Synthesis of *N*-(Substituted Phenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridines as Potential Nonsteroidal Anti-inflammatory Agents

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Received February 1, 2000

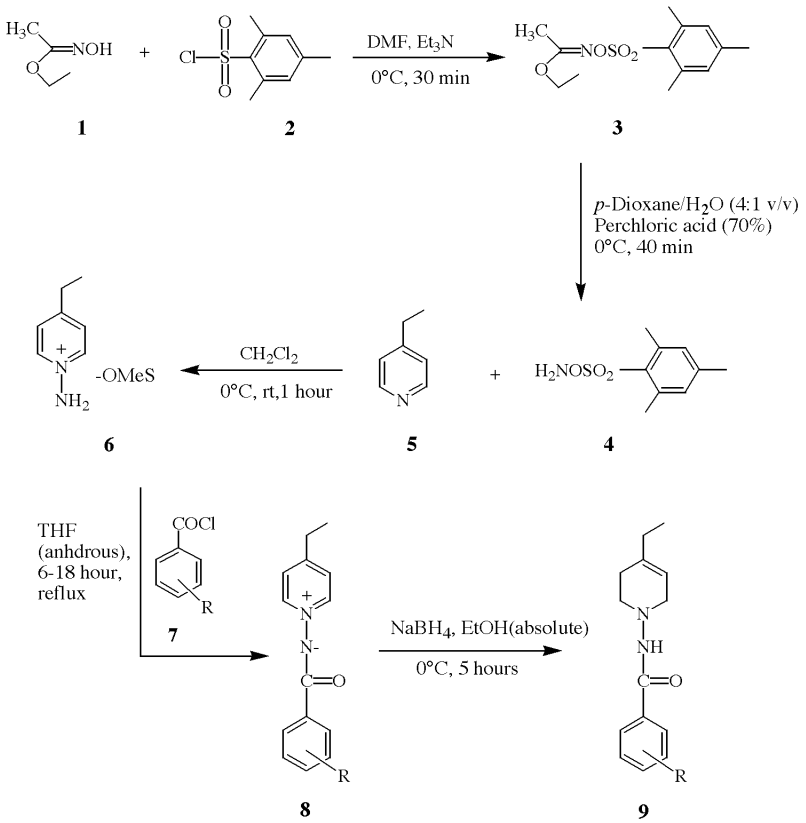
Fourteen novel *N*-(substituted phenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridines **9** were synthesized in fair to good yields. 4-Ethylpyridine **5** reacted with *O*-mesitylenesulfonylhydroxylamine (*O*-MSH) **4** to furnish *N*-amino-4-ethylpyridinium mesitylenesulfonate **6**. The reaction of **6** with substituted acid chlorides **7** gave the stable crystalline pyridinium ylides **8a**-**8n**. A sodium borohydride reduction of **8** in absolute ethanol furnished the target compounds *N*-(substituted phenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridines **9a**-**9n**.

J. Heterocyclic Chem., **38**, 69 (2001).

Compounds consisting of a reduced pyridine ring system are known to possess a variety of biological activities [1-4]. Earlier work [5-7] by Knaus and co-workers indicated the synthesis of a series of *N*-(carbonylamino)-1,2,3,6-tetrahydropyridines (THPs) which showed that anti-inflammatory, analgesic, and hyperglycemic activities with no observed toxicities after preliminary pharmacological tests. It became obvious that the pharmacological activities of the THP derivatives depended greatly on the nature of the substituents on the THP ring structure [8,9]. Previously, toxicological evaluation of 1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) and its analogs by Fries *et al.*, indicated that less or no toxicity was observed when alkyl groups were introduced on the tetrahydropyridine ring [10].

Several *N*-[phenyl(pyridyl)carbonylamino]-1,2,3,6-tetrahydropyridines were synthesized and reported [8,9,11]. Nucleophilic attack of pyridine derivatives on

Scheme 1



1 **2** **3** **4** **5** **6** **7** **8** **9**

1-chloro-2,4-dinitrobenzene resulted in the formation of the 2,4-dinitrophenyl pyridinium chlorides. Benzoyl hydrazide and/or pyridyl hydrazides reacted with pyridinium chlorides furnishing the 2,4-dinitroaniline derivatives, which were subsequently hydrolyzed to yield the pyridinium ylides. Sodium borohydride reduction of the ylides afforded the 1,2,3,6-tetrahydropyridine analogs.

In a recent approach the carbonyl group of the THPs was replaced with a sulfonyl group producing new derivatives with significantly enhanced anti-inflammatory activities [12]. Other previous reports indicated that the alkyl groups on the tetrahydropyridine ring system possessed reasonably higher anti-inflammatory activity [8,9,11].

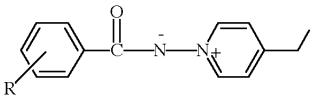
In our current report, the tetrahydropyridines were prepared using an alternative method of incorporating electron-donating ethyl groups on the THP ring structure. In addition, several substituents that tend to exert electronic, lipophilic and steric influences on the tetrahydropyridine analogs were introduced on the phenyl ring. These changes in turn are expected to influence the biological activities of the tetrahydropyridine derivatives. Using a similar method, electron withdrawing groups were introduced on the tetrahydropyridine ring system and their anti-inflammatory activities were tested [13,14].

The synthetic pathway is outlined in Scheme 1. The *O*-mesitylenesulfonylhydroxylamine (MSH) **4** was used to prepare the *N*-amine salt as an aminating agent [15]. Mesitylene sulfonylchloride **2** was added with stirring to a solution of ethyl acetohydroxamate **1** and triethylamine in dimethylforamide at 0 °C. After one hour, the reaction mixture was poured into ice/water to give ethyl *O*-mesitylenesulfonylacetohydroxamate **3** in 92% yield. Stirring the mixture of **3** in *p*–dioxane:water (4:1 v/v) with 70% perchloric acid and allowing them to react for 40 minutes, gave white crystals of MSH **4** in 79% yield. 4-Ethylpyridine **5** was reacted with MSH **4** in dichloromethane to produce *N*-amino-4-ethyl pyridinium mesitylenesulfonate **6**. Reaction of **6** with substituted acid chlorides **7** in anhydrous tetrahydrofuran at 70 °C gave stable ylides **8a**-**8n**. Sodium borohydride reduction of **8** in absolute ethanol furnished the target compounds *N*-(substituted phenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridines **9a**-**9n**.

