[Chem. Pharm. Bull. 32(12)4866—4872(1984)]

Reductive Amination of Ethynylpyridines with Sodium Cyanoborohydride

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(Received April 14, 1984)

In order to investigate the structure–activity relationship of betahistine derivatives, a general synthesis of methylated 2-(2-methylaminoethyl)pyridines was developed based on the addition of methylamine hydrochloride to methylated 2-ethynylpyridines under reductive conditions. In addition, the scope and limitations of the reductive addition were briefly examined. For example, the reaction proceeded smoothly with *p*-nitrophenylacetylene, whereas phenylacetylene itself did not react with methylamine.

Keywords——ethynylpyridine; sodium cyanoborohydride; reductive amination; betahistine; palladium-catalyzed reaction; ethyl pyridineacetate; 2-(2-pyridyl)ethylamine

Betahistine, 2-(2-methylaminoethyl)pyridine (**3a**)[1] is clinically used as an antivertigo agent and is prepared by the Michael-type addition of methylamine to 2-vinylpyridine.[2] In order to investigate the structure–activity relationships extensively in this field, it is necessary to develop a widely applicable method for the preparation of N-heteroaromatics containing a phenylethylamine like structure, because suitable vinyl-N-heteroaromatics are not always readily available.

From the above point of view, we have investigated the construction of the desired C–C–N linkage on monoazine and diazine rings. In connection to this subject, the following findings have been obtained.

i) Ethynyl-N-heteroaromatics can be generally prepared by the cross-coupling reaction of the corresponding halogeno derivatives with trimethylsilylacetylene in the presence of a palladium catalyst.[3]

ii) Hydrolysis of 4-(1-hexynyl)pyrimidine gives butyl 4-pyrimidinyl ketone in the presence of piperidine,[4] *via* the formation of an enamine as an intermediate.

iii) Sodium cyanoborohydride reduces the enamines to the corresponding saturated amines.[5]

On the basis of the above results, the reduction of ethynylpyridines with sodium cyanoborohydride in the presence of an appropriate amine hydrochloride was examined for our purpose. The present paper deals with the synthesis of betahistine analogs, and describes the scope and limitations of the reductive amination employed.

Heating of 2-ethynylpyridine (**2a**) with 1.5 eq of sodium cyanoborohydride and 5 eq of methylamine hydrochloride in ethanol for 24 h gave a colorless liquid. No depression of melting point was observed on admixture of the hydrochloride of the product with that of authentic **3a**. Similarly, four kinds of methyl homolog (**2b—e**), prepared by the cross-coupling reaction of the corresponding 2-bromomethylpyridines (**1b—e**) with trimethylsilylacetylene, were reductively aminated with methylamine hydrochloride and sodium cyanoborohydride. Except for the 5-methyl homolog (**3d**), the yields of methyl-2-(2-methylaminoethyl)pyridines (**3b—e**) were satisfactory.

The same compounds (**3b—e**) were alternatively synthesized by utilizing the reactivity of

the 2-methyl group on the pyridine ring. Namely, metallation of the dimethylpyridines (**6a**, **d**, **e**) except **6c** with *n*-butyllithium at room temperature followed by condensation with diethyl carbonate at −60 °C afforded ethyl methyl-2-pyridineacetates (**5b**, **d**, **e**). On the other hand, the reaction of 2,4-dimethylpyridine (**6c**) gave ethyl 2-methyl-4-pyridineacetate (**5'c**), instead of the 2-pyridineacetate (**5c**), under the above conditions. Preparation of the desired ethyl-2-pyridineacetate (**5c**) was achieved by lithiation at −60 °C, followed by carbonation with diethyl carbonate at the same temperature. Condensation of the pyridineacetates (**5b**—**e**) with aqueous methylamine in a sealed tube gave the *N*-methyl-2-pyridineacetamides (**4b**—**e**). The reduction of **4b**—**e** with diborane generated from sodium borohydride and boron trifluoride etherate proceeded smoothly to give the desired amines (**3b**—**e**).

