STUDY OF AMINO–IMINO TAUTOMERISM IN DERIVATIVES OF 2-, 4- AND 6-AMINONICOTINIC ACID

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^{13}C NMR spectra of *p*-nitrobenzoyl 2-, 4-, and 6-aminopyridine-3-carboxylates, their hydrochlorides, trifluoroacetates and 1-benzyl derivatives were studied. As found from the chemical shifts of pyridine carbon atoms C-2, C-4 and C-6, the free bases exist in the amino form whereas hydrochlorides and 1-substituted pyridinium derivatives in the imino form. Trifluoroacetates of the 2- and 6-amino derivatives have structure similar to that of amidiniumcarboxylates (parallel hydrogen bonds and partially ionic character) whereas trifluoroacetate of the 4-amino derivative is structurally close to the corresponding hydrochloride. The found structures were confirmed by ^{1}H NMR and IR spectroscopy.

Most of antivirals are based on nucleoside analogs. Structure–activity studies of cytostatic and antiviral effect of nucleosides led to modification of the base by replacement of the =N– by the =CH– group as realized in the synthesis of deazapurine or deazapyrimidine (pyridine) derivatives[1]. Since in natural nucleosides the heterocyclic nucleus bears an amino group as well as a nitrogen-bound sugar component, the preparation of aminopyridine derivatives substituted in position 1 was of interest. Unlike the purine and pyrimidine nucleosides, the mentioned compounds contain a quaternary nitrogen atom whose presence markedly influences the properties of the molecule. It affects e.g. the transport of the molecule through biological membranes or, due to interaction with enzymes, influences also other parameters that determine behaviour of the molecule in biological systems. It is appropriate to compensate the positive charge of the nucleus by a carboxy group or a similar functionality. Interestingly, 1-substituted 4-aminonicotinic acid exists in nature as a part of the CNS-active alkaloid clitidin[2].

In contrast to 3-amino derivatives of pyridine, the 2- and 4-amino derivatives can exist in two tautomeric forms: in the amino and in the imino form. In free bases the amino form prevails; this fact is explained by loss of aromatic resonance energy in the imino form[3,4]. However, already protonation of 2- and 4-aminopyridines, which takes

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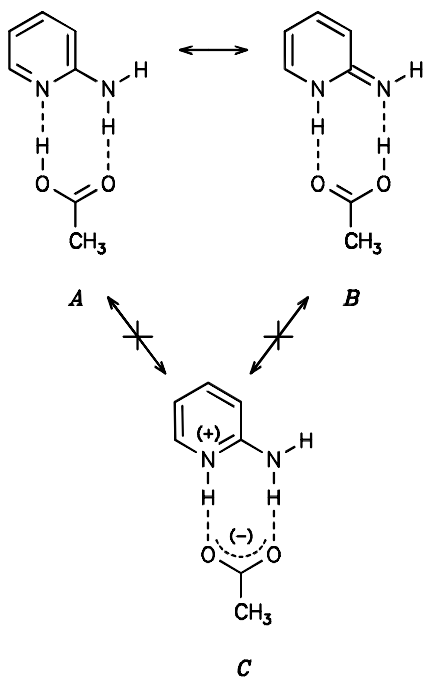
place exclusively at the ring nitrogen, disturbs the aromatic character of the molecule and the compound exists in the imino form: the salt formed is thus not an aminopyridinium but a 1,2-dihydropyridin-2-iminium or 1, 4-dihydropyridin-4-iminium salt[5]. If the 2-aminopyridine in question forms a complex with acetic acid, its structure can be depicted by the limiting formulae (*A*) and (*B*) in Scheme 1 (refs[6,7]). According to quantum chemical calculations, the structure (*C*) in the ground state is unstable and its existence is improbable.