The results of the synthesis of the pyridinium ylides **8** and the corresponding 1,2,3,6-tetrahydropyridines **9** are presented in Table 1 and Table 2. Scheme 2 shows the numbering of the pyridinium ylides **8** and tetrahydropyridines **9** systems. The tetrahydropyridines **9** show typical ^{1}H nmr absorption at approximately δ 3.1 as a multiplet which correspond to C_2-protons coupled to the C_3-protons. Since C_2–protons are directly connected to N-atom, C_3–protons are expected to absorb at around δ 2.2 when compared to C_2–protons. C_6–protons generally absorb at δ 3.5. Since C_6–protons are connected with both N-atom and vinyl group, they are further down field-shifted. The broad singlet at around δ 3.5 was assigned to C_6–protons which have very weak coupling with the C_5-proton. The vinyl proton of the tetrahydropyridines on C_5–proton was typically observed at δ 5.3. The infrared (ir) spectrum (potassium bromide) confirmed the presence of structural features in targeted compounds which typically display absorption approximately at ν 3200 (NH), 1640 (CO) cm^{-1}. The pharmacological evaluation of the compounds for anti-inflammatory and analgesic activity is underway.

Table 1

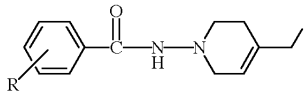
Pyridinium Ylides **8a-8n** synthetic data



	R	mp (°C)	Yield (%)	F.W.
8a	4-OCH_3	117-119	81	256.31
8b	3-OCH_3	138-140	49	256.31
8c	3-CF_3	120-122	28	294.28
8d	4-CH_3	164-166	12	240.31
8e	4-C_2H_5	151-153	72	254.34
8f	4-*n*Bu	174-176	33	282.39
8g	4-*t* Bu	194-196	66	282.39
8h	2-CH_3	136-138	53	240.31
8i	4-F	182-184	22	244.27
8j	3-F	130-132	48	244.27
8k	2-F	168-170	49	244.27
8l	4-Cl	189-191	42	260.73
8m	4-Br	169-171	26	305.18
8n	3,5-Cl_2	141-143	35	295.17

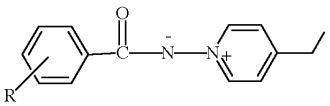
Table 2

1,2,3,6-Tetrahydropyridines **9a-9n** synthetic data



	R	mp (°C)	Yield (%)	F.W.
9a	4-OCH_3	167-169	32	260.34
9b	3-OCH_3	133-135	32	260.34
9c	3-CF_3	119-121	44	298.31
9d	4-CH_3	149-151	30	244.34
9e	4-C_2H_5	143-145	26	258.37
9f	4-*n*Bu	125-127	64	286.42
9g	4-*t* Bu	158-160	52	286.42
9h	2-CH_3	157-159	78	244.34
9i	4-F	164-166	31	248.30
9j	3-F	142-144	33	248.30
9k	2-F	125-127	38	248.30
9l	4-Cl	180-182	64	264.76
9m	4-Br	187-189	36	309.21
9n	3,5-Cl_2	120-122	83	299.20

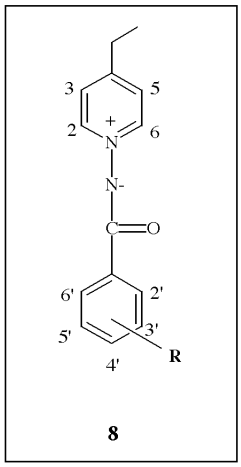
Elemental Analysis of the Pyridinium Ylides (**8a-8n**)



Compound	R	Molecular Formula	MW	%C	%H	%N	Elemental Analysis
8a	4-OCH_3	$C_{15}H_{16}N_2O_2 \cdot 0.25\ H_2O$	260.81	69.08	6.38	10.74	Calcd.
				69.17	6.41	10.51	Found
8b	3-OCH_3	$C_{15}H_{16}N_2O_4 \cdot 0.125\ H_2O$	258.56	69.68	6.33	10.83	Calcd.
				69.69	6.33	10.81	Found
8c	3-CF_3	$C_{15}H_{13}N_2OF_3 \cdot 0.125H_2O$	296.53	60.30	4.55	9.38	Calcd.
				60.09	4.66	9.01	Found
8d	4-CH_3	$C_{15}H_{16}N_2O$	240.31	74.97	6.71	11.66	Calcd.
				74.72	6.82	11.34	Found
8e	4-C_2H_5	$C_{16}H_{18}N_2O$	254.33	75.56	7.13	11.01	Calcd.
				75.56	7.25	10.86	Found
8f	4-*n*-Bu	$C_{18}H_{22}N_2O$	282.39	76.56	7.85	9.92	Calcd.
				76.97	8.04	9.79	Found
8g	4-*t*-Bu	$C_{18}H_{22}N_2O \cdot 0.25H_2O$	286.89	75.36	7.91	9.76	Calcd.
				75.35	8.03	9.69	Found
8h	2-CH_3	$C_{15}H_{16}N_2O$	240.31	74.97	6.71	11.66	Calcd.
				75.21	6.82	11.55	Found
8i	4-F	$C_{14}H_{13}N_2OF$	244.27	68.84	5.36	11.47	Calcd.
				68.69	5.46	11.37	Found
8j	3-F	$C_{14}H_{13}N_2OF$	244.27	68.84	5.36	11.47	Calcd.
				68.67	5.45	11.34	Found
8k	2-F	$C_{14}H_{13}N_2OF \cdot 0.125\ H_2O$	246.52	68.21	5.42	11.36	Calcd.
				68.14	5.39	11.22	Found
8l	4-Cl	$C_{14}H_{13}N_2OCl$	265.23	63.40	5.13	10.56	Calcd.
				63.08	4.97	10.41	Found
8m	4-Br	$C_{14}H_{13}N_2OBr \cdot 0.5\ H_2O$	314.19	53.52	4.49	8.92	Calcd.
				53.67	4.22	8.94	Found
8n	3,5-Cl_2	$C_{14}H_{12}N_2OCl_2 \cdot 0.25H_2O$	299.62	56.11	4.20	9.35	Calcd.
				56.22	4.03	9.35	Found

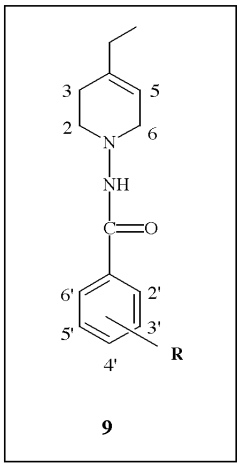
Scheme 2

Structure and numbering of *N*-(Substituted Phenylcarbonylamino)-4-ethylpyridinium ylides (**8a-8n**) and *N*-(Substituted Phenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridines (**9a-9n**).