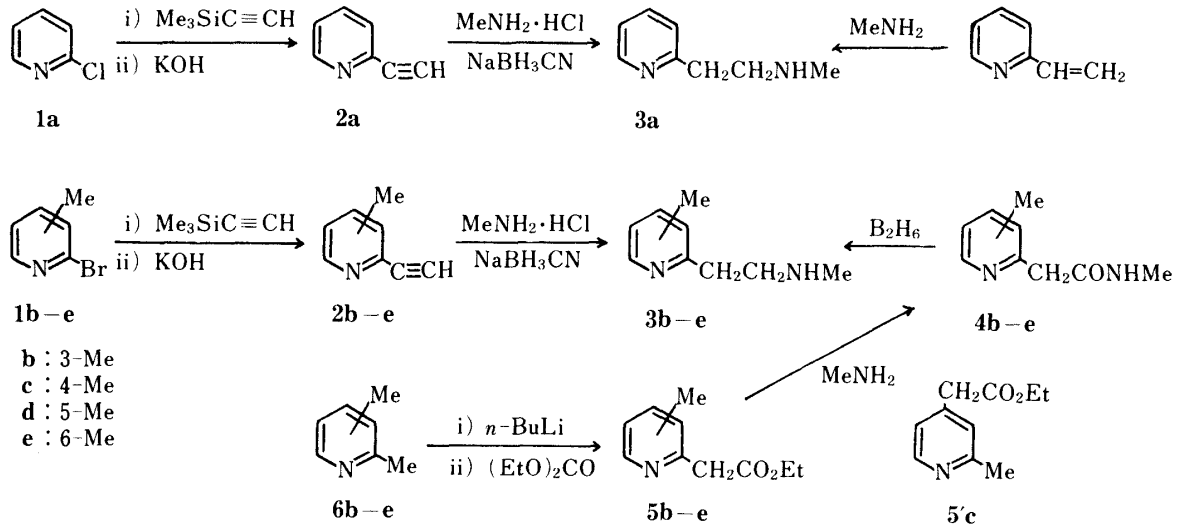

Chart 1

The reductive amination of ethynylpyridines (**2b**—**e**) seemed to offer experimental simplicity in the preparation of the betahistine-type compounds as compared with the synthetic route to **3b**—**c** from **6b**—**e**. Therefore, further work was done to explore the scope and limitations of this reductive amination. The cross-coupling reaction of trimethylsilylacetylene with 2,3-dihalopyridines such as 3-chloro-2-bromo- (**1g**) and 2,3-dibromopyridine (**1h**) proceeded site-selectively to give the corresponding 2-ethynylpyridines (**2g**, **h**). These ethynyl compounds (**2g**, **h**) and 3-ethyl-2-ethynylpyridine (**2f**) derived from 3-ethyl-2-iodopyridine (**1f**) were smoothly converted by the reductive amination into the 3-substituted betahistines (**3f**—**h**). These results demonstrated that the reductive amination is not synthetically restricted by the presence of an *ortho*-substituent.

When **2a** was allowed to react with dimethylamine hydrochloride and sodium cyanoborohydride, 2-(2-dimethylaminoethyl)pyridine (**7a**) was obtained in 93% yield. In contrast, the reductive amination of **2a** with ammonium chloride did not proceed, and the reaction with aniline hydrochloride gave the expected product, 2-(2-anilinoethyl)pyridine (**8**), in a low yield. These results suggest an important role of the nucleophilicity of the amines in the reaction.

While 2-(1-propynyl)pyridine (**9**) adequately accepted dimethylamine as an attacking amine, 2-phenylethynylpyridine (**10**) did not. These findings may provide a basis for the construction of compounds with branched aminoethyl groups at the 2-position.

Finally, the electron withdrawing effect of aromatic nuclei on the reductive amination was briefly investigated. 3-Ethynylpyridine (**12**) and 5-ethynyl-2,4-dimethylpyrimidine (**14**) reacted with dimethylamine hydrochloride under the same conditions to give 3-(2-dimethylamino)pyridine (**13**) and 2,4-dimethyl-5-(2-dimethylaminoethyl)pyridine (**15**), re-

spectively, but the yields of these products (**13** and **15**) were less than 20%.