The structure of quaternary 2- and 4-aminopyridinium salts remained unsolved because no suitable method of study has been found so far. Alkylation of 2-aminopyridine with methyl iodide afforded the 1-methyl derivative which upon mild treatment with alkali was converted into 2-imino-1-methyl-1,2-dihydropyridine[8]; this fact is regarded as the only proof of preference of imino form in 1-substituted 2-aminopyridinium salts.

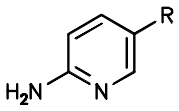
In our present paper we investigate the structure of quaternary salts derived from 2- , 4- and 6-aminopyridines bearing an ester functionality in the position 3. We have found a suitable method utilizing ^{13}C NMR spectroscopy for the proof of structure and character of an amino group, not only in these compounds but also in other aminoazaheterocycles. The method is based on the fact that chemical shifts of the corresponding atoms of the pyridine nucleus in free bases, their salts and 1-substituted compounds



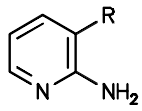
SCHEME 1

vary in the range of 7 ppm in a defined way, according to the character of the amino group (limiting cases are "pure" amino form, $-NH_2$, and "pure" iminium form, $=NH_2^+$).

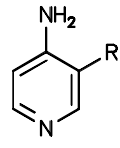
For the study of character of the amino group we have chosen *p*-nitrobenzyl esters of 6- (*Ia*), 2- (*IIa*) and 4-aminonicotinic acid (*IIIa*), their trifluoroacetates *Ib – IIIb*, hydrochlorides *Ic – IIIc* and 1-benzyl derivatives *Id – IIId*. For comparison, we studied the corresponding deaza derivatives, i.e. *p*-nitrobenzyl esters of 4- (*IVa*) and 2-aminobenzoic acid (*Va*) and their hydrochlorides *IVb* and *Vb*, as well as the corresponding deamino derivatives, i.e. *p*-nitrobenzyl ester of nicotinic acid (*VIa*), its hydrochloride *VIb* and 1-benzyl derivative *VIc*.



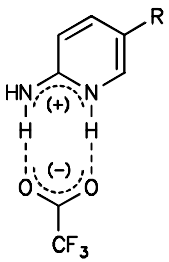
Ia



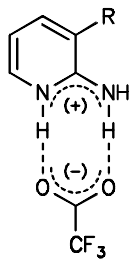
IIa



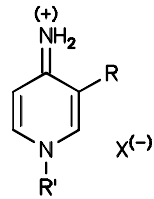
IIIa



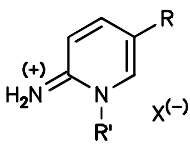
Ib



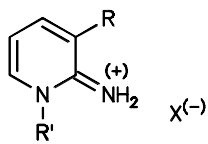
IIb



IIIb, R' = H; X = CF_3COO
IIIc, R' = H; X = Cl
IIId, R' = benzyl; X = Br



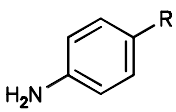
Ic, Id



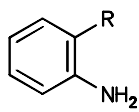
IIc, IId

In formulae *I – III* : R = *p*-nitrobenzyloxycarbonyl
In formulae *Ic, IIc* : R' = H; X = Cl
In formulae *Id, IId* : R' = benzyl; X = Br

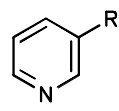
Esters *Ia*, *IIa*, *IVa – VIa* were synthesized[9] by reaction of cesium salt of the appropriate carboxylic acid with *p*-nitrobenzyl bromide. Ester *IIIa* was prepared by reesterification of methyl 4-aminonicotinate with *p*-nitrobenzyl alcohol. Methyl 4-aminonicotinate was synthesized by the following reaction sequence. 3-Methylpyridine 1-oxide[10] was nitrated to give the nitro derivative which was oxidized to 4-nitronicotinic acid 1-oxide[11]. Its silver salt was methylated with methyl iodide[12] and the obtained methyl ester was catalytically hydrogenated. Esters *Ia – VIa* served as starting compounds for the preparation of trifluoroacetates *Ib – IIIb* by treatment with trifluoroacetic acid in acetone; analogously, on reaction with hydrochloric acid we obtained hydrochlorides *Ic – IIIc* and *IVb*. Compounds *Vb* and *VIb* were prepared only in the NMR tube and were not isolated. Benzyl derivatives *Id* and *IId* were obtained by reaction of the corresponding *p*-nitrobenzyl esters *Ia* and *IIa* with benzyl bromide in dimethylformamide at elevated temperature. Since under these conditions the compound *VIa* underwent transesterification, the quaternization leading to compounds *IIId* and *VIc* was performed in dioxane at room temperature.