8

N-(Substituted Phenylcarbonylamino)-4-ethylpyridinium ylide (**8a-8n**)



9

N-(Substituted Phenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridines (**9a-9n**)

EXPERIMENTAL

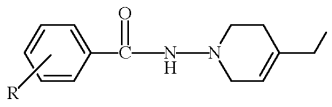
Melting points were determined on a Mettler Toledo Type Fp 62 Melting Point Apparatus and were uncorrected. Infrared spectra were recorded on a Perkin-Elmer FTIR 1430 spectrophotometer, using KBr pellets. ^{1}H-nmr spectra were obtained with a Brucker HX-300 spectrometer and the chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane as an internal standard. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee. Silica gel (Merck, 250-400 mesh) was used for flash column chromatographic separations. The homogeneity of products and intermediates was monitored by TLC on Merck 60F-254 plates, with visualization under UV light. All the solvents and chemicals were purchased from Fisher Scientific Company (Orlando, Florida) and Aldrich Chemical Company (Milwaukee, Wisconsin).

General Procedure A.

N-Amino-4-ethylpyridinium Mesitylenesulfonate (**6**).

To an ice-cold solution of 4-ethyl pyridine (3.12 g, 29.11 mmoles) in dichloromethane (10 ml) was added dropwise a solution of *O*-MSH (*O*-mesitylene sulfonyl hydroxylamine, **4**,

Elemental Analysis of the Tetrahydropyridine (**9a-9n**)



Compound	R	Molecular Formula	MW	Elemental Analysis %C	%H	%N	
9a	4-OCH_3	$C_{15}H_{20}N_2O_2$.	260.34	69.20	7.74	10.76	Calcd.
				69.18	7.90	10.54	Found
9b	3-OCH_3	$C_{15}H_{20}N_2O_2$	260.34	69.20	7.74	10.76	Calcd.
				69.40	7.80	10.75	Found
9c	3-CF_3	$C_{15}H_{17}N_2OF_3$· 0.125H_2O	302.81	59.94	5.78	9.32	Calcd.
				59.69	5.80	9.27	Found
9d	4-CH_3	$C_{15}H_{20}N_2O$	240.31	73.74	8.25	11.46	Calcd.
				73.73	8.46	11.45	Found
9e	4-C_2H_5	$C_{17}H_{25}N_2O$	258.37	74.38	8.58	10.84	Calcd.
				74.65	8.66	10.85	Found
9f	4-*n*-Bu	$C_{18}H_{26}N_2O$	286.42	75.48	9.15	9.78	Calcd.
				75.78	9.33	9.73	Found
9g	4-*t*-Bu	$C_{18}H_{26}N_2O$	286.42	75.48	9.15	9.78	Calcd.
				75.38	9.31	9.77	Found
9h	2-CH_3	$C_{15}H_{20}N_2O$	244.34	73.74	8.25	11.46	Calcd.
				73.40	8.26	11.34	Found
9i	4-F	$C_{14}H_{17}N_2OF$	248.30	67.72	6.90	11.28	Calcd.
				67.47	7.00	11.16	Found
9j	3-F	$C_{14}H_{17}N_2OF$	248.30	67.72	6.90	11.28	Calcd.
				67.45	7.08	11.23	Found
9k	2-F	$C_{14}H_{17}N_2OF$	248.30	67.72	6.90	11.28	Calcd.
				67.79	6.99	11.21	Found
9l	4-Cl	$C_{14}H_{17}N_2OCl$	264.76	63.51	6.47	10.58	Calcd.
				63.92	6.61	10.68	Found
9m	4-Br	$C_{14}H_{17}N_2OBr$	309.21	54.38	5.54	9.06	Calcd.
				54.26	5.64	8.86	Found
9n	3,5-Cl_2	$C_{14}H_{12}N_2OCl_2$· 0.5H_2O	308.21	54.56	5.56	9.09	Calcd.
				54.89	5.38	9.07	Found

6.26 g, 29.11 mmoles) in dichloromethane. The resulting mixture was stirred in an ice bath for 30 minutes, stirred at room temperature for 20 minutes and excess ether was added. A dark brown oil weighing 5.14 g was extracted (57% yield). This product, **6**, was used for the next step without further purification. 1H nmr (deuteriochloroform): δ 1.19 (t, J = 7.6 Hz, 3H, CH_2CH_3), 2.15 (s, 3H, CH_3), 2.49 (s, 6H, CH_3 x 2), 2.87 (q, J = 7.6 Hz, 2H, CH_2CH_3), 4.01 (br s, 2H, NH_2), 6.74 (s, 2H, phenyl protons), 7.82-7.91 (dd, J = 5.8, 5.8 Hz, 2H, pyridinium protons), 8.66-8.80 (dd, J = 5.8, 5.8 Hz, 2H, pyridinium protons).

General Procedure B.

N-(4-Methoxyphenylcarbonylimino)-4-ethylpyridinium Ylide (**8a**).

To an ice-cold solution of *N*-amino-4-ethylpyridinium salt **6** (7.5 g, 23.3 mmoles) in anhydrous tetrahydrofuran (100 ml) was added *para*-anisoyl chloride (11.9 g, 69.9 mmoles) dropwise via a syringe. The reaction was allowed to reflux for 24 hours at 70 °C. After cooling to room temperature, the reaction was quenched by adding 40 ml of a saturated aqueous sodium bicarbonate solution. The mixture was shaken repeatedly in a 500 ml separatory funnel and allowed to stand for a few minutes. The solution was extracted with chloroform (3 x 90 ml). Drying over magnesium sulfate, filtration and removal of solvent *in vacuo* gave a yellowish semi-crystal residue. This residue was crystallized from hexane/ether (10:1, v/v) to afford 4.8 g (81%) of off-white crystals, mp 117-119 °C. The other derivatives were similarly prepared and purified. ir (potassium bromide): ν 1605 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.25 (t, J = 7.8 Hz, 3H, CH_2CH_3), 2.80-2.88 (q, J = 7.8 Hz, 2H, CH_2CH_3), 3.80 (s, 3H, OCH_3), 6.90 (d, J = 8.8 Hz, 2H, phenyl protons), 7.45 (d, J = 6.8 Hz, 2H, C_3, C_5-H), 8.10 (d, J = 8.8 Hz, 2H, phenyl protons), 8.62 (d, J = 6.8 Hz, 2H, C_2, C_6-H).

