMR (CDCl₃) δ 8.23 (d, 1 H, J = 9.0 Hz), 8.04 (dd, 1 H, J = 7.8, 9.0 Hz), 7.74 (s, 1 H), 7.32 (d, 1 H, J = 7.8 Hz), 4.21 (s, 3 H), 3.34-3.42 (m, 1 H), 3.33 (s, 3 H), 3.12 (s, 3 H), 1.48 (d, 6 H, J = 6.9 Hz); ¹³C NMR (CDCl₃) δ 150.06, 145.47, 141.95, 140.49, 134.92, 107.92, 107.57, 106.10, 37.57, 37.48, 33.33, 24.71, 21.40. Anal. Calcd for C_{14}H_{20}IN_{3}O_{2}.1/2H₂O: C, 42.22; H, 5.32; N, 10.55. Found: C, 42.19; H, 5.36; N, 10.45.
2-Phenylimidazo[1,2-a]pyridin-5-ol (13b)  A solution of 2-bromoacetophenone (19.9 g, 0.1 mol) in dry THF (60 mL) was added dropwise to a mixture of 2,6-diaminopyridine (10.9 g, 0.1 mol) in THF (80 mL) at reflux temperature. The mixture was stirred at reflux overnight. Additional 2,6-diaminopyridine (3 g) was added to the mixture which was refluxed for a further 5 h. The solvent was evaporated to dryness and the resulting residue was washed with Et₂O (3 x 100 mL) and then dissolved in methanol (150 mL). Conc'd HBr solution (3 mL) was added and the mixture was stirred at reflux for 30 min. Solvent was evaporated to dryness. The residue was neutralized with sat'd NaHCO₃ solution and the mixture was extracted with CHCl₃ (4 x 100 mL). The organic layers were washed with brine, dried (anhydrous Na₂SO₄) and filtered via a column of silica gel, eluted with a mixture of 20% hexane in ethyl acetate to give 5-amino-2-phenylimidazo[1,2-a]pyridine (5.27 g, 25.2%): Rf = 0.44 (EtOAc-hexane, 4:1); ¹H NMR (CDCl₃) δ 7.94, (dd, 2 H, J = 1.4, 8.4 Hz), 7.64 (s, 1 H), 7.37-7.43 (m, 2 H), 7.29-7.34 (m, 1 H), 7.17 (d, 1 H, J = 8.8 Hz), 7.09 (dd, 1 H, J = 7.2, 8.8 Hz), 6.04 (dd, 1 H, J = 1.1, 7.2 Hz), 4.45 (br s, 2 H). The treatment of 5-amino-2-phenylimidazo[1,2-a]pyridine (2.83 g, 13.5 mmol) with an aqueous 70% H₂SO₄ solution as described for 10a gave 13b (2.62 g, 92.2%) as an olive green solid: Rf = 0.68 (CHCl₃-MeOH, 9:1); ¹H NMR (DMSO-d₆) δ 8.24 (s, 1 H), 7.89 (d, 2 H, J = 7.8 Hz), 7.35-7.50 (m, 5 H), 6.24 (d, 1 H, J = 7.8 Hz), 5.72 (d, 1 H, J = 8.4 Hz).

2-Phenyl-5-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridine (13c) Carbamoylation of 13b (2.6 g, 12.3 mmol) with sodium hydride (0.2 g, 8.6 mmol) and N,N-dimethylcarbamoyl chloride (0.79 mL, 8.6 mmol) in dry DMF (25 mL) as described earlier for 12c afforded a crude product which was purified by column chromatography (silica gel; 2% of MeOH in CHCl₃) to give 13c (0.67 g, 42%) as a yellow solid from EtOAc/hexane: mp 152-153°C; Rf = 0.57 (CHCl₃-MeOH, 24:1); ¹H NMR (CDCl₃) δ 7.98 (d, 2 H, J = 7.2 Hz), 7.78 (s, 1 H), 7.51 (d, 1 H, J = 9.0 Hz), 7.43 (dd, 2 H, J = 7.2, 7.8 Hz), 7.32 (m, 1 H), 7.22 (dd, 1 H, J = 7.5, 9.0 Hz), 6.65 (d, 1 H, J = 7.5 Hz), 3.24 (s, 3 H), 3.09 (s, 3 H); ¹³C NMR (CDCl₃) δ 151.68, 147.18, 145.85, 140.66, 133.63, 128.60, 128.00, 126.19, 125.17, 113.80, 103.55, 101.97, 37.16, 36.78. Anal. Calcd for C₁₆H₁₅N₃O₂: C, 68.31; H, 5.37; N, 14.94. Found: C, 68.24; H, 5.40; N, 14.89.
1-Methyl-2-phenyl-5-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridinium Iodide (13d) (PN-III-236, BN38874) Following the general procedure for Quaternization, the reaction of 13c (0.78 g, 2.8 mmol) with an excess of methyl iodide in dry THF (5 mL) gave 13d (0.92 g, 78.5 %) as white needles from (CH<sub>3</sub>)<sub>2</sub>CO/Et<sub>2</sub>O: mp 156-157 °C; IR (KBr)<sub>vmax</sub> 1755 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 8.16 (d, 1 H, J = 9.0 Hz), 8.04 (dd, 1 H, J = 8.0, 9.0 Hz), 7.96 (s, 1 H), 7.61-7.75 (m, 2 H), 7.57 - 7.62 (m, 3 H), 7.36 (dd, 1 H, J = 0.6, 8.0 Hz), 4.15 (s, 3 H), 3.29 (s, 3 H), 3.11 (s, 3 H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 150.22, 142.09, 140.90, 138.93, 135.35, 131.22, 130.29, 129.38, 124.28, 108.76, 108.16, 108.04, 37.58, 34.18. Anal. Calcd for: C<sub>17</sub>H<sub>18</sub>N<sub>3</sub>O<sub>2</sub>: C, 48.24; H, 4.29; N, 9.93. Found: C, 48.08; H, 4.32; N, 9.93.

5-Hydroxy-2-(p-nitrophenylazo)pyridine. (7) To a solution of p-nitroaniline (7.4 g, 53.5 mmol) in hydrochloric acid (60 mL, 1 part of water and 1 part of conc HCl) was added an ice cold solution of sodium nitrite (5.5 g, 79.9 mmol) in water (12 mL). The addition was done at -5 °C. The diazonium chloride solution was then added to a cold solution of 3-hydroxypyridine (5.0 g, 52.5 mmol) and sodium hydroxide (2.1 g, 52.5 mmol) in water (100 mL) in such a way that the pH of the reaction mixture was maintained close to neutral. After stirring for an additional hour the mixture was acidified with glacial acetic acid, filtered and dried. The solid obtained was a mixture of two isomers and the mixture was used without crystallization for the next step.

5-Benzoyloxy-2-(p-nitrophenylazo)pyridine. To a solution of the above azo dye (mixture of isomers) (5.46 g, 22.3 mmol) and potassium carbonate (6.1 g, 44.0 mmol) in water (150 mL) was added benzoyl chloride (3.8 mL, 32.7 mmol) at rt. The mixture was stirred for 1 hour and the precipitate obtained was filtered, and washed thoroughly with water, dried and crystallized from benzene to give 5.2 g (67%) of the desired 5-benzoyloxy-2-(p-nitrophenylazo)pyridine.

2-Amino-5-benzoyloxypyridine (14) To a suspension of 5-benzoyloxy-2-(p-nitrophenylazo)pyridine (9.5 g, 27.2 mmol) and 10%-Pd/C (0.490 g) in ethanol (250 mL) was added a solution of sodium hypophosphite (20.7 g, 195 mmol) in water (125 mL). The reaction mixture was heated to reflux for 1.5 h and the combined filtrate
was cooled and neutralized with saturated sodium bicarbonate solution. The crystalline solid obtained was filtered and dried to give 4.5 g (77%) of the amine.