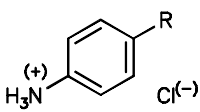
IVa



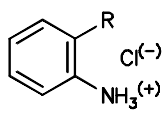
Va



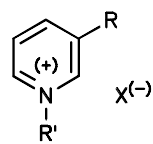
VIa



IVb



Vb



VIb, R' = H; X = Cl

VIc, R' = benzyl; X = Br

In formulae *IV – VI* : R = *p*-nitrobenzyloxycarbonyl

The free bases (esters *Ia – IIIa*) were unequivocally assigned the amino structure on the basis of literature data (vide supra) as well as our spectroscopic studies (vide infra). On the other hand, hydrochlorides *Ic – IIIc* invariably exist in the iminium form.

The best method for determining the structure of quaternary salts proved to be the ^{13}C NMR spectroscopy. The signals of the individual carbon atoms were assigned on the basis of experimental distinction of tertiary and quaternary carbon atoms by the APT (Attached Proton Test) method. The observed chemical shifts of carbon atoms in compounds *I – VI* are given in Table I.

As follows from Table I, the ^{13}C NMR spectra of bases *Ia* – *IIIa* and their hydrochlorides *Ic* – *IIIc* are considerably different, particularly as concerns the carbon atoms C-2, C-4 and C-6 or atoms in the immediate vicinity of the amino group. The differences between the corresponding signals are in the range 3 – 11 ppm. Worth notice is the fact that in the case of 6- and 2-amino derivatives *I* and *II* (compounds of the amidine type) the chemical shifts change evenly in the order base – trifluoroacetate – hydrochloride – benzyl derivative whereas the spectra of compounds *IIIb* – *IIId* are similar to each other but different from that of the base *IIIa*. To assess the magnitude of the effect of the ring nitrogen atom on the chemical shifts, we synthesized esters of 4-aminobenzoic acid *IVa* and *Va* and their respective hydrochlorides *IVb* and *Vb*. As

TABLE I
^{13}C NMR spectra (δ, ppm) of compounds[a] *I* – *VI*

Compound	C-2	C-3	C-4	C-5	C-6	C=O
Ia	151.2	113.2	138.3	108.0	162.7	165.0
Ib	145.5	114.0	140.6	111.2	159.1	163.8
Ic	146.4	114.3	141.9	113.2	156.8	163.2
Id	144.3	116.0	141.3	116.1	155.9	162.8
IIa	159.7	104.4	140.0	112.3	154.5	166.2
IIb	156.1	107.6	143.7	111.9	148.0	164.4
IIc	153.9	110.0	143.5	111.9	146.4	163.4
IId	152.8	112.6	145.8	112.5	146.5	163.6
IIIa	152.6	106.1	155.4	111.0	152.0	166.4
IIIb	141.1	108.1	158.0	112.0	145.4	163.8
IIIc	140.3	106.7	158.4	112.4	144.8	163.9
IIId	141.0	107.1	157.2	113.4	147.4	163.2
IVa[b]	131.7	115.6	131.7	113.1	154.2	165.8
IVb[b]	131.5	120.4	131.5	117.2	148.1	165.5
Va[b]	151.9	108.4	130.8	116.8	134.6	167.0
Vb[b]	144.6	117.3	131.8	123.3	135.2	166.1
VIa	153.7	125.1	136.8	123.8	149.9	164.2
VIb	153.6	127.7	136.0	126.8	144.1	162.1
VIc	153.0	130.6	136.2	128.9	146.2	162.0