Anal. Calcd. for $C_{15}H_{16}N_2O_2$•0.25H_2O: C, 69.08; H, 6.38; N, 10.74. Found: C, 69.17; H, 6.41; N, 10.51.

N-(3-Methoxyphenylcarbonylimino)-4-ethylpyridinium Ylide (**8b**).

The compound **8b** was obtained following General Procedure B as off-white needles, 393 mg (49%), mp 138-140 °C; ir (potassium bromide): ν 1686 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.30 (t, J = 7.8 Hz, 3H, CH_2CH_3), 2.78-2.87 (q, J = 7.8 Hz, 2H, CH_2CH_3), 3.85 (s, 3H, CH_3), 6.94 (m, 1H, phenyl proton), 7.24-7.31 (m, 1H, phenyl proton), 7.44 (d, J = 6.8 Hz, 2H, C_3, C_5-H), 7.74-7.69 (m, 2H, phenyl protons), 8.61 (d, J = 6.8 Hz, 2H, C_2, C_6-H).

Anal. Calcd. for $C_{15}H_{16}N_2O_2$•0.125H_2O: C, 69.68; H, 6.33; N, 10.83. Found: C, 69.69; H, 6.33; N, 10.81.

N-(3-Trifluoromethylphenylcarbonylimino)-4-ethylpyridinium Ylide (**8c**).

The compound **8c** was obtained following General Procedure B using 3 equivalents of 3-trifluoromethyl benzoylchloride to furnish ivory crystals in 28% yield, mp 120-122 °C; ir (potassium bromide): ν 1613 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.38 (t, J = 7.8 Hz, 3H, CH_2CH_3), 2.90 (q, J = 7.8 Hz, 2H, CH_2CH_3), 7.55 (d, J = 6.8 Hz, 3H, phenyl protons), 7.70 (d, J = 7.7 Hz, 1H, $C_{2'}$-H), 8.40 (d, J = 6.8 Hz, 2H, C_2, C_6-H), 8.71 (d, J = 6.8 Hz, 2H, C_2, C_6-H).

Anal. Calcd. for $C_{15}H_{13}N_2OF_3$•0.125H_2O: C, 60.30; H, 4.55; N, 9.38. Found: C, 60.09; H, 4.66; N, 9.01.

N-(4-Methylphenylcarbonylimino)-4-ethylpyridinium Ylide (**8d**).

The compound **8d** was obtained following General Procedure B. The product was recrystallized in 100% ethyl acetate and obtained as a solid, 12% yield, mp 164-166 °C; ir (potassium bromide): 1585 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.35 (t, J = 7.8 Hz, 3H, CH_2CH_3), 2.40 (s, 3H, CH_3), 2.85 (q, J = 7.8 Hz, 2H, CH_2CH_3), 7.20 (d, J = 7.5 Hz, 2H, phenyl protons), 7.45 (d, J = 7.5 Hz, 2H, C_3, C_5-H), 8.05 (d, J = 7.5 Hz, 2H, phenyl protons), 8.60 (d, J = 7.5 Hz, 2H, C_2, C_6-H).

Anal. Calcd. for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66. Found: C, 74.72; H, 6.82; N, 11.34.

N-(4-Ethylphenylcarbonylimino)-4-ethylpyridinium Ylide (**8e**).

The compound **8e** was obtained following General Procedure B using 3 equivalents of 4-ethyl benzoylchloride. The resulting crude compound was purified on a column of silica-gel and the eluent ethyl acetate:methanol (9:1 v/v, 1,000 ml) furnished **8e** as white crystals in 72% yield, mp 151-153 °C; ir (potassium bromide): ν 1591 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.90 (t, J = 7.3 Hz, 3H, CH_2CH_3), 1.03 (t, J = 7.8 Hz, 3H, CH_2CH_3), 2.63-2.72 (q, J = 7.3 Hz, 2H, CH_2CH_3), 2.80-2.88 (q, J = 7.8 Hz, 2H, CH_2CH_3), 6.86 (d, J = 8.3 Hz, 2H, $C_{2'}$ & $C_{6'}$-H), 7.46 (d, J = 6.8 Hz, 2H, C_3, C_5-H), 8.05 (d, J = 8.3 Hz, 2H, $C_{3'}$, $C_{5'}$-H), 8.63 (d, J = 6.8 Hz, 2H, C_2, C_6-H).

Anal. Calcd. for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13; N, 11.01. Found: C, 75.56; H, 7.25; N, 10.86.

N-(4-*n*-Butylphenylcarbonylimino)-4-ethylpyridinium Ylide (**8f**).

The compound **8f** was obtained following General Procedure B by using 3 equivalents of 4-*n*-butyl benzoylchloride. The resulting crude mixture was recrystallized in 100% ethyl acetate to give 1.1 g (33% yield) of white crystals, mp 174-176 °C; ir (potassium bromide): ν 1593 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.92 (t, J = 7.6 Hz, 3H, CH_2CH_3), 1.34 (m, 5H, $CH_2CH_2CH_2CH_3$), 1.60-1.70 (m, 2H, $CH_2CH_2CH_2CH_3$), 2.65 (t, J = 7.6 Hz, 2H, $CH_2CH_2CH_2CH_3$), 2.86 (q, J = 7.6 Hz, 2H, -CH_2CH_3), 7.23 (d, J = 8.3 Hz, $C_{3'}$, $C_{5'}$-H), 7.45 (d, J = 6.8 Hz, 2H, C_3, C_5-H), 8.05 (d, J = 8.3 Hz, 2H, $C_{2'}$, $C_{6'}$-H), 8.61 (d, J = 6.8 Hz, 2H, C_2, C_6-H).

Anal. Calcd. for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92. Found: C, 76.97; H, 8.04; N, 9.79.