6-Benzoyloxyimidazo[1,2-a]pyridine (15a) A mixture of 2-amino-5-benzoyloxypyridine (6.52 g, 30.4 mmol) and chloroacetaldehyde (6.37 g, 36.5 mmol, 45% w/w in water) in acetone (150 mL) was gently refluxed. The reaction mixture was evaporated to dryness under aspirator pressure. The resulting residue was neutralized with sat'd NaHCO₃ solution and extracted with CHCl₃ (4 x 100 mL). The organic layers were washed with brine (2 x 100 mL), dried (anhydrous Na₂SO₄), filtered and evaporated to dryness. Purification of the crude by column chromatography (silica gel, 20% of hexane in EtOAc) gave 15a (3.34 g, 46%) as a tan solid from EtOAc/hexane: mp 144-145 °C; Rf = 0.25 (EtOAc-hexane, 5:1); ¹H NMR (CDCl₃) δ 8.28 (d, 1 H, J = 2.1 Hz), 8.19-8.22 (m, 2 H), 7.51-7.70 (m, 6 H), 7.12 (dd, 1 H, J = 2.1, 9.6 Hz); ¹³C NMR (CDCl₃) δ 164.87, 154.77, 143.76, 139.69, 134.63, 134.02, 130.20, 128.69, 121.13, 118.54, 117.80, 113.40. Anal. Calcd for C₁₄H₁₀N₂O₂: C, 70.58; H, 4.23; N, 11.76. Found: C, 70.47; H, 4.22; N, 11.75.

6-(N,N-Dimethylcarbamoyloxy)imidazo[1,2-a]pyridine (15b) A mixture of 15a (1.80 g, 7.6 mmol) and sodium methoxide (0.61 g, 11.3 mmol) in dry pyridine (50 mL) was stirred at 75 °C overnight. N,N-dimethylcarbamoyl chloride (1.18 mL, 12.8 mmol) was added slowly via syringe. The reaction mixture was stirred for 10 h. Solvent was removed to dryness and the resulting residue was partitioned between a sat'd solution of NaHCO₃ and CHCl₃. The aqueous phase was extracted with CHCl₃ (4 x 30 mL). The organic layers were washed with brine, dried (anhydrous Na₂SO₄) and filtered. Removal of solvent to dryness gave a crude which was purified by column chromatography (silica gel, CHCl₃-MeOH, 50:1) to give 15b (1.37 g, 88.8%) as a pale yellow solid from EtOAc/hexane: mp 123-123.5 °C; Rf = 0.23 (CHCl₃-MeOH, 50:1); ¹H NMR (CDCl₃) δ 8.13 (ca, 1 H), 7.63 (d, 1 H, J = 1.2 Hz), 7.57 (d, 1 H, J = 9.6 Hz), 7.55 (s, 1 H), 7.03 (dd, 1 H, J = 2.1, 9.6 Hz), 3.11 (s, 3 H), 3.03 (s, 3 H); ¹³C NMR (CDCl₃) δ 143.67, 140.21, 134.36, 121.70, 118.48, 117.39, 113.19, 36.86, 36.47. Anal. Calcd for C₁₀H₁₁N₃O₂: C, 58.53; H, 5.40; N, 20.48. Found: C, 58.67; H, 5.52; N, 20.54.
1-Methyl-6-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridinium p-Toluenesulfonate (15c) (PN-III-268, BN40481) Following the general procedure for Quaternization, the reaction of 15b (0.103 g, 0.5 mmol) with methyl p-toluenesulfonate (0.14 g, 0.75 mmol) in dry THF (5 mL) gave 15c (0.19 g, 97 %) as a white solid: mp 176-177 °C; IR (KBr) νmax 3138, 3045, 1732, 1184 cm⁻¹; ¹H NMR (CDCl₃) δ 9.05 (d, 1 H, J = 1.8 Hz), 8.65 (d, 1 H, J = 1.8 Hz), 8.13 (d, 1 H, J = 1.8 Hz), 7.99 (d, 1 H, J = 9.6 Hz), 7.79 (d, 2 H, J = 8.1 Hz), 7.66 (dd, 1 H, J = 1.8, 9.6 Hz), 7.13 (d, 2 H, J = 8.1 Hz), 4.12 (s, 3 H), 3.09 (s, 3 H), 3.01 (s, 3 H), 2.33 (s, 3 H); ¹³C NMR (CDCl₃) δ 153.23, 143.98, 143.22, 139.08, 136.96, 130.66, 128.55, 127.47, 125.81, 122.85, 116.10, 110.61, 36.94, 36.60, 34.60, 21.22. Anal. Calcd for C₁₈H₂₁N₃0₅S: C, 55.23; H, 5.41; N, 10.73. Found: C, 55.49; H, 5.40; N, 10.72.

2-Methyl-6-benzoyloxyimidazo[1,2-a]pyridine (16a) A mixture of 2-amino-5-benzoyloxypyridine (1.79 g, 8.36 mmol) and chloroacetone (0.77 mL, 9.2 mmol) in absolute ethanol (35 mL) was refluxed for 10 h. Two more portions of chloroacetone were added (0.3 mL each) over a period of 10 h. The solvent was then removed to dryness under reduced pressure. The resulting residue was treated with a sat. d NaHCO₃ solution. The aqueous mixture was extracted with CHCl₃ (4 x 25 mL) and dried (anhydrous Na₂SO₄). Removal of solvent to dryness gave a crude, which was purified by column chromatography (silica gel, EtOAc-hexane, 2:1) to give 16a (0.88 g, 41.8%) as off-white needles from EtOAc/hexane: mp 178-180 °C; Rf = 0.25 (EtOAc-hexane, 2:1); ¹H NMR (CDCl₃) δ 8.20 (ca, 1 H), 8.15-8.17 (m, 2 H), 7.62-7.68 (m, 1 H), 7.49-7.54 (m, 3 H), 7.34 (d, 1 H, J = 0.3 Hz), 7.05 (dd, 1 H, J = 2.1, 9.6 Hz), 2.46 (s, 3 H); ¹³C NMR (CDCl₃) δ 164.87, 144.47, 143.26, 139.21, 133.88, 130.10, 128.60, 120.42, 117.95, 116.55, 110.51, 14.33. Anal. Calcd for C₁₅H₁₂N₂O₂: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.25; H, 4.91; N, 11.22.

2-Methyl-6-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridine (16b) The reaction of 16a (3.3 g, 13.1 mmol) with sodium methoxide (1.06 g, 19.6 mmol) and N,N-dimethylcarbamoyl chloride (2.4 mL, 26.2 mmol) in dry pyridine (25 mL) at 95 °C (oil bath temperature) as described for 15b gave 16b (0.89 g, 31%) after purification by column chromatography (silica gel, gradient elution, 2-14% of ethanol in EtOAc). Decolorization of 16b with charcoal in MeOH followed by
Recrystallization in EtOAc/hexane gave pale yellow needles: mp 133-134 °C; \( R_f = 0.40 \) (EtOAc-EtOH, 9:1); \(^1\)H NMR (CDCl\(_3\)) \& 8.02 (d, 1 H, \( J = 2.1 \) Hz), 7.44 (d, 1 H, \( J = 9.6 \) Hz), 7.30 (s, 1 H), 6.97 (dd, 1 H, \( J = 2.1, 9.6 \) Hz), 3.10 (s, 3 H), 3.02 (s, 3 H), 2.44 (s, 3 H); \(^{13}\)C NMR (CDCl\(_3\)) \& 154.40, 144.20, 143.22, 139.78, 121.04, 117.98, 116.22, 110.34, 36.80, 36.42, 14.37. Anal. Calcd for C\(_{17}\)H\(_{13}\)N\(_3\)O\(_2\): C, 60.26; H, 5.98; N, 19.17. Found: C, 60.33; H, 6.02; N, 19.15.

**1,2-Dimethyl-6-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridinium**

**p-Toluenesulfonate (16c) (PN-IV-33, BN40507)** Following the general procedure for Quaternization, the treatment of 16b (55 mg, 0.25 mmol) with methyl p-toluenesulfonate (70 mg, 0.37 mmol) in dry THF (2 mL) gave 16c (95 mg, 94 %) as a white solid from MeOH/Et\(_2\)O: mp 223-224 °C; IR (KBr)\(_{\nu}\max \) 3113, 3049, 1716, 1184 cm\(^{-1}\); \(^1\)H NMR (DMSO-d\(_6\)) \& 8.97 (d, 1 H, \( J = 1.9 \) Hz), 8.18 (d, 1 H, \( J = 9.8 \) Hz), 8.15 (s, 1 H), 7.92 (dd, 1 H, \( J = 1.9, 9.8 \) Hz), 7.46 (d, 2 H, \( J = 7.9 \) Hz), 7.08 (d, 2 H, \( J = 7.9 \) Hz), 3.90 (s, 3 H), 3.08 (s, 3 H), 2.95 (s, 3 H), 2.49 (s, 3 H), 2.27 (s, 3 H); \(^{13}\)C NMR (DMSO-d\(_6\)) \& 152.93, 145.85, 142.44, 137.28, 137.10, 135.84, 129.37, 127.79, 125.32, 121.56, 112.42, 110.68, 36.43, 36.09, 30.79, 20.59, 9.22. Anal. Calcd for C\(_{19}\)H\(_{23}\)N\(_3\)O\(_5\)S: C, 56.28; H, 5.72; N, 10.36. Found: C, 56.37; H, 5.78; N, 10.36.