[a] *p*-Nitrobenzyl group (compounds *I* – *VI*): 65.0 (CH_2), 123.9 (C-3 and C-5), 128.7 (C-2 and C-6), 144.7 (C-1), 147.5 (C-4). Benzyl group (*Id* – *IIId*): 56.3 (CH_2), 128.0 (C-2 and C-6), 129.0 (C-4), 129.5 (C-3 and C-5), 134.2 (C-1). Benzyl group (*VIc*) 63.9 (CH_2), 129.0 (C-2 and C-6), 129.3 (C-4), 129.5 (C-3 and C-5). [b] The data are given in the order C-2, C-1, C-6, C-5, C-4 and C=O.

shown in Table I, the formation of salts affects considerably not only the shift of the carbon atom bearing the amino group but also the signals of C-3 and C-5 in the heterocycle (4 – 9 ppm). To study the effect of the amino group on the spectral changes due to protonation or quaternization, we prepared model compounds *VI*. Upon protonation (compound *VIb*) or quaternization (compound *VIc*), the spectrum of the nicotinic ester *VIa* also shows changes of only the C-3 and C-5 signals (5 ppm). The C-2 signal is not affected and the C-6 shift relative to the base is greater for the hydrochloride (5 ppm) than for the benzyl derivative (3 ppm). For compound *VIc*, the benzyl methylene signal is shifted 7.6 ppm downfield which indicates a greater positive charge on nitrogen than in the amino derivatives *Id* – *IIId*.

Of interest are the spectra of trifluoroacetates *Ib* and *IIb* whose chemical shifts are located between those of the base and the hydrochloride (Table I). This fact can be explained by the amidinium structure of the studied compounds: they are capable of forming two strong hydrogen bonds between the amidine group and the carboxyl group of trifluoroacetic acid. The aromatic character of the nucleus is thus disturbed only partially because the positive charge is delocalized between the atoms of the amidinium group. Both bonds N–C–N are then almost equivalent (as far as allowed by the asymmetric substitution) and the structure of trifluoroacetates *Ib* and *IIb* can be well described by formulae with delocalized π-electrons. The mentioned facts are in accord with the conclusions of our earlier studies on amidinium carboxylates (see e.g. refs[13,14]). In compound *IIIb* the mentioned parallel hydrogen bonds cannot exist and therefore its spectrum is very similar to that of hydrochloride *IIIc*.

If the base is quaternized, its ^{13}C NMR signals (in compounds *I* – *III*) are invariably located outside the interval given by signals of the base or the hydrochloride (Table I). Since no such shifts were observed on benzylation of a compound without an amino group, this proved unequivocally that 1-substituted derivatives of 2-, 4- or 6-aminonicotinic acid exist in the form of iminium salts.

Table II shows ^{1}H NMR spectra of the compounds synthesized. The proton shifts exhibit relationships similar to those found in the ^{13}C NMR spectra discussed above. Worth notice is the signal of the $=NH_2^+$ protons in compound *IIIb* and particularly *IIIc* where the nonequivalence of the iminium protons due to hydrogen bond to the carbonyl oxygen is indicated by the presence of two sharp singlets ($\Delta\delta$ = 0.81 ppm).

The structure of the studied compounds determined by NMR data has been confirmed also by their IR spectra. The spectra of bases *Ia* – *Va* exhibit bands characteristic of an amino group: two or three vibration bands in the region 3 200 – 3 500 cm^{-1} and a deformation band at about 1 635 cm^{-1} (Table III). In addition to the deformation band, compounds *Ia* – *IIIa* and *VIa* display a strong band at 1 600 – 1 605 cm^{-1} due to skeletal vibrations of the pyridine nucleus[15,16]. This band is also present in the spectra of 1-benzylpyridine derivatives containing an amino group (*Id* – *IIId*) and salts (*Ib* – *IIIb*, *Ic* – *IIIc*). Although in these compounds the band is somewhat weaker and is