N-(4-*t*-Butylphenylcarbonylimino)-4-ethylpyridinium Ylide (**8g**).

The compound **8g** was obtained following General Procedure B by using 3 equivalents of 4-*t*-butylbenzoyl chloride. The resulting crude mixture was recrystallized in 100% ethyl acetate to give a white compound, 66% yield, mp 194-196 °C; ir (potassium bromide): ν 1588 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.30 (t, J = 7.8 Hz, 3H, CH_2CH_3), 1.34 (s, 9H, CH_3 x 3), 2.79-2.88 (q, J = 7.8 Hz, 2H, CH_2CH_3), 7.38 (d, J = 7.8 Hz, $C_{3'}$, $C_{5'}$-H), 7.43 (d, J = 7.3 Hz, C_3, C_5-H), 8.03 (d, J = 7.8 Hz, $C_{2'}$, $C_{6'}$-H), 8.58 (d, J = 7.3 Hz, C_2, C_6-H).

Anal. Calcd. for $C_{18}H_{22}N_2O$•0.25H_2O: C, 75.36; H, 7.91; N, 9.76. Found: C, 75.35; H, 8.03; N, 9.69.

N-(2-Methylphenylcarbonylimino)-4-ethylpyridinium Ylide (**8h**).

The compound **8h** was obtained following General Procedure B by using 3 equivalents of 2-methyl benzoylchloride to give an ivory compound in 53% yield, mp 136-138 °C; ir (potassium bromide): ν 1581 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.32 (t, J = 7.8 Hz, 3H, CH_2CH_3), 2.55 (s, 3H, CH_3), 2.78-2.87 (q, J = 7.8 , 7.8 Hz, 2H, CH_2CH_3), 7.20 (m, 3H, $C_{3'}$, $C_{4'}$, $C_{5'}$-H), 7.45 (d, J = 6.8 Hz, 2H, C_3, C_5-H), 7.65 (m, 1H, $C_{6'}$-H), 8.64 (d, J = 6.8 Hz, 2H, C_2, C_6-H).

Anal. Calcd. for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66. Found: C, 75.21; H, 6.82; N, 11.55.

N-(4-Fluorophenylcarbonylimino)-4-ethylpyridinium Ylide (**8i**).

The compound **8i** was obtained following General Procedure B by using 3 equivalents of 4-fluorobenzoylchloride. Recrystallization using 100% ethyl acetate gave a white needle-like compound in 22% yield, mp 182-184 °C; ir (potassium bromide): ν 1602 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.32 (t, J = 7.8 Hz, 3H, CH_2CH_3), 2.78-2.87 (q, J = 7.8 Hz, 2H, CH_2CH_3), 7.01-7.07 (m, 2H, phenyl protons), 7.44 (d, J = 6.8 Hz, 2H, C_3, C_5-H), 8.09-8.15 (m, 2H, phenyl protons), 8.59 (d, J = 6.8 Hz, 2H, C_2, C_6-H).

Anal. Calcd. for $C_{14}H_{13}N_2OF$: C, 68.84; H, 5.36; N, 11.47. Found: C, 68.89; H, 5.46; N, 11.37.

N-(3-Fluorophenylcarbonylimino)-4-ethylpyridinium Ylide (**8j**).

The compound **8j** was obtained following General Procedure by using 3 equivalents of 3-fluorobenzoylchloride with ethyl acetate:methanol (9:1,v/v) as an eluent for column chromatography followed by recrystallization with 100% ethyl acetate to give ivory crystals in 85% yield, mp 130-132 °C; ir (potassium bromide): ν 1689 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.29 (t, J = 7.8 Hz, 3H, CH_2CH_3), 2.78-2.87 (q, J = 7.8 Hz, 2H, CH_2CH_3), 7.20-7.38 (m, 3H, $C_{4'}$, $C_{5'}$, $C_{6'}$-H), 7.83 (d, J = 6.8 Hz, 2H, C_3, C_5-H), 7.95 (d, J = 7.3 Hz, 1H, $C_{2'}$-H), 8.90 (d, J = 6.8 Hz, 2H, C_2, C_6-H).

Anal. Calcd. for $C_{14}H_{13}N_2OF$: C, 68.84; H, 5.36; N, 11.47. Found: C, 68.67; H, 5.45; N, 11.34.

N-(2-Fluorophenylcarbonylimino)-4-ethylpyridinium Ylide (**8k**).

The compound **8k** was obtained following General Procedure B by using 3 equivalents of 2-fluorobenzoylchloride to give a white compound in 49% yield, mp 168-170 °C; ir (potassium bromide): ν 1600 (CO) cm^{-1}; ^1H nmr (deuteriumchloroform): δ 1.28 (t, J = 7.8 Hz, 3H, CH_2CH_3), 2.78-2.86 (q, J = 7.8 Hz, 2H, CH_2CH_3), 7.02-7.17 (m, 3H, phenyl protons), 7.50 (d, J = 6.8 Hz, 2H, C_3, C_5-H), 7.82-7.90 (dd, J = 6.9 Hz, 1H, phenyl proton), 8.62 (d, J = 6.8 Hz, 2H, C_2, C_6-H).

Anal. Calcd. for $C_{14}H_{13}N_2OF$•0.125H_2O: C, 68.21; H, 5.42; N, 11.36. Found: C, 68.14; H, 5.39; N, 11.22.

N-(4-Chlorophenylcarbonylimino)-4-ethylpyridinium Ylides (**8l**).

The compound **8l** was obtained following General Procedure B by using 3 equivalents of 4-chlorobenzoylchloride. Recrystallization under 100% ethyl acetate gave an ivory compound in 42% yield, mp 189-191 °C; ir (potassium bromide): ν 1596 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.26 (t, J = 7.5 Hz, 3H, CH_2CH_3), 2.74-2.82 (q, J = 7.5 Hz, 2H, CH_2CH_3), 7.25 (d, J = 8.4 Hz, 2H, phenyl protons), 7.45 (d, J = 6.6 Hz, 2H, C_3, C_5-H), 7.97 (d, J = 8.4 Hz, 2H, phenyl protons), 8.53 (d, J = 6.6 Hz, 2H, C_2, C_6-H).

Anal. Calcd. for $C_{14}H_{13}N_2OCl$: C, 63.40; H, 5.13; N, 10.56. Found: C, 63.08; H, 4.97; N, 10.41.