**2-(2-Propyl)imidazo[1,2-a]pyridin-6-ol (17a)** A mixture of 2-amino-5-benzoyloxypyridine (0.89 g, 4.2 mmol) and 1-bromo-3-methylbutan-2-one (6) (0.75 g, 4.6 mmol) in dry THF (15 mL) was refluxed for 16 h. Solvent was removed to dryness and the resulting residue was treated with aqueous 20% KOH solution. The mixture was stirred at 100 °C (oil bath temperature) for 1 h, then cooled and neutralized with Conc HCl solution to give solid 17a (0.52 g, 71 %): \( R_f = 0.43 \) (CHCl\(_3\)-MeOH, 9:1); \(^1\)H NMR (CDCl\(_3\)) \& 7.76 (d, 1 H, \( J = 1.8 \) Hz), 7.19 (overlapped d, 1 H, \( J = 9.6 \) Hz), 7.18 (overlapped s, 1 H), 7.02 (dd, 1 H, \( J = 1.8, 9.6 \) Hz), 3.08 (septet, 1 H, \( J = 7.1 \) Hz), 1.32 (d, 6 H, \( J = 7.1 \) Hz); \(^{13}\)C NMR (CDCl\(_3\)) \& 151.97, 147.48, 140.81, 121.46, 115.01, 110.72, 107.87, 27.92, 22.46.

**2-(2-Propyl)-6-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridine (17b)** A mixture of 17a (0.21 g, 1.2 mmol) and N,N-dimethylcarbamoyl chloride (0.19 g, 1.8 mmol) in dry pyridine (10 mL) was stirred at 80 °C overnight. Solvent was then
evaporated to dryness under reduced pressure and the resulting residue was partitioned between a sat d NaHCO₃ solution and CHCl₃. The aqueous phase was extracted with CHCl₃ (6 x 20 mL). The organic layers were washed with brine (2 x 20 mL), dried (anhydrous Na₂SO₄), filtered and evaporated to dryness. Purification of the crude by column chromatography (silica gel; EtOAc-hexane, 4:1) afforded 17b (0.21 g, 70%) as a thick oil: Rf = 0.29 (EtOAc-hexane, 4:1); ¹H NMR (CDCl₃) δ 7.95 (d, 1 H, J = 2.2 Hz), 7.39 (d, 1 H, J = 9.9 Hz), 7.20 (s, 1 H), 6.87 (dd, 1 H, J = 2.2, 9.9 Hz), 2.92-3.07 (overlapped m, 4 H), 2.91 (s, 3 H), 1.26 (d, 6 H, J = 6.9 Hz); ¹³C NMR (CDCl₃) δ 154.75, 154.20, 142.90, 139.51, 120.89, 118.06, 116.19, 108.15, 36.50, 36.19, 28.21, 22.20.

1-Methyl-2-(2-propyl)-6-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridinium Iodide (17c) (PN-III-240, BN38883) Following the general procedure for Quaternization, 17b (1.27 g, 5.1 mmol) was reacted with an excess of methyl iodide in dry THF to give 17c (1.65 g, 82.5 %) as an off-white solid from CH₃CN/Et₂O: mp 180-181 °C; IR (KBr) v_max 3068, 3032, 1734 cm⁻¹; ¹H NMR (CDCl₃) δ 9.10 (d, 1 H, J = 2.1 Hz), 8.58 (s, 1 H), 8.28 (d, 1 H, J = 9.9 Hz), 7.77 (dd, 1 H, J = 2.1, 9.9 Hz), 4.15 (s, 3 H), 3.28 (septet, 1 H, J = 6.9 Hz), 3.14 (s, 3 H), 3.02 (s, 3 H), 1.43 (d, 6 H, J = 6.9 Hz); ¹³C NMR (CDCl₃) δ 153.11, 145.49, 143.40, 137.49, 130.52, 121.77, 112.09, 111.40, 37.10, 36.84, 33.04, 24.96, 21.55. Anal. Calcd for C₁₄H₂₀IN₃O₂: C, 43.20; H, 5.18; N, 10.80. Found: C, 43.04; H, 5.23; N, 10.79.

2-Amino-4-(N,N-dimethylcarbamoyloxy)pyridine (19) To a suspension of NaH (2.10 g, 52.5 mmol) (washed with hexane) in dry THF (100 mL), was added portionwise powdery 2-amino-4-hydroxypyridine (5.50 g, 50 mmol). The mixture was refluxed for 17.5 h. N,N-Dimethylcarbamoyl chloride (5.0 mL, 53 mmol) was then added dropwise. The mixture was refluxed further for 30 h. After cooling, the mixture was filtered and washed with THF. The filtration was evaporated to dryness to afford 19 as a yellow solid (7.75 g, 85 %). Purification by flash column chromatography (silica gel, acetone:MeOH:CH₂Cl₂=10:1:40) followed by recrystallization from acetone/ether gave a white solid: mp 104-5 °C; IR (KBr) v_max 3420, 3311, 3161, 2942, 1724, 1647, 1602, 1566, 1485, 1448, 1392, 1346, 1306, 1267, 1175, 953, 847, 799, 747 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.99 (d, J = 6.0
7-(N,N-Dimethylcarbamoyloxy)imidazo[1,2-a]pyridine (20a) A mixture of α-chloroacetylaldehyde (3.14 g, 18 mmol) and 2-amino-4-(N,N-dimethylcarbamoyloxy)pyridine (2.72 g, 15 mmol) were refluxed in THF for 13 h. The solvent was removed under reduced pressure. The residue was taken up by CH₂Cl₂ (100 mL) and washed with sat d NaHCO₃ (2x10 mL) and brine (10 mL). The aqueous washings were combined and extracted with CH₂Cl₂ (4x20 mL). The CH₂Cl₂ were combined and dried over anhydrous MgSO₄, and CH₂Cl₂ was evaporated. The residue was purified by flash column chromatography (silica gel, 5% to 10% MeOH in CH₂Cl₂) to afford 20a (2.122 g, 69%) as a white solid from ether: mp 98-100 °C; IR (KBr) vmax 3433, 3117, 3052, 2942, 1721, 1645, 1532, 1508, 1472, 1441, 1389, 1316, 1277, 1235, 1182, 1151, 1121, 1078, 1011, 910, 858, 829, 808, 735 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 8.07 (d, J = 7.2 Hz, 1H), 7.61 (s, 1H), 7.54 (s, 1H), 7.35 (d, J = 2.4 Hz, 1H), 6.73 (dd, J = 2.4, 7.2 Hz, 1H), 3.12 (s, 3H), 3.03 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 154.49, 149.13, 146.11, 134.70, 126.28, 112.53, 110.22, 108.81, 37.27, 37.02; MS (El) m/z 206 (M+1, 8.9), 205 (M, 31.6). Anal. Calcd for C₁₀H₁₁N₃O₂: C, 58.53; H, 5.40; N, 20.48. Found: C, 58.62; H, 5.40; N, 20.39.

2-Methyl-7-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridine (21a) A mixture of α-chloroacetone (4 mL, 50.0 mmol), 2-amino-4-(N,N-dimethylcarbamoyloxy)pyridine (1.81 g, 10.0 mmol) and toluensulfonic acid (57 mg, 0.30 mmol) in benzene (30 mL) were refluxed in a round bottom flask (100 mL) equipped with Dean-Stock distillation apparatus. After 9 h, additional α-chloroacetone (4 mL, 50.0 mmol) was added, and the reaction was refluxed further for 17 h. The benzene was removed under reduced pressure. The residue was taken up by CH₂Cl₂ (100 mL) and washed with sat d NaHCO₃ (2x10 mL) and brine (10 mL). The aqueous washings were combined and extracted with CH₂Cl₂ (4x20 mL). The CH₂Cl₂ were combined and dried over anhydrous MgSO₄, and CH₂Cl₂ was evaporated. The residue was purified by flash column chromatography (silica gel, CH₂Cl₂:EtOAc:MeOH =
50:50:1) to afford 21a (0.752 g, 34 %) as white crystals from ether: mp 95-6 °C; IR (KBr) $v_{max}$ 3043, 2931, 1726, 1643, 1528, 1508, 1584, 1476, 1445, 1385, 1327, 1275, 1246, 1173, 1015, 855, 754, 719 cm$^{-1}$; $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ 8.31 (d, $J = 7.2$ Hz, 1H), 7.53 (s, 1H), 7.14 (d, $J = 1.8$ Hz, 1H), 6.67 (dd, $J = 1.8$, 7.2 Hz, 1H), 3.10 (s, 3H), 2.96 (s, 3H), 2.31 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 154.56, 148.88, 145.72, 144.54, 125.68, 109.53, 109.46, 107.90, 37.24, 36.99, 14.81; MS (Cl, methane) m/z 220 (M+1, 100). Anal. Calcd for C$_{11}$H$_{13}$N$_3$O$_2$: C, 60.26; H, 5.98; N, 19.17. Found: C, 60.37; H, 5.99; N, 19.14.