shifted to higher wavenumbers (1 605 – 1 612 cm^{-1}), this shift is not so large as to correspond to protonation or quaternization of the pyridine nucleus (ref.[15] reports a hypsochromic shift to 1 631 – 1 647 cm^{-1}; for compound *VIc* we have found 1 630 cm^{-1}, see Table III). This fact, together with appearance of amidinium bands (1 600 – 1 700 cm^{-1}), shows a delocalization of the positive charge, not only in the amidine structures (compounds *I* and *II*) but also in the amidine vinylogs (compounds *III*).

Of diagnostic importance is the stretching vibration band ν(C=O) in the pyridine trifluoroacetates[17,18], since the formation of hydrogen bond reduces the difference be-

TABLE II
^{1}H NMR spectra (δ, ppm; *J*, Hz) of compounds[a] *I* – *VI*

Compound	Chemical shifts					*J*(H,H)			
	H-2	H-4	H-5	H-6	NH_2	4,5	5,4	5,6	6,5
Ia	8.59	7.91	6.50	–	7.01	8.7	8.8	–	–
Ib	8.62	8.12	6.83	–	8.20	8.5	8.7	–	–
Ic	8.63	8.23	7.06	–	8.65	8.6	9.3	–	–
Id	8.92	8.31	7.27	–	[c]	9.4	8.2	–	–
IIa	–	8.15	6.64	8.23	7.20	7.8	7.7	7.3	7.5
IIb	–	8.32	6.87	8.45	8.20	5.5	5.2	8.0	7.9
IIc	–	8.40	6.98	8.68	8.40	5.5	5.0	6.4	7.1
IId	–	8.69	7.14	9.10	[c]	5.0	4.8	4.9	5.5
IIIa	8.78	–	6.70	8.09	7.30	–	–	6.1	–
IIIb	8.91	–	7.04	8.21	8.50[d]	–	–	7.5	8.7
IIIc	8.87	–	7.12	8.23	8.56[e]	–	–	7.1	8.0
IIId	9.18	–	7.10	8.66	[c]	–	–	7.4	–
IVa[b]	7.68	7.68	6.59	–	6.06	8.0	8.6	–	–
IVb[b]	7.87	7.87	6.99	–	8.62	6.9	7.0	–	–
Va[b]	–	7.79	6.54	7.27	6.67	8.0	8.5	6.1	6.0
Vb[b]	–	7.91	7.11	7.52	[c]	8.1	7.9	7.0	7.0
VIa	9.17	8.36	7.61	8.85	–	8.2	7.7	5.9	5.1
VIb	9.32	8.91	8.10	9.08	–	8.1	7.9	6.2	5.1
VIc	9.81	9.04	8.32	9.44	–	8.1	6.4	6.1	6.1

[a] *p*-Nitrobenzyl group (compounds *I* – *VI*): 5.45 s, 2 H (CH_2); 7.80 d, 2 H, *J* = 8.5 (H-2 and H-6); 8.25 d, 2 H, *J* = 8.4 (H-3 and H-5); benzyl group (*Id* – *IIId*, *VIc*): 5.55 s, 2 H (CH_2); 7.20 – 7.45 m, 5 H (H-arom.). [b] The data are given in the order H-2, H-6, H-5, H-4, NH_2, *J*(6,5), *J*(5,6), *J*(5,4), *J*(4,5). [c] Not observed. [d] Another NH_2 signal at 9.0 ppm. [e] Another NH_2 signal at 9.37 ppm.

tween the carbonyl and carboxyl absorption bands. In our case (compounds *Ib* – *IIIb*), however, the situation is more complicated because of the presence of the amino and the ester carbonyl groups. Nevertheless, from the position of the C=O band in the spectrum of trifluoroacetate (1 703 – 1 717 cm^{-1}; thus between ν(COO^-) and ν(C=O); Table III) we can conclude that in the complex aminopyridine–trifluoroacetic acid both electrostatic interaction between the ions and parallel hydrogen bonds participate.