N-(4-Bromophenylcarbonylimino)-4-ethylpyridinium Ylides (**8m**).

The compound **8m** was obtained following General Procedure B by using 3 equivalents of 4-bromobenzoylchloride. The resulting crude product was purified on a column of silica gel with ethyl acetate:methanol (9:1, v/v, 1,000 ml) eluent to give a white compound in 26% yield, mp 169-171 °C; ir (potassium bromide): ν 1595 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.29 (t, J = 7.8 Hz, 3H, CH_2CH_3), 2.79-2.87 (q, J = 7.3 ,7.8 Hz, 2H, CH_2CH_3), 7.45-7.55 (m, 4H, phenyl protons, C_3, C_5-H), 8.20 (d, J = 8.7 Hz, 2H, phenyl protons), 8.63 (d, J = 6.8 Hz, 2H, C_2, C_6-H).

Anal. Calcd. for $C_{14}H_{13}N_2OBr•0.5H_2O$: C, 53.52; H, 4.49; N, 8.92. Found: C, 53.67; H, 4.22; N, 8.94.

N-(3,5-Dichlorophenylcarbonylimino)-4-ethylpyridinium Ylides (**8n**).

The compound **8n** was obtained following General Procedure B by using 3 equivalents of 3,5-dichlorobenzoylchloride to give an ivory compound in 35% yield, mp 141-143 °C; ir (potassium bromide): ν 1595 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.33 (t, J = 7.8 Hz, 3H, CH_2CH_3), 2.80-2.88 (q, J = 7.8 Hz, 2H, CH_2CH_3), 7.36 (m, 1H, $C_{4'}$-H), 7.50 (d, J = 6.8 Hz, 2H, C_3, C_5-H), 8.00 (m, 2H, $C_{2'}$, $C_{6'}$-H), 8.60 (d, J = 6.8 Hz, 2H, C_2, C_6-H).

Anal. Calcd. for $C_{14}H_{12}N_2OCl_2•0.25H_2O$: C, 56.11; H, 4.20; N, 9.35. Found: C, 56.22; H, 4.03; N, 9.35.

General Procedure C.

N-(4-Methoxycarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridine (**9a**).

N-(4-Methoxyphenylcarbonylimino)-4-ethylpyridinium ylide **8a** (4 g, 15.6 mmoles) was dissolved in 100 ml of absolute ethanol and cooled to 0 °C while stirring. Sodium borohydride (2.95 g, 78.03 mmoles) in 20 ml of absolute ethanol was added and stirring continued at 0 °C for 5 hours. The excess sodium borohydride was treated with distilled water (100 ml) and the reaction mixture allowed to warm up to room temperature. It was then extracted with chloroform (3 x 75 ml) and dried over anhydrous sodium sulfate. Evaporation of the filtered chloroform solution *in vacuo* resulted in obtaining ivory crystals. This crude product was purified on a silica-gel column using ethyl acetate:hexane (2:1, v/v, 1,000 ml) as an eluent to furnish **9a** as an ivory white solid, 1.31 g (32% yield) of the desired tetrahydropyridine, mp 167-169 °C; ir (potassium bromide): ν 3206 (NH), 1635 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.98 (t, J = 7.4 Hz, 3H, CH_2CH_3), 2.00 (q, J = 7.4 Hz, 2H, CH_2CH_3), 2.25 (s, 2H, C_3-H), 3.08 (m, 2H, C_2-H), 3.45 (br s, 2H, C_6-H), 3.80 (s, 3H, OCH_3), 5.32 (s, 1H, C_5-H), 6.90 (d, J = 8.6 Hz, 2H, phenyl protons), 7.0 (br s, 1H, N*H*, deuterium oxide exchangeable), 7.70 (m, 2H, phenyl protons).

Anal. Calcd. for $C_{15}H_{20}N_2O_2$: C, 69.20; H, 7.74; N, 10.76. Found: C, 69.18; H, 7.90; N, 10.54.

N-(3-Methoxyphenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridine (**9b**).

The compound **9b** was obtained following General Procedure C by using 100% ethyl acetate for recrystallization of the crude product to give a white solid in 32% yield, mp 133-135 °C; ir (potassium bromide): ν 3200 (NH), 1644 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.98 (t, J = 7.3 Hz, 3H, CH_2CH_3), 1.95-2.03 (q, J = 7.3 Hz, 2H, CH_2CH_3), 2.25 (m, 2H, C_3-H), 3.10 (m, 2H, C_2-H), 3.47 (s, 2H, C_6-H), 3.83 (s, 3H, -OCH_3), 5.33 (s, 1H, C_5-H), 6.95 (br s, 1H, N*H*, deuterium oxide exchangeable), 7.00 (m, 1H, $C_{2'}$-H), 7.20-7.33 (m, 3H, $C_{4'}$, $C_{5'}$, $C_{6'}$-H).

Anal. Calcd. for $C_{15}H_{20}N_2O_2$: C, 69.20; H, 7.74; N, 10.76. Found: C, 69.40; H, 7.80; N, 10.75.

N-(3-Trifluoromethylphenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridine (**9c**).

The compound **9c** was obtained following General Procedure C except using methanol:diethyl ether (40:1, v/v) for recrystallization of the crude mixture to furnish 44% yield of white compound, mp 119-121 °C ; ir (potassium bromide): ν 3217 (NH), 1635 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.02 (t, J = 7.5 Hz, 3H, CH_2CH_3), 2.01 (q, J = 7.5 Hz, 2H, CH_2CH_3), 2.27 (s, 2H, C_3-H), 3.10 (m, 2H, C_2-H), 3.49 (s, 2H, C_6-H), 5.35 (s, 1H, C_5-H), 7.00 (s, 1H, N*H*, deuterium oxide exchangeable), 7.55 (m, 1H, $C_{5'}$-H), 7.72 (d, J = 7.7 Hz, 1H, $C_{6'}$-H), 7.90 (d, J = 7.7 Hz, 1H, $C_{4'}$-H), 8.0 (s, 1H, $C_{2'}$–H).

Anal. Calcd. for $C_{15}H_{17}N_2OF_3•0.125H_2O$: C, 59.94; H, 5.78; N, 9.32. Found: C, 59.69; H, 5.80; N, 9.27.

N-(4-Methylphenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridine (**9d**).