2-Isopropyl-7-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridine (22a) A mixture of 1-bromo-3-methylbutan-2-one (6) (1.98 g, 12.0 mmol), 2-amino-4-(N,N-dimethylcarbamoyloxy)pyridine (1.81 g, 10.0 mmol) and toluensulfonic acid (57 mg, 0.30 mmol) in toluene (30 mL) was refluxed for 24 h. The toluene was removed under reduced pressure. The residue was taken up by CH$_2$Cl$_2$ (100 mL) and washed with sat d NaHCO$_3$ (2x10 mL) and brine (10 mL). The aqueous washings were combined and extracted with CH$_2$Cl$_2$ (5x20 mL). The CH$_2$Cl$_2$ were combined and dried over anhydrous MgSO$_4$, and CH$_2$Cl$_2$ was evaporated. The residue was purified by flash column chromatography (silica gel, 20% acetone in CH$_2$Cl$_2$) to afford 22a (1.516 g, 61 %) as white needle crystals from ether: mp 106-7 °C; IR (KBr) $v_{max}$ 3144, 3080, 2953, 2868, 1719, 1640, 1526, 1505, 1470, 1437, 1393, 1287, 1238, 1181, 1015, 868, 799, 789, 737 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.97 (d, $J = 7.2$ Hz, 1H), 7.27 (s, 1H), 7.25 (d, $J = 2.4$ Hz, 1H), 6.64 (dd, $J = 2.4$, 7.2 Hz, 1H), 3.11 (s, 3H), 3.09 (m, 1H), 3.02 (s, 3H), 1.35 (d, $J = 6.9$ Hz, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 155.40, 154.54, 148.87, 145.60, 125.94, 109.41, 108.12, 107.47, 37.21, 36.98, 28.89, 22.87; MS (Cl, methane) m/z 248 (M+1, 100). Anal. Calcd for C$_{13}$H$_{17}$N$_3$O$_2$: C, 63.14; H, 6.93; N, 16.99. Found: C, 63.22; H, 6.99; N, 16.97.

2-Phenyl-7-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridine (23a) A mixture of $\alpha$-bromoacetophenone (1.99 g, 10.0 mmol), 2-amino-4-(N,N-dimethylcarbamoyloxy)pyridine (1.81 g, 10.0 mmol) and toluensulfonic acid (57 mg, 0.30 mmol) were refluxed in toluene for 22 h. The toluene was removed under reduced pressure. The residue was taken up by CH$_2$Cl$_2$ (100 mL) and washed with sat d NaHCO$_3$ (2x10 mL) and brine (10 mL). The aqueous washings were combined
and extracted with CH₂Cl₂ (4x20 mL). The CH₂Cl₂ were combined and dried over anhydrous MgSO₄, and CH₂Cl₂ was evaporated. The residue was purified by flash column chromatography (silica gel, 5% MeOH in CH₂Cl₂) to afford 23a (1.524 g, 54%) as white needle crystals from acetone: mp 184-5 °C; IR (KBr) νmax 3136, 3084, 2942, 1725, 1642, 1526, 1505, 1472, 1443, 1391, 1370, 1254, 1204, 1184, 1169, 1074, 1009, 872, 787, 775, 719, 694 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 8.06 (dd, J = 0.9, 7.2 Hz, 1H), 7.94 (m, 2H), 7.82 (s, 1H), 7.46-7.28 (m, 4H), 6.73 (dd, J = 2.4, 7.2 Hz, 1H), 3.13 (s, 3H), 3.04 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 154.46, 149.39, 147.06, 146.43, 134.22, 129.20, 128.45, 126.53, 126.09, 110.27, 108.52, 108.27, 37.31, 37.06; MS (EI) m/z 282 (M⁺, 4.8), 205 (M, 30.0), 209 (M-Me₂NCO, 4.5), 72 (Me₂NCO, 100). Anal. Calcd. for C₁₆H₁₅N₃O₂: C, 68.31; H, 5.37; N, 14.94. Found: C, 68.41; H, 5.41; N, 14.98.

General Procedure for Quaternization of 7-(N,N-dimethylcarbamoyloxy)-imidazo[1,2-a]pyridine derivatives  A mixture of appropriate carbamate (1 equiv) and methyl iodide (1.5-10 equiv) in dry THF was stirred at 50 °C (oil bath) for 12-43 hours. The mixture was cooled to rt and filtered. The product was washed with dry THF and dried in vacuo at rt.

1-Methyl-7-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridinium Iodide (20b) (SJ-II-43)  Following the general procedure for Quaternization, 20a (0.584 g, 2.84 mmol) was reacted with an excess of methyl iodide (0.27 mL, 4.27 mmol) in dry THF (5 mL) for 12 h to give 20b (0.920 g, 93%) as a light yellow solid from MeOH/Et₂O: mp 147-8 °C; IR (KBr) νmax 3071, 3034, 1740, 1655, 1547, 1456, 1377, 1271, 1260, 1200, 1144, 1099, 1007, 841, 808, 773, 729, 638 cm⁻¹; ¹H NMR (300 MHz, acetone-d₆) δ 9.21 (d, J = 7.5 Hz, 1H), 8.59 (d, J = 1.8 Hz, 1H), 8.25 (d, J = 1.8 Hz, 1H), 8.08 (d, J = 2.1 Hz, 1H), 7.51 (dd, J = 2.1, 7.5 Hz, 1H), 4.22 (s, 3H), 3.16 (s, 3H), 3.03 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 156.18, 152.48, 140.91, 131.44, 127.38, 115.36, 114.21, 101.67, 37.61, 37.54, 35.85. Anal. Calcd for C₁₆H₁₄N₃O₂I: C, 38.06; H, 4.06; N, 12.10; I, 36.56. Found: C, 38.16; H, 4.03; N, 12.15; I, 36.65.

1-Methyl-2-methyl-7-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridinium Iodide (21b) (SJ-II-100)  Following the general procedure for Quaternization, 21a
(1.417 g, 6.47 mmol) was reacted with an excess of methyl iodide (2.01 mL, 30.85 mmol) in dry THF (10 mL) for 24 h to give 21b (2.20 g, 94%) as an off-white solid from MeOH/Et₂O: mp 216-8 °C; IR (KBr) v_max 2978, 1734, 1549, 1499, 1476, 1433, 1399, 1256, 1209, 1198, 1146, 1007, 893, 800, 725 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 9.25 (d, J = 7.2 Hz, 1H), 8.50 (s, 1H), 7.83 (s, 1H), 7.19 (dd, J = 2.1, 7.5 Hz, 1H), 3.93 (s, 3H), 3.11 (s, 3H), 2.99 (s, 3H), 2.52 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 155.79, 152.59, 141.00, 135.55, 130.90, 113.86, 112.98, 101.66, 37.58, 37.51, 32.80, 11.23. Anal. Calcd for C₁₂H₁₆N₃O₂: C, 39.91; H, 4.47; N, 11.63, I, 35.14. Found: C, 40.00; H, 4.43; N, 11.56; I, 35.06.