EXPERIMENTAL

The melting points were determined on a Boetius block and are uncorrected. The NMR spectra (δ, ppm; *J*, Hz) were measured on a Gemini-300HC instrument in hexadeuteriodimethyl sulfoxide. Experimental parameters: for ^1H NMR 300.075 MHz, digital resolution 0.3 Hz/point; for ^{13}C NMR 75.462 MHz, digital resolution 0.6 Hz/point; APT technique. The IR spectra were recorded on a Bruker IFS 88 spectrometer in KBr pellets.

TABLE III
Infrared spectra of compounds *I* – *VI*

Compound	ν(NH_2)	δ(NH_2)	ν(C=N)	ν(C=O)
Ia	3 409, 3 315	1 652	1 600	1 603
IIa	3 449, 3 274, 3 216	1 635	1 606	1 698
IIIa	3 481, 3 444, 3 371	1 624	1 605	1 699
IVa	3 468, 3 354, 3 232	1 640	–	1 682
Va	3 475, 3 370	1 618	–	1 688
VIa	–	–	1 605	1 724
Ib	3 322[a]	–	1 607	1 706
IIb	3 361	–	1 607	1 713, 1 681
IIIb	3 396	1 671[a]	1 605	1 717, 1 685
Ic	3 404	1 687[a]	1 610	1 720
IIc	3 383[a]	1 643	1 612	1 709
IIIc	3 393	1 655	1 605	1 714
IVb	3 419	1 632	–	1 723
Id	3 416	1 666	1 601	1 720
IId	3 320[a]	1 650	1 601	1 704
IIId	3 379[a]	1 671	1 605	1 723
VIc	–	–	1 630	1 729

[a] Broad band.

2-Aminonicotinic and trifluoroacetic acids were purchased from Fluka, 6-aminonicotinic acid from Aldrich. Methyl 4-nitronicotinate 1-oxide was obtained from 3-methylpyridine 1-oxide according to a published procedure[10–12].

Methyl 4-Aminopyridine-3-carboxylate

Methyl 4-nitronicotinate 1-oxide (5.7 g, 29 mmol) was hydrogenated in methanol (120 ml) over 10% Pd/C (2.7 g) at atmospheric pressure and 40 °C for 3 h (consumption 2 910 ml, 130 mmol H_2). The catalyst was filtered through a layer of microcrystalline cellulose and washed with methanol (2 × 50 ml). After evaporation of the solvent, the crystalline residue was sublimed at 120 °C/2 kPa to give 1.75 g (40%) of methyl 4-aminopyridine-3-carboxylate, m.p. 174.5 – 175.5 °C. For $C_7H_8N_2O_2$ (152.2) calculated: 55.25% C, 5.29% H, 18.41% N; found: 55.17% C, 5.31% H, 18.01% N. ^{1}H NMR spectrum: 3.82 s, 3 H (OCH_3); 7.15 d, 1 H, *J*(5,6) = 7.4 (H-5); 7.45 bs, 2 H (NH_2); 8.11 d, 1 H, *J*(6,5) = 7.1 (H-6); 8.30 s, 1 H (H-2).

p-Nitrobenzyl Esters *Ia*, *IIa*, *IVa – VIa*. General Procedure[7]

A mixture of the appropriate carboxylic acid (1 mmol), water (10 ml) and cesium carbonate (163 mg, 0.5 mmol) was stirred at room temperature to dissolution (about 2 h). After evaporation of the solvent under diminished pressure and codistillation of the residue with dimethylformamide (3 × 5 ml), the colourless crystalline material was dissolved in anhydrous dimethylformamide (15 ml). *p*-Nitrobenzyl bromide (216 mg, 1 mmol) was added to this solution under vigorous stirring. The reaction mixture was stirred at room temperature overnight, and the dimethylformamide was evaporated under diminished pressure. The residue was codistilled with toluene (6 × 20 ml), mixed with hot acetone, the suspension was filtered and the filtrate was evaporated under diminished pressure. The yellow crystalline residue was crystallized from acetone–ethanol (9 : 1). For yields, elemental analyses and melting points see Table IV.