The compound **9d** was obtained following General Procedure C. After recrytallization in 100% ethyl acetate, the product was collected as a white solid, 30% yield, mp 149-151 °C; ir (potassium bromide): ν 3211 (NH), 1636 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.02 (t, J = 7.4 Hz, 3H, CH_2CH_3), 2.01 (q, J = 7.4 Hz, 2H, CH_2CH_3), 2.27 (br s, 2H, C_3-H), 3.11 (m, 2H, C_2-H), 3.49 (s, 2H, C_6-H), 5.35 (s, 1H, C_5-H), 7.23 (d, J = 8.0 Hz, 2H, phenyl protons), 7.65 (d, J = 8.0 Hz, 2H, phenyl protons).

Anal. Calcd. for $C_{15}H_{20}N_2O$: C, 73.74; H, 8.25; N, 11.46. Found: C, 73.73; H, 8.46; N, 11.45.

N-(4-Ethylphenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridine (**9e**).

The compound **9e** was obtained following General Procedure C after recrystallization in 100% ethyl acetate as a white solid, 27% yield, mp 143-145 °C ; ir (potassium bromide): ν 3230 (NH), 1644 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.05 (t, J = 7.3 Hz, 3H, CH_2CH_3 of THP ring), 1.25 (t, J = 7.8 Hz, 3H, CH_2CH_3), 2.0 (q, J = 7.3 Hz, 2H, CH_2CH_3), 2.24 (m, 2H, C_3-H), 2.62-2.70 (q, J = 7.8 Hz, 2H, CH_2CH_3), 3.08 (m, 2H, C_2-H), 3.46 (s, 2H, C_6-H), 5.32 (s, 1H, C_5-H), 6.95 (br s, 1H, N*H*, deuterium oxide exchangeable), 7.20 (d, J = 8.3 Hz, 2H, $C_{3'}$, $C_{5'}$-H), 7.63 (d, J = 8.3 Hz, 2H, $C_{2'}$, $C_{6'}$-H).

Anal. Calcd. for $C_{17}H_{25}N_2O$: C, 74.38; H, 8.58; N, 10.84. Found: C, 74.65; H, 8.66; N, 10.85.

N-(4-*n*-Butylphenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridine (**9f**).

The compound **9f** was obtained following General Procedure C. After flash column chromatography of the crude product using ethyl acetate:methanol (9:1, v/v) as an eluent to provide a white solid, 64% yield, mp 125-127 °C; ir (potassium bromide): ν 3229 (NH), 1644 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.87 (t, J = 7.3 Hz, 3H, $CH_2CH_2CH_2CH_3$), 0.97 (t, J = 7.3 Hz, 3H, CH_2CH_3), 1.28-1.39 (m, 2H, $CH_2CH_2CH_2CH_3$), 1.52-1.63 (m, 2H, $CH_2CH_2CH_2CH_3$), 1.95-2.03 (q, J = 7.8 Hz, 2H, CH_2CH_3), 2.24 (br s, 2H, C_3-H), 2.59 (t, J = 7.8 Hz, 2H, $CH_2CH_2CH_2CH_3$), 3.09 (m, 2H, C_2-H), 3.46 (s, 2H, C_6-H), 5.32 (s, 1H, C_5-H), 7.01 (br s, 1H, N*H*, deuterium oxide exchangeable), 7.18 (d, J = 7.8 Hz, 2H, $C_{3'}$, $C_{5'}$-H), 7.62 (d, J = 7.8 Hz, 2H, $C_{2'}$, $C_{6'}$-H).

Anal. Calcd. for $C_{18}H_{26}N_2O$: C, 75.48; H, 9.15; N, 9.78. Found: C, 75.78; H, 9.33; N, 9.73.

N-(4-*t*-Butylphenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridine (**9g**).

The compound **9g** was obtained following General Procedure C. The compound was collected, after recrystallization in 100% ethyl acetate, as a white solid, 52% yield, mp 158-160 °C; ir (potassium bromide): ν 3220 (NH), 1647 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.02 (t, J = 7.5 Hz, 3H, CH_2CH_3), 1.31 (s, 9H, CH_3 in t-butyl), 2.01 (q, J = 7.5 Hz, 2H, CH_2CH_3), 2.27 (br s, 2H, C_3-H), 3.10 (m, 2H, C_2-H), 3.49 (s, 2H, C_6-H), 5.35 (s, 1H, C_5-H), 6.98 (s, 1H, N*H*, deuterium oxide exchangeable), 7.40 (d, J = 7.9 Hz, 2H, $C_{3'}$, $C_{5'}$-H), 7.65 (d, J = 7.9 Hz, 2H, $C_{2'}$, $C_{6'}$-H).

Anal. Calcd. for $C_{18}H_{26}N_2O$: C, 75.48; H, 9.15; N, 9.78. Found: C, 75.38; H, 9.31; N, 9.77.

N-(2-Methylphenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridine (**9h**).

The compound **9h** was obtained following General Procedure C. A white solid was collected with 78% yield after recrystallization in 100% ethyl acetate, mp 157-159 °C; ir (potassium bromide): ν 3193 (NH), 1645 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.97 (t, J = 7.3 Hz, 3H, CH_2CH_3), 1.94-2.02 (q, J = 7.3 Hz, 2H, CH_2CH_3), 2.25 (m, 2H, C_3-H), 2.43 (s, 3H, CH_3), 3.09 (m, 2H, C_2-H), 3.45 (s, 2H, C_6-H), 5.32 (s, 1H, C_5-H), 6.60 (br s, 1H, N*H*, deuterium oxide exchangeable), 7.14-7.32 (m, 4H, phenyl protons).

Anal. Calcd. for $C_{15}H_{20}N_2O$: C, 73.74; H, 8.25; N, 11.46. Found: C, 73.40; H, 8.26; N, 11.34.

N-(4-Fluorophenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridine (**9i**).

The compound **9i** was obtained following General Procedure C. After recrystallization in 100% ethyl acetate, a white solid was collected, 31% yield, mp 164-166 °C; ir (potassium bromide): ν 3210 (NH), 1638 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.98 (t, J = 7.5 Hz, 3H, CH_2CH_3), 1.99-2.02 (q, J = 7.5 Hz, 2H, CH_2CH_3), 2.31 (m, 2H, C_3-H), 3.26 (m, 2H, C_2-H), 3.63 (s, 2H, C_6-H), 5.33 (s, 1H, C_5-H), 7.06-7.11 (m, 2H, $C_{2'}$, $C_{6'}$-H), 7.18 (br s, 1H, N*H*, deuterium oxide exchangeable), 7.80 (m, 2H, $C_{3'}$, $C_{5'}$-H).