1-Methyl-2-isopropyl-7-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridinium Iodide (22b) (SJ-II-95) Following the general procedure for Quaternization, 22a (1.05 g, 4.25 mmol) was reacted with an excess of methyl iodide (1.32 mL, 21.25 mmol) in dry THF (25 mL) for 24 h to give 22b (1.56g, 94%) as an off-white solid from MeOH/Et₂O: mp 196-7 °C; IR (KBr) v_max 3049, 3023, 2972, 1746, 1657, 1547, 1534, 1464, 1379, 1252, 1198, 1150, 1007, 847, 808, 783, 748 cm⁻¹; ¹H NMR (300 MHz, acetone-d₆) δ 9.02 (dd, J = 0.6, 7.2 Hz, 1H), 8.35 (s, 1H), 8.05 (d, J = 2.4 Hz, 1H), 7.48 (dd, J = 2.4, 7.2 Hz, 1H), 4.13 (s, 3H), 3.42 (m, 1H), 3.15 (s, 3H), 3.02 (s, 3H), 1.44 (d, J = 6.6 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 155.94, 152.56, 145.39, 141.19, 131.22, 113.92, 111.61, 101.72, 37.56, 37.50, 32.91, 25.24, 21.96. Anal. Calcd for C₁₄H₂₀N₃O₂I: C, 43.20; H, 5.18; N, 10.80, I, 32.60. Found: C, 43.28; H, 5.17; N, 10.83; I, 32.50.

1-Methyl-2-phenyl-7-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridinium Iodide (23b) (SJ-II-39) Following the general procedure for Quaternization, 23a (1.554 g, 5.524 mmol) was reacted with an excess of methyl iodide (1.72 mL, 27.6 mmol) in dry THF (25 mL) for 24 h. Another portion of methyl iodide (1.72 mL, 27.6 mmol) was added, and the reaction was stirred further for 19 h to give 23b (2.134 g, 91%) as a light yellow solid from MeOH/Et₂O: mp 212-4 °C; IR (KBr) v_max 3142, 2996, 2934, 1736, 1659, 1537, 1489, 1443, 1387, 1265, 1204, 1157, 1017, 891, 810, 779, 758, 748, 727, 702 cm⁻¹; ¹H NMR (300 MHz, acetone-d₆) δ 9.28 (d, J = 7.2 Hz, 1H), 8.77 (s, 1H), 8.15 (d, J = 1.8 Hz, 1H), 7.80-7.72 (m, 2H), 7.68-7.63 (m, 3H), 7.55 (dd, J = 1.8, 7.2 Hz, 1H), 4.09 (s, 3H), 3.18 (s, 3H), 3.04 (s, 3H); ¹³C NMR (75...
MHz, CDCl\textsubscript{3} \( \delta \) 156.22, 152.52, 141.53, 138.79, 131.51, 131.39, 130.44, 129.94, 125.08, 114.18, 113.24, 102.08, 37.57, 37.50, 33.64. Anal. Calcd for C\textsubscript{17}H\textsubscript{18}N\textsubscript{3}O\textsubscript{2}: C, 48.24; H, 4.29; N, 9.93; I, 29.98. Found: C, 48.15; H, 4.29; N, 9.84; I, 30.02.

**General Procedure for Carbamoylation of 8-Hydroxyimidazo[1,2-a]pyridine Derivatives**  A mixture of 8-hydroxyimidazo[1,2-a]pyridine derivative (1 equiv) and N,N-dimethylcarbamoyl chloride (1.5 equiv) in pyridine was stirred at 80 °C for 16 h. Solvent was evaporated under reduced pressure to dryness and the resulting residue was neutralized with saturated NaHCO\textsubscript{3} solution. The aqueous mixture was extracted with CHCl\textsubscript{3} (6x). The organic layers were washed with water, brine and dried (Na\textsubscript{2}SO\textsubscript{4}). Removal of solvent gave a crude product.

8-(N,N-Dimethylcarbamoyloxy)imidazo[1,2-a]pyridine (25b) Following the general procedure for carbamoylation, the reaction of 8-hydroxyimidazo[1,2-a]pyridine (9) 25a (8.5 g, 5.0 mmol) with N,N-dimethylcarbamoyl chloride (0.69 mL, 7.5 mmol) in pyridine (5 mL) gave 25b (0.67 g, 65%) as a white solid after purification by column chromatography (silica gel; CHCl\textsubscript{3}-MeOH, 25:1) followed by recrystallization in EtOAc/hexane: mp 128-129.5 °C; R\textsubscript{f} = 0.29 (CHCl\textsubscript{3}-MeOH, 25:1); \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \( \delta \) 7.86 (br d, 1 H, J = 6.9 Hz), 7.48 (br d, 2H, J = 8.7 Hz), 6.86 (br d, 1 H, J = 7.4 Hz), 6.57 (dd, 1 H, J = 6.9, 7.4 Hz), 3.12 (s, 3 H), 2.94 (s, 3 H). \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \( \delta \) 153.70, 140.95, 140.72, 133.46, 123.06, 115.35, 113.19, 111.42, 36.80, 36.67. Anal. Calcd for C\textsubscript{10}H\textsubscript{11}N\textsubscript{3}O\textsubscript{2}: C, 58.53; H, 5.40 N, 20.48. Found: C, 58.46 H, 5.46; N, 20.53.

1-Methyl-8-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridinium \textit{p}-Toluenesulfonate (25c) (PN-II-278, BN36049) Following the general procedure for Quaternization, the reaction of 25b (0.96 g, 4.68 mmol) with methyl p-toluenesulfonate (1.3 g, 7.0 mmol) in THF (20 mL) gave 25c (1.38 g, 75%) as white solid from CH\textsubscript{3}CN/Et\textsubscript{2}O: mp 145-145.5 °C; IR (KBr)\textsubscript{vmax} 3107, 3086, 1751, 1199 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \( \delta \) 9.12 (d, 1 H, J = 6.8 Hz), 8.79 (d, 1 H, J = 2.1 Hz), 8.33 (d, 1 H, J = 2.1 Hz), 7.78 (d, 2 H, J = 8.0 Hz), 7.51 (d, 1 H, J = 7.8 Hz), 7.25 (dd, 1 H, J = 6.8, 7.8 Hz), 7.12 (d, 2 H, J = 8.0 Hz), 4.20 (s, 3 H), 3.15 (s, 3 H), 3.04 (s, 3 H), 2.13 (s, 3 H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \( \delta \) 152.72, 144.07, 139.13, 136.66, 134.17, 128.61,
Anal. Calcd for C_{18}H_{21}N_{3}O_{5}S: C, 55.23; H, 5.41; N, 10.73. Found: C, 55.29; H, 5.40; N, 10.72.

**2-Methyl-8-hydroxyimidazo[1,2-a]pyridine (26a)** A mixture of 2-amino-3-hydroxypyridine (1.10 g, 10 mmol) and 2-chloroacetone (0.8 mL, 10 mmol) in dry THF (30 mL) was gently refluxed for 5 h. Then another 0.8 mL of 2-chloroacetone was added and the reaction mixture was stirred at reflux temperature overnight. Solvent was then evaporated to dryness and the resulting residue was quenched with a saturated aqueous solution of NaHCO₃. The mixture was filtered to yield 26a (0.52 g, 35%) as a tan solid. The aqueous filtrate was extracted with CHC₃ (4 x 10 mL). The combined organic layers were washed with brine and dried (Na₂SO₄). Removal of solvent gave another 0.26 g (18%) of 26a: ¹H NMR (D₂O) δ 7.96 (dd, 1 H, J = 1.2, 6.3 Hz); 7.61 (d, 1 H, J = 0.9 Hz), 7.06 (dd, 1 H, J = 6.3, 7.8 Hz), 7.01 (dd, 1 H, J = 1.2, 7.8 Hz), 2.38 (d, 3 H, J = 0.9 Hz); ¹³C NMR (DMSO-d₆) δ 142.60, 133.31, 132.90, 119.29, 117.35, 112.81, 112.43, 10.21.

**2-Methyl-8-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridine (26b)** Following the general procedure for carbamoylation of 8-hydroxyimidazo[1,2-a]pyridine derivatives, 26a (0.74 g, 5 mmol) and N,N-dimethylcarbamoyl chloride in dry pyridine yielded 26b (0.8 g, 74%) as an off-white solid from EtOAc/hexane: mp 80.5-81.5 °C; Rₚ = 0.41 (CHCl₃-MeOH, 19:1); ¹H NMR (CDCl₃) δ 7.88 (dd, 1 H, J = 0.9, 6.8 Hz), 7.35 (s, 1 H), 6.92 (dd, 1 H, J = 0.9, 7.5 Hz), 6.67 (dd, 1 H, J = 6.8, 7.5 Hz), 3.21 (s, 3 H), 3.03 (s, 3 H), 2.46 (d, 3 H, J = 0.9 Hz); ¹³C NMR (CDCl₃) δ 153.91, 143.46, 140.60, 139.87, 122.46, 115.20, 110.84, 110.52, 36.83, 36.78, 14.50. Anal. Calcd for C₁₁H₁₃N₃O₂: C, 60.26; H, 5.98; N, 19.17. Found: C, 60.19; H, 6.01; N, 19.21.