p-Nitrobenzyl 4-Aminopyridine-3-carboxylate (*IIIa*)

A mixture of methyl 4-aminopyridine-3-carboxylate (110 mg, 0.72 mmol), *p*-nitrobenzyl alcohol (137 mg, 0.89 mmol) and Amberlite GC-120 (H^+ form, 20 mg) was heated at 95 °C and 5 kPa for 17 h. The reaction mixture was filtered and codistilled with toluene (5 × 5 ml). The residue was washed with acetone (–30 °C) and crystallized from acetone–ethanol (9 : 1). For yield, elemental analysis and melting point see Table IV.

Trifluoroacetates *Ib – IIIb*. General Procedure

p-Nitrobenzyl ester *Ia – IIIa* (82 mg, 0.3 mmol) was dissolved in warm mixture of acetone (2 ml) and ethanol (1 ml). Trifluoroacetic acid (23 μl, 34 mg, 0.3 mmol) was then added to the solution and the reaction mixture was stirred at 40 °C for 30 min. Upon cooling, the colourless crystalline product was collected. For yields, melting points and elemental analyses see Table IV.

Hydrochlorides *Ic – IIIc* and *IVb*. General Procedure

p-Nitrobenzyl ester *Ia – IVa* (0.39 mmol) was dissolved in a warm mixture of acetone (2 ml) and methanol (0.5 ml). Hydrochloric acid (0.1 ml) was added to the solution and the colourless crystalline hydrochloride deposited immediately. For physical characteristics and yields see Table IV.

TABLE IV
Characteristic data of compounds *I – VI*

Compound	Formula (M.w.)	M.p., °C Yield, %	Calculated/Found		
			% C	% H	% N
Ia	$C_{13}H_{11}N_3O_4$	226 – 227	57.13	4.06	15.38
	(273.2)	68	56.99	4.10	15.52
Ib	$C_{15}H_{12}F_3N_3O_6$	167 – 168	46.50	3.12	10.85
	(387.2)	85	46.32	3.15	10.53
Ic	$C_{13}H_{12}ClN_3O_4 . 2 H_2O$	180 – 182	45.16	4.66	12.15
	(345.7)	78	44.94	4.15	12.23
Id	$C_{20}H_{18}BrN_3O_4 . H_2O$	224 – 225	51.96	4.36	9.08
	(462.3)	67	51.74	4.32	9.34
IIa	$C_{13}H_{11}N_3O_4$	199 – 200	57.13	4.06	15.38
	(273.2)	60	57.23	4.10	14.92
IIb	$C_{15}H_{12}F_3N_4O_6$	156 – 159	46.50	3.12	10.85
	(387.2)	50	46.55	3.22	10.50
IIc	$C_{13}H_{12}ClN_3O_4$	174 – 177	50.48	3.91	13.59
	(309.7)	43	50.47	4.13	13.59
IId	$C_{20}H_{18}BrN_3O_4$	206 – 209	54.17	4.09	9.48
	(444.3)	56	54.09	3.89	9.81
IIIa	$C_{13}H_{11}N_3O_4 . 0.5 H_2O$	171 – 172	55.27	4.25	14.88
	(282.2)	50	54.92	4.51	14.41
IIIb	$C_{15}H_{12}F_3N_3O_6$	155 – 158	46.50	3.12	10.85
	(387.2)	74	46.44	2.95	10.40
IIIc	$C_{13}H_{12}ClN_3O_4 . 1.5 H_2O$	215 – 216	46.37	4.45	12.48
	(336.7)	85	46.78	3.99	12.31
IIId	$C_{20}H_{18}BrN_3O_4$	226 – 228	54.17	4.09	9.48
	(444.3)	[a]	53.89	3.94	9.10
IVa	$C_{14}H_{12}N_2O_4 . 0.5 H_2O$	124 – 125	61.75	4.44	10.29
	(281.3)	55	61.42	4.76	9.94
IVb	$C_{14}H_{13}ClN_2O_4$	150 – 152	54.54	4.25	9.09
	(308.8)	82	54.78	4.41	8.86
Va	$C_{14}H_{12}N_2O_4$	127 – 129	61.75	4.44	10.29
	(272.3)	64	61.51	4.83	10.15
VIa	$C_{13}H_{10}N_2O_4$	137 – 138	60.47	3.90	10.85
	(258.2)	62	60.26	3.62	10.57
VIc	$C_{20}H_{17}N_2O_4$	180 – 182	55.96	3.91	6.53
	(429.3)	47	55.58	3.90	6.12