Anal. Calcd. for $C_{14}H_{17}N_2OF$: C, 67.72; H, 6.90; N, 11.28. Found: C, 67.47; H, 7.00; N, 11.16.

N-(3-Fluorophenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridine (**9j**).

The compound **9j** was obtained following General Procedure C. This compound was collected after recrystallization in ethyl acetate:hexane (9:1, v/v) as a white solid, 33% yield, mp 142-144 °C; ir (potassium bromide): ν 3222 (NH), 1643 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.02 (t, J = 7.3 Hz, 3H, CH_2CH_3), 2.00 (q, J = 7.3 Hz, 2H, CH_2CH_3), 2.27 (br s, 2H, C_3-H), 3.11 (m, 2H, C_2-H), 3.48 (s, 2H, C_6-H), 5.35 (s, 1H, C_5-H), 7.05 (br s, 1H, N*H*, deuterium oxide exchangeable), 7.20-7.40 (m, 3H, phenyl protons), 7.50 (s, 1H, $C_{2'}$-H).

Anal. Calcd. for $C_{14}H_{17}N_2OF$: C, 67.72; H, 6.90; N, 11.28. Found: C, 67.45; H, 7.08; N, 11.23.

N-(2-Fluorophenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridine (**9k**).

The compound **9k** was obtained following General Procedure C. This compound was collected after recrystallization in 100% ethyl acetate as a white solid, 38% yield, mp 125-127 °C; ir (potassium bromide): ν 3204 (NH), 1644 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.98 (t, J = 7.3 Hz, 3H, CH_2CH_3), 1.96-2.04 (q, J = 7.3 Hz, 2H, CH_2CH_3), 2.25 (br s, 2H, C_3-H), 3.13 (m, 2H, C_2-H), 3.52 (s, 2H, C_6-H), 5.33 (s, 1H, C_5-H), 7.04-7.12 (dd, J = 8.0 Hz, 1H, $C_{5'}$-H), 7.21-7.26 (d, J = 8 Hz, 1H, $C_{4'}$-H), 7.40-7.48 (m, 1H, $C_{6'}$-H), 7.70 (br s, 1H, N*H*, deuterium oxide exchangeable), 8.00-8.10 (m, 1H, $C_{3'}$-H).

Anal. Calcd. for $C_{14}H_{17}N_2OF$: C, 67.72; H, 6.90; N, 11.28. Found: C, 67.79; H, 6.99; N, 11.21.

N-(4-Chlorophenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridine (**9l**).

The compound **9l** was obtained following General Procedure C. This compound was collected after recrystallization in 100% ethyl acetate as a white solid, 64% yield, mp 180-182 °C; ir (potassium bromide): ν 3204 (NH), 1643 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.06 (t, J = 7.8 Hz, 3H, CH_2CH_3), 2.04-2.12 (q, J = 7.8 Hz, 2H, CH_2CH_3), 2.33 (s, 2H, C_3-H), 3.17 (m, 2H, C_2-H), 3.55 (s, 2H, C_6-H), 5.41 (s, 1H, C_5-H), 7.05 (br s, 1H, N*H*, deuterium oxide exchangeable), 7.45 (d, J = 7.8 Hz, 2H, $C_{2'}$, $C_{6'}$-H), 7.75 (d, J = 7.8 Hz, 2H, $C_{3'}$, $C_{5'}$-H).

Anal. Calcd. for $C_{14}H_{17}N_2OCl$: C, 63.51; H, 6.47; N, 10.58. Found: C, 63.92; H, 6.61; N, 10.68.

N-(4-Bromophenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridine (**9m**).

The compound **9m** was obtained following General Procedure C. This compound was collected after recrystallization in 100% ethyl acetate as a white solid, 36% yield, mp 187-189 °C; ir (potassium bromide): ν 3208 (NH), 1646 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.97 (t, J = 7.3 Hz, 3H, CH_2CH_3), 1.95-2.03 (q, J = 7.3 Hz, 2H, CH_2CH_3), 2.24 (s, 2H, C_3-H), 3.06 (m, 2H, C_2-H), 3.45 (s, 2H, C_6-H), 5.32 (s, 1H, C_5-H), 6.95 (br s, 1H, N*H*, deuterium oxide exchangeable), 7.50-7.61 (m, 4H, phenyl protons).

Anal. Calcd. for $C_{14}H_{17}N_2OBr$: C, 54.38; H, 5.54; N, 9.06. Found: C, 54.26; H, 5.64; N, 8.86.

N-(3,5-Dichlorophenylcarbonylamino)-4-ethyl-1,2,3,6-tetrahydropyridine (**9n**).

The compound **9n** was obtained following General Procedure C. This compound was collected after recrystallization in 100%

ethyl acetate as a white solid, 83% yield, mp 120-122 °C; ir (potassium bromide): ν 3195 (NH), 1645 (CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.98 (t, J = 7.3 Hz, 3H, CH_2CH_3), 1.97-2.02 (q, J = 7.3 Hz, 2H, CH_2CH_3), 2.29 (br s, 2H, C_3-H), 3.19 (m, 2H, C_2-H), 3.56 (s, 2H, C_6-H), 5.32 (s, 1H, C_5-H), 6.70 (br s, 1H, N*H*, deuterium oxide exchangeable), 7.45 (s, 1H, $C_{4'}$-H), 7.65 (s, 2H, $C_{2'}$, $C_{6'}$-H).

Anal. Calcd. for $C_{14}H_{16}N_2OCl_2 \cdot 0.5H_2O$: C, 54.56; H, 5.56; N, 9.09. Found: C, 54.89; H, 5.38; N, 9.07.

Acknowledgements.

We are grateful to the National Institute of Health, Division of Research Resources, MBRS research funding program, NIH No. GM 08111 and the Research Center at Minority Institutions (RCMI) Grant RR 03020. We are also grateful to Dr. Thomas Gedris, Chemistry Department, NMR Unit, Florida State University, Tallahassee, Florida, for recording all the nmr spectra of our compounds.

REFERENCES AND NOTES

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