**1,2-Dimethyl-8-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridinium Tosylate (26c) (PN-II-222, BN34830)** Following the general procedure for Quaternization, the reaction of 26b (0.4 g, 1.82 mmol) and methyl p-toluenesulfonate (0.5 g, 2.7 mmol) in THF (5 mL) afforded 26c (0.52 g, 70%) as an off-white solid from methanol/ether: mp 205-207 °C; IR (KBr)₉max 3136, 3049, 1728 cm⁻¹; ¹H NMR (CDCl₃) δ 9.06 (dd, 1 H, J = 0.6, 6.6 Hz), 8.57 (s, 1 H), 7.73 (d, 2 H, J = 8.1 Hz), 8.27 (d, 2 H, J = 6.6 Hz), 7.98 (dd, 1 H, J = 0.6, 8.1 Hz), 7.87 (d, 1 H, J = 0.6 Hz), 7.65 (s, 1 H), 7.38 (d, 2 H, J = 8.1 Hz), 7.06 (d, 1 H, J = 0.6 Hz), 3.94 (s, 3 H), 3.80 (s, 3 H), 2.48 (d, 3 H, J = 0.6 Hz); ¹³C NMR (CDCl₃) δ 153.91, 143.46, 140.60, 139.87, 122.46, 115.20, 110.84, 110.52, 36.83, 36.78, 14.50. Anal. Calcd for C₁₇H₁₈N₃O₄S: C, 60.92; H, 5.98; N, 19.17. Found: C, 60.93; H, 6.01; N, 19.17.
7.47 (dd, 1 H, J = 0.6, 7.8 Hz), 7.21 (dd, 1 H, J = 6.6, 7.8 Hz), 7.06 (dd, 2 H, J = 8.1 Hz), 3.99 (s, 3 H), 3.18 (s, 3 H), 3.04 (s, 3 H), 2.44 (s, 3 H), 2.28 (s, 3 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 152.67, 144.23, 138.72, 136.02, 135.62, 134.18, 128.31, 127.42, 125.74, 125.55, 116.43, 114.34, 37.21, 36.78, 32.77, 21.13, 9.92. Anal. Calcd for: C$_{19}$H$_{23}$N$_3$O$_5$S: C, 56.28; H, 5.72; N, 10.36. Found: C, 56.25; H, 5.73; N, 10.31.

8-Hydroxy-2-(2-propyl)imidazo[1,2-a]pyridine (27a) To a hot solution of 2-amino-3-hydroxypyridine (3.3 g, 30 mmol) in absolute ethanol (30 mL) and THF (30 mL) was added dropwise a solution of 1-bromo-3-methylbutan-2-one (6) (4.95 g, 30 mmol). The reaction mixture was gently refluxed overnight and solvent was removed under reduced pressure. The residue was dissolved in methanol and a few drops of Conc. HBr were added. The mixture was heated on a steam bath for 1 h. Removal of solvent to dryness gave a brown solid, which was quenched with saturated NaHCO$_3$ solution. The mixture was extracted with CHCl$_3$ (6 x 30 mL). The organic layers were washed with H$_2$O (30 mL), brine (2 x 30 mL) and dried (Na$_2$SO$_4$). Evaporation of solvent gave a crude product. Purification of the crude by column chromatography on silica gel (CHCl$_3$-MeOH, 19:1) afforded 27a (3.9 g, 74%) as white solid from MeOH/Et$_2$O: mp 162-163 °C; $R_f$ = 0.35 (CHCl$_3$-MeOH, 19:1); $^1$H NMR (CDCl$_3$) $\delta$ 7.6 (dd, 1 H, J = 4.5 Hz), 7.23 (d, 1 H, J = 0.6 Hz), 6.66-6.71 (m, 2 H), 3.09-3.22 (m, 1 H), 1.28 (d, 6 H, J = 6.9 Hz), 0.47 (br s, 1 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 151.06, 146.98, 140.18, 116.54, 113.99, 108.28, 108.07, 27.62, 22.39. Anal. Calcd for C$_{10}$H$_{12}$N$_2$O: C, 68.16; H, 6.86; N, 15.90. Found: C, 68.11; H, 6.90; N, 15.83.

8-(N,N-Dimethylcarbamoyloxy)-2-(2-propyl)imidazo[1,2-a]pyridine (27b) Following the general procedure for carbamoylation of 8-hydroxyimidazo[1,2-a]pyridine derivatives, the reaction of 27a (2.7 g, 15.3 mmol) with N,N-dimethylcarbamoyl chloride (2.1 mL, 23.0 mmol) in pyridine (30 mL) gave a crude product, which was purified by column chromatography (silica gel; EtOAc-hexane, 4:1) to give 27b (2.71 g, 71%) as a white solid from EtOAc/hexane: mp 100-101 °C; $R_f$ = 0.33 (EtOAc-hexane, 4:1); $^1$H NMR (CDCl$_3$) $\delta$ 7.90 (dd, 1 H, J = 0.9, 6.9 Hz), 7.35 (s, 1 H), 6.91 (dd, 1 H, J = 0.9, 7.5 Hz), 6.65 (dd, 1 H, J = 6.9, 7.5 Hz), 3.22 (s, 3 H), 3.08-3.20 (m, 1 H), 3.02 (s, 3 H), 1.34 (d, 6 H, J = 6.9 Hz). Anal. Calcd for C$_{13}$H$_{17}$N$_3$O$_2$: C, 63.14; H, 6.93; N, 16.99. Found: C, 63.01; H, 6.92; N, 16.98.
1-Methyl-2-(2-propyl)-8-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]-pyridinium p-Toluenesulfonate (27c) (PN-III-28, BN36058) Following the general procedure for Quaternization, the reaction of 27b (1.1 g, 4.45 mmol) with methyl p-toluenesulfonate (1.24 g, 6.67 mmol) in CH$_3$CN (20 mL) gave 27c (1.72 g, 89 %) as white solid from CH$_3$CN/Et$_2$O: mp 125-126 °C; IR (KBr)$_{\text{vmax}}$ 3099, 3040, 1734, 1720, 1219 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 9.19 (d, 1 H, J= 6.7 Hz), 8.63 (s, 1 H), 7.76 (d, 2 H, J = 7.8 Hz), 7.48 (d, 1 H, J = 7.8 Hz), 7.22 (dd, 1 H, J = 6.7; 7.8 Hz), 7.06 (d, 2 H, J = 7.9 Hz), 4.03 (s, 3 H), 3.20 (s, 3 H), 3.08-3.18 (m, 1 H), 3.05 (s, 3 H), 2.28 (s, 3 H), 1.31 (d, 6 H, J = 6.9 Hz); $^{13}$C NMR (CDCl$_3$) $\delta$ 152.73, 145.16, 144.34, 138.61, 136.02, 134.37, 128.24, 128.06, 125.83, 125.79, 116.44, 113.05, 37.23, 36.00, 32.78, 24.22, 21.17, 21.11. Anal. Calcd for C$_{21}$H$_{27}$N$_3$0$_5$S: C, 58.18; H, 6.28; N, 9.69. Found: C, 57.98; H, 6.33; N, 9.58.

8-Hydroxy-2-phenylimidazo[1,2-a]pyridine (28a) A mixture of 2-amino-3-hydroxypyridine (1.10 g, 10 mmol) and 2-bromoacetophenone (1.99 g, 10 mmol) in acetone (30 mL) was stirred at 60 °C overnight. The volume of solvent was reduced and the mixture was cooled in an ice bath. The resulting solid was filtered, then dissolved in methanol, followed by addition of a few drops of Conc. HBr solution. The mixture was heated on a steam bath for 1 h. Solvent was evaporated to dryness. The residue was quenched with saturated NaHCO$_3$ solution. The aqueous mixture was extracted with CHCl$_3$ (6 x 20 mL). The organic layers were washed with brine (2 x 20 mL) and dried (Na$_2$SO$_4$). Removal of solvent gave 28a (1.38 g, 66%) as a solid: $R_f = 0.56$ (CHCl$_3$-MeOH, 9:1); $^1$H NMR (DMSO-d$_6$) $\delta$ 8.75 (s, 1 H), 8.35 (d, 1 H, J = 6.6 Hz), 8.00 (d, 2 H, J = 7.6 Hz), 7.51-7.60 (m, 3 H), 7.28 (dd, 1 H, J = 6.6, 7.5 Hz), 7.16 (d, 1 H, J = 7.8 Hz).