[a] Quantitative yield.

1-Benzyl-5- (*Id*) and 1-Benzyl-3-(*p*-nitrobenzyloxycarbonyl)-1,2-dihydropyridin-2-iminium Bromide (*IId*)

Benzyl bromide (73 mg, 0.43 mmol) was added in portions to a solution of compound *Ia* or *IIa* (73 mg, 0.27 mmol) in anhydrous dimethylformamide (2 ml) and the mixture was heated at 70 °C for 6 h. The solvent was evaporated under diminished pressure and the residue was codistilled with toluene (6 × 5 ml). The solid residue was washed with ether and dried. For physical characteristics and yields see Table IV.

1-Benzyl-3-(*p*-nitrobenzyloxycarbonyl)-1,4-dihydropyridin-4-iminium Bromide (*IIId*) and 1-Benzyl-3-(*p*-nitrobenzyloxycarbonyl)pyridinium Bromide (*VIc*)

Benzyl bromide (85 mg, 0.5 mmol) was added to a solution of compound *IIIa* or *VIa* (0.27 mmol) in dry dioxane (3 ml) and the reaction mixture was set aside at ambient temperature for 10 days. The deposited colourless crystals were collected and dried. For melting points and elemental analyses of the products see Table IV.

1-Benzyl-3-benzyloxycarbonylpyridinium Bromide

Benzyl bromide (143 mg, 0.84 mmol) was added dropwise to a solution of compound *VIa* (100 mg, 0.39 mmol) in anhydrous dimethylformamide (10 ml) and the reaction mixture was heated at 70 °C for 14 h. The solvent was evaporated under diminished pressure and the residue was codistilled with toluene (6 × 5 ml). The solid residue was dissolved in acetone (5 ml), filtered and *tert*-butyl methyl ether (15 ml) was added. The deposited crystalline product was collected on filter and dried; yield 78 mg (52%) of the title compound, m.p. 182.5 – 184 °C. ^{1}H NMR spectrum: 5.48 s, 2 H (OCH_2); 6.06 s, 2 H (N^+–CH_2); 7.34 – 7.66 m, 10 H (H-arom.); 8.32 dd, 1 H, *J*(5,4) = 6.4, *J*(5,6) = 6.1 (H-5); 9.05 d, 1 H, *J*(4,5) = 8.1 (H-4); 9.44 d, 1 H, *J*(6,5) = 6.0 (H-6); 9.81 s, 1 H (H-2). ^{13}C NMR spectrum: 63.9 (N^+–CH_2), 68.4 (OCH_2), 128.7 (2 C) + 129.0 (2 C) + 129.3 (1 C) + 129.5 (2 C) + 129.7 (2 C) + 129.9 (1 C) (C-arom.); 130.3 (C-5), 130.6 (C-3), 134.4 + 135.5 (C′-1 and C″-1), 136.2 (C-4), 146.2 (C-6), 152.0 (C-2), 161.9 (C=O).

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