8-(N,N-Dimethylcarbamoyloxy)-2-phenylimidazo[1,2-a]pyridine (28b) Following the general procedure for carbamoylation of 8-hydroxyimidazo[1,2-a]-pyridine derivatives, treatment of 28a (1.1 g, 5.2 mmol) with N,N-dimethylcarbamoyl chloride (0.72 mL, 7.8 mmol) in pyridine (10 mL) gave a crude product. Purification of the crude by column chromatography (silica gel; CHCl$_3$-MeOH, 20:1) afforded 28b (1.2 g, 82%) as an off-white solid: mp 132-132.5 °C; $R_f = 0.58$ (CHCl$_3$-MeOH,
1-Methyl-2-phenyl-8-(N,N-dimethylcarbamoyloxy)imidazo[1,2-a]pyridinium Iodide (28c) (PN-II-258, BN36030) Following the general procedure for Quaternization, the reaction of 28b (2.0 g, 7.1 mmol) with methyl iodide (1.32 mL, 21.3 mmol) in THF (25 mL) yielded 28c (2.47 g, 82%) as white needles from CH₃CN/Et₂O: mp 165-165.5 °C; IR (KBr)νmax 3057, 1741, 1143 cm⁻¹; ¹H NMR (CDCl₃) δ 9.38 (d, 1 H, J = 6.7 Hz), 8.95 (s, 1 H), 7.68 (d, 1 H, J = 7.8 Hz), 7.52-7.62 (m, 5 H), 7.36 (dd, 1 H, J = 6.7, 7.8 Hz), 4.00 (s, 3 H), 3.27 (s, 3 H), 3.09 (s, 3 H); ¹³C NMR (CDCl₃) δ 152.60, 138.73, 136.75, 134.86, 131.05, 130.15, 129.30, 126.92, 126.44, 123.96, 117.07, 113.88, 37.34, 37.19, 34.63. Anal. Calcd for C₁₇H₁₈IN₃O₂: C, 48.24; H, 4.29; N, 9.93. Found: C, 48.34; H, 4.25; N, 9.97.

3-(N,N-dimethylcarbamoyloxy)pyridine (29a) Sodium hydride (3.3 g, 0.11 mol, 80% dispersion in mineral oil) was added in small portions to an ice-cooled solution of 3-pyridinol (9.51 g, 0.1 mol) in DMF (70 mL). The mixture was stirred in an ice bath for 10 min, then at room temperature for 30 min. The mixture was cooled and N,N-dimethylcarbamoyl chloride (0.13 mol, 11.96 mL) was added via syringe. The reaction mixture was then stirred at 80 °C for 2 h, cooled and poured into cold aqueous 1% KOH solution. The mixture was saturated with NaCl then extracted with benzene:pentane ether (4:1) (3 x 80 mL). The combined organic layers were washed with H₂O (150 mL), then extracted with 5% HCl solution (3 x 75 mL). The cooled aqueous phase was basified with 20% KOH solution and extracted with benzene:pentane ether (4:1) (3 x 80 mL). The combined organic layers were washed with brine and dried (Na₂SO₄). Removal of solvent gave a pale yellow liquid 29a (11.05 g, 66.4%): ¹H NMR (CDCl₃) δ 8.43-8.45 (br s, 1 H), 7.51 (ddd, 1 H, J = 1.3 Hz, J = 2.5 Hz, J = 8.3 Hz), 7.30 (dd, 1 H, J = 4.7 Hz, J = 8.3 Hz), 3.12 (s, 3 H),
3.02 (s, 3 H): $^{13}$C NMR (CDCl$_3$) $\delta$ 154.48, 148.03, 146.10, 143.48, 129.16, 123.52, 36.65, 36.35.

1-Methyl-3-(N,N-dimethylcarbamoyloxy)pyridinium Iodide (29b) A mixture of 29a (9.8 g, 58.97 mmol) and methyl iodide (7.3 mL, 118 mmol) in dry THF (50 mL) was magnetically stirred overnight. The resulting precipitate was filtered and recrystallized with acetone/ether to give 29b as a white solid (14.25 g, 78.4%): $^1$H NMR (CDCl$_3$) $\delta$ 8.83 (s, 1 H), 8.68 (d, 1 H, $J = 6.0$ Hz), 8.37 (d, 1 H, $J = 8.7$ Hz), 8.03-8.08 (dd, 1 H, $J = 6.0$ Hz, $J = 8.7$ Hz), 4.76 (DO-H), 4.40 (s, 3 H), 3.13 (s, 3 H), 3.00 (s, 3 H).

1-Methyl-1,2,5,6-tetrahydro-3-(N,N-dimethylcarbamoyloxy)pyridine (29c) To an ice-cooled solution of 29b (1.54 g, 5 mmol) in MeOH (25 mL) was added NaBH$_4$ (0.75 g, 20 mmol) in small portions. The mixture was stirred in an ice bath for 30 min, then at room temperature for 1 h. The volume of solvent was carefully reduced and H$_2$O (10 mL) was added. The solution was saturated with NaCl then extracted with ether (3 x 20 mL). The combined organic layers were washed with brine (2 x 20 mL) and dried (MgSO$_4$). Removal of solvent gave a pale yellow liquid 29c (0.86 g, 96.6%): $^1$H NMR (CDCl$_3$) $\delta$ 5.44 (ca. 1 H), 3.02 (dd, 2 H, $J = 2.4$ Hz, $J = 3.9$ Hz), 2.95 (s, 3 H), 2.93 (s, 3 H), 2.54 (t, 2 H, $J = 5.9$ Hz), 2.38 (s, 3 H), 2.23-2.29 (br m, 2 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 145.84, 110.97, 55.13, 51.23, 45.21, 36.46, 36.30, 24.04.

1,1-Dimethyl-1,2,5,6-tetrahydro-3-(N,N-dimethylcarbamoyloxy)pyridinium Tosylate (29d) (PN-226, BM17825) A mixture of 29c (0.85 g, 4.78 mmol) and methyl tosylate (1.78 g, 9.57 mmol) in ether (5 mL) was stirred at room temperature for 1 h. The precipitate was filtered and washed several times with ether to give 29d (1.63 g, 93%), as white solid from CH$_3$CN/ether: mp 146-7 °C; IR (KBr) $\nu_{max}$ 3040, 3028, 1718, 1697 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 7.74 (d, 2 H, $J = 7.9$ Hz), 7.14 (d, 2 H, $J = 7.9$ Hz), 5.61 (t, 1 H, $J = 3.4$ Hz), 4.04 (br s, 2 H), 3.75 (t, 2 H, $J = 6.1$ Hz), 3.41 (s, 6 H), 2.92 (s, 3 H), 2.89 (s, 3 H), 2.50 (br m, 2 H), 2.33 (s, 3 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 153.66, 143.82, 139.50, 139.11, 128.56, 125.70, 110.77, 60.55, 57.91, 51.65, 36.49, 36.32, 21.18, 19.96. Anal. Calcd for C$_{17}$H$_{30}$O$_5$N$_2$S: C, 55.12; H, 7.07; N, 7.56. Found: C, 55.19; H, 7.10; N, 7.61.
3-(N-Methylcarbamoyloxy)pyridine (30a) 3-Hydroxypyridine (4.75 g, 50 mmol) was carbamoylated as described for 2c with methyl isocyanate (6 mL, 0.1 mol) in the presence of a catalytic amount of Bu₂Sn(OAc)₂ in dry THF (40 mL). Column chromatography of the crude product on silica gel (CHCl₃-MeOH, 9:1) gave 30a (5.47 g, 72%) as a colorless oil: Rf = 0.42 (CHCl₃-MeOH, 9:1); ¹H NMR (CDCl₃) δ 8.41-8.45 (ca, 1 H), 7.51-7.55 (m, 1 H), 7.27-7.32 (m, 1 H), 6.13 (br s, 1 H), 2.83 (d, 3 H, J = 4.8 Hz); ¹³C NMR (CDCl₃) δ 154.47, 147.70, 145.77, 143.13, 129.07, 123.57, 27.40.

1-Methyl-3-(N-methylcarbamoyloxy)pyridinium Iodide (30b) A mixture of 30a (2.43 g, 16 mmol) and methyl iodide (2 mL, 32 mmol) in dry THF (30 mL) was stirred at room temperature for 16 h and then evaporated to dryness to give a yellow oil. Crystallization of the crude product gave 30b (3.28 g, 66%) as a yellow solid from MeOH/ether: ¹H NMR (D₂O) δ 8.84 (s, 1 H), 8.67 (d, 1 H, J = 6.2 Hz), 8.37 (d, 1 H, J = 8.6 Hz), 8.01 (dd, 1 H, J = 6.2, 8.6 Hz), 4.40 (s, 3 H), 2.83 (s, 3 H).

1-Methyl-1,2,5,6-tetrahydro-3-(N-methylcarbamoyloxy)pyridine (30c) To an ice-cooled solution of 30b (1.84 g, 6.25 mmol) in methanol (10 mL) was added NaBH₄ (0.97 g, 25 mmol) in small portions. The mixture was stirred at 0 °C for 30 min, then at room temperature for 1 h. The organic solvent was evaporated under vacuum and the white residue was dissolved in H₂O. The aqueous mixture was extracted with CH₂Cl₂ (6 x 30 mL). The combined organic layers were dried (MgSO₄) and evaporated to dryness to give a brown oil. Purification of the crude product by column chromatography on silica gel (CHCl₃-MeOH, 9:1) gave 30c (0.74 g, 70%) as white crystals from acetone/hexane: mp 86.5-87.5 °C; Rf = 0.27 (CDCl₃-MeOH, 9:1); IR (KBr)νmax 1730 cm⁻¹; ¹H NMR (CDCl₃) δ 5.46 (br s, 1 H), 4.80 (br s, 1 H), 3.01 (br s, 2 H), 2.82 (d, 3 H, J = 4.8 Hz), 2.53 (t, 2 H, J = 5.7 Hz), 2.38 (s, 3 H), 2.24 - 2.28 (m, 2 H). Anal. Calcd for C₈H₁₄N₂O₂: C, 56.45; H, 8.29; N, 16.46. Found: C, 56.36; H, 8.27; N, 16.39.

1,1-Dimethyl-1,2,5,6-tetrahydro-3-(N-methylcarbamoyloxy)pyridinium Iodide (30d) (PN-II-198, BN34821) Following the general procedure for Quaternization, the reaction of 30c (0.45 g, 2.64 mmol) with methyl iodide (0.5 mL, 7.9 mmol) in dry
THF (4 mL) gave 30d (0.75 g, 91%) as a white solid from CH₃CN/ether: mp 172-173 °C; IR (KBr)νmax 1730, 1709 cm⁻¹; ¹H NMR (DMSO-d₆) δ 7.59 (br m, 1 H), 5.67 (br s, 1 H), 4.00 (br s, 2 H), 3.45 (t, 2 H, J = 6.2 Hz), 3.12 (s, 6 H), 2.59 (d, 3 H, J = 4.5 Hz), 2.46 - 2.54 (m, 2 H); ¹³C NMR (DMSO-d₆) δ 153.88, 138.76, 110.25, 59.49, 57.27, 50.79, 26.93, 19.23. Anal. Calcd for C₉H₁₇N₂O₂: C, 34.63; H, 5.50; N, 8.97. Found: C, 34.72; H, 5.51; N, 9.02.

1-Methyl-4-(N,N-dimethylcarbamoyloxy)pyridinium Iodide (31b) (15) To an ice-cooled solution of 4-hydroxypyridine (4.75 g, 50 mmol) in dry DMF (70 mL) was added NaH (1.65 g, 55 mmol) in small portions. After being stirred at room temperature for 30 min, the mixture was cooled in an ice bath and N,N-dimethylcarbamoyl chloride (10.75 g, 0.1 mol) was added slowly via a syringe. The reaction mixture was then stirred at 80 °C for 5 h, cooled and quenched with H₂O (30 mL) followed by aqueous 10% HCl solution (50 mL), saturated with NaCl, then extracted with CH₂Cl₂ (3 x 30 mL). The aqueous phase was basified with 20% NaOH solution and extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine, dried (Na₂SO₄) and filtered through a short column of silica gel. Removal of the solvent gave 31a as a yellow liquid (3.53g, 42%): ¹H NMR (CDCl₃) δ 8.57 (d, 2 H, J = 4.8 Hz), 7.13 (d, 2 H, J = 4.8 Hz), 3.10 (s, 3 H), 3.02 (s, 3 H).

A mixture of 31a (0.86 g, 5.18 mmol) and methyl iodide (0.64 mL) in dry THF (10 mL) was stirred at room temperature overnight. The precipitate was filtered and recrystallized with methanol/ether to give 31b (1.50 g, 94%): mp 149-150 °C (lit. 131-132 °C).

1-Methyl-1,2,5,6-tetrahydro-4(N,N-dimethylcarbamoyloxy)pyridine (31c) Following the procedure described for 29c, the reduction of 31b (1.17 g, 3.8 mmol) with NaBH₄ (0.58 g, 15.2 mmol) in methanol (15 mL) gave 31c as a liquid (0.65 g, 96%): ¹H NMR (CDCl₃) δ 5.32-5.37 (ca, 1 H), 3.02 (ddd, 2 H, J = 2.7 Hz, J = 3.5 Hz, J = 9.2 Hz), 2.93 (br s, 6 H), 2.65 (dd, 2 H, J = 5.7 Hz, J = 12.3 Hz), 2.30-2.40 (overlapped, 5 H); ¹³C NMR (CDCl₃) δ 154.53, 146.85, 111.04, 52.77, 51.75, 45.02, 36.29, 36.20, 27.74.
1,1-Dimethyl-1,2,5,6-tetrahydro-4(N,N-dimethylcarbamoyloxy)pyridinium Tosylate (32) (PN-236, BM17834) To a solution of 31c (0.63 g, 3.53 mmol) in dry CH$_3$CN (20 mL) was added methyl tosylate (1.316 g, 7.00 mmol). After being stirred at room temperature for 2 h, the reaction mixture was warmed on a steam bath and ether was added. The reaction mixture was then cooled on an ice bath to give a white solid 32 (1.07 g, 83%): mp 159-9.5 °C from CH$_3$CN/ether; IR (KBr) $\nu$max 3032, 3022, 1718, 1190 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 7.72 (d, 2 H, J = 7.9 Hz), 7.14 (d, 2 H, J = 7.9 Hz), 5.33 (br s, 1 H), 4.16 (br d, 2 H, J = 3.0 Hz), 3.78 (t, 2 H, J = 6.5 Hz), 3.41 (s, 6 H), 2.95 (s, 3 H), 2.92 (s, 3 H), 2.56 (br m, 2 H), 2.33 (s, 3 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 153.6, 145.4, 143.8, 139.2, 128.7, 125.7, 106.5, 60.0, 58.7, 51.2, 36.5, 36.3, 23.8, 21.2. Anal. Calcd for C$_{17}$H$_{30}$O$_5$N$_2$S: C, 55.12; H, 7.07; N, 7.56. Found: C, 55.12; H, 7.12; N, 7.53.

2-(4-Hydroxyphenyl)imidazo[1,2-a]pyridine A general procedure (16) was followed in the synthesis of 2-(4-hydroxyphenyl)-imidazo[1,2-a]pyridine hydrobromide from 2-aminopyridine and $\alpha$-bromo-4-hydroxyacetophenone. The resulting salt was suspended in water and excess sodium bicarbonate was added. The mixture was stirred vigorously for 12 h. The product was obtained after filtration and washed with water.

1-Methyl-2-(4-hydroxyphenyl)imidazo[1,2-a]pyridinium Chloride (KC012, BM14306) A general procedure for Quaternization was followed, which included methylation with iodomethane and anion anion exchange with Amberlite resin. Recrystallization from hot acetonitrile gave 72% yield of the desired product: mp 233-235 °C; IR (KBr) $\nu$max 3397, 3073, 3051, 1614, 1504, 1282 cm$^{-1}$; $^1$H NMR (D$_2$O) $\delta$ 8.58 (d, 1 H), 7.99 (s, 1 H), 7.89 (m, 2 H), 7.43 (m, 3 H), 6.93 (d, 2 H). Anal. Calcd for C$_{14}$H$_{13}$ClN$_2$O. 0.25 H$_2$O: C, 63.39; H, 5.13; N, 10.57; Cl, 13.37. Found: C, 62.98; H, 5.12; N, 10.61; Cl, 13.34.
References:


(14) Prepared from 2-(lithiomethyl)-1-methyl-1H-imidazole and ethylene oxide.


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