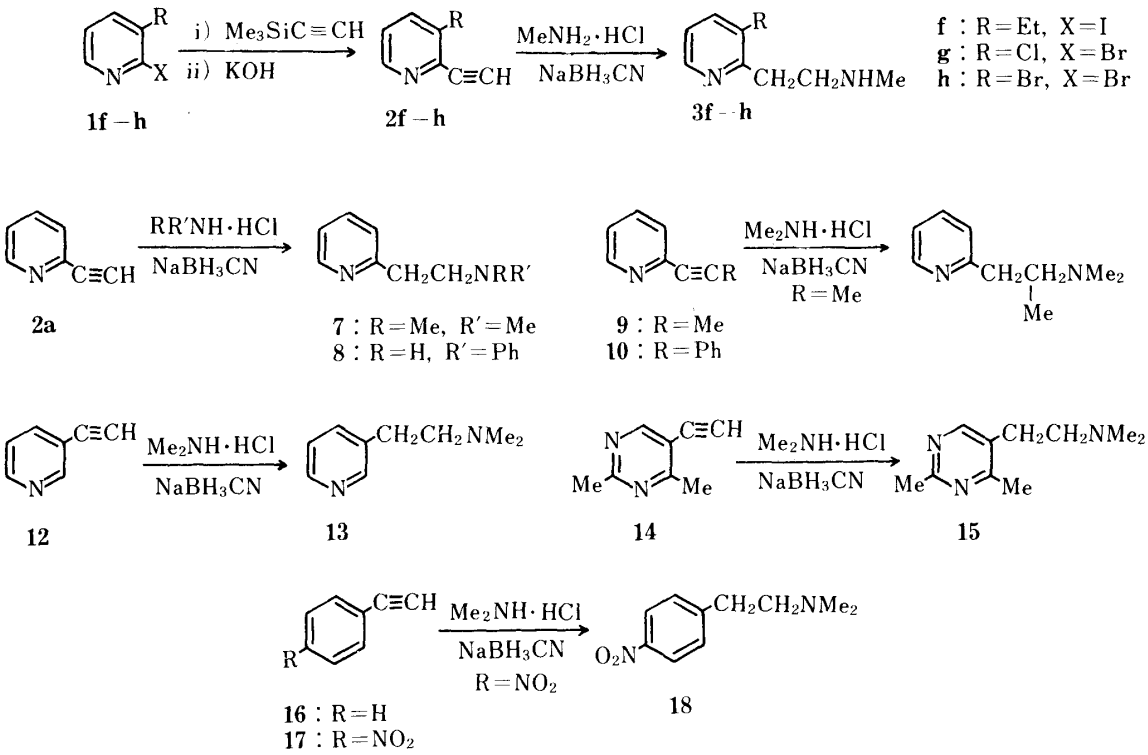

Chart 2

In addition, the reductive amination of 4-nitroethynylbenzene (**17**) with dimethylamine and sodium cyanoborohydride gave *N*, *N*-dimethyl-4-nitrophenylethylamine (**18**) in 94% yield, whereas the reaction of ethynylbenzene (**16**) resulted in recovery of the starting material.

Experimental

All melting points and boiling points are uncorrected. Infrared (IR) spectra were measured with a JASCO IRA-1 spectrometer. Proton magnetic resonance (^{1}H-NMR) spectra were taken at 60 MHz with a JEOL JNM-PMX 60 spectrometer. Chemical shifts are expressed in δ (ppm) values. The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, dd = double doublet, m = multiplet, and br = broad.

3-Ethyl-2-iodopyridine (1f)——A mixture of 2-chloro-3-ethylpyridine (5.54 g, 39 mmol), NaI (34 g, 230 mmol), 57% HI (6 ml), and 2-butanone (120 ml) was refluxed for 26 h. After removal of the solvent under reduced pressure, the reaction mixture was diluted with water. The solution was made alkaline with solid K_2CO_3 and extracted with $CHCl_3$. The $CHCl_3$ extract was washed with aq. Na_2SO_3 and dried over K_2CO_3. The crude product was fractionated, and the fraction boiling at 134—138 °C (24 mmHg) was collected. Yield 5.16 g (57%). ^{1}H-NMR (CCl_4): 1.23 (3H, t, J=7.0 Hz), 2.68 (2H, q, J=7.0 Hz), 7.10 (1H, dd, J=7.0 and 5.0 Hz), 7.30 (1H, dd, J=7.0 and 2.0 Hz), 8.07 (1H, dd, J=5.0 and 2.0 Hz). Picrate: mp 92—94 °C, yellow needles (acetone–hexane). *Anal.* Calcd for $C_{13}H_{11}IN_4O_7$ (picrate): C, 33.79; H, 2.40; N, 12.12. Found: C, 33.52; H, 2.42; N, 12.12.

Cross-Coupling Reaction of Halogenopyridines (1) with Trimethylsilylacetylene——General Procedure: A mixture of halogenopyridine (40 mmol), trimethylsilylacetylene (4.7 g, 48 mmol), $Pd(PPh_3)_2Cl_2$ (0.94 g, 1.3 mmol), CuI (0.47 g, 2.5 mmol), and Et_3N (50 ml) was stirred at room temperature for 14 h (for the case of **1b**, **d**) or refluxed for 3 h (for the case of **1c**, **e**—**h**). After removal of the Et_3N, the reaction mixture was diluted with water, and extracted with ether. The ethereal extract was distilled under reduced pressure, and the distillate was dissolved in MeOH (30 ml). The MeOH solution was added to 1 N KOH (120 ml), and the mixture was stirred at room temperature for 1 h. The reaction mixture was acidified with 3 N HCl and concentrated under reduced pressure. The residue was dissolved in water, made alkaline with solid K_2CO_3, and extracted with ether. Removal of the ether gave the crude ethynyl compound, which was purified by SiO_2 column chromatography using C_6H_6 as an eluent. Distillation of the product obtained from the benzene eluent afforded the pure ethynylpyridines.

TABLE I. Ethynylpyridines

Compd. No.	Yield (%)	bp (°C) [mmHg]	IR (neat) cm^{-1} –C≡C–	^{1}H-NMR (CCl_4) δ (ppm) –C≡CH	Ring protons	Other protons
2b	31	60 [3]	2125	3.23 (1H, s)	7.09 (1H, dd, J=8.0, 5.0 Hz) 7.43 (1H, dd, J=8.0, 1.0 Hz) 8.35 (1H, dd, J=5.0, 1.0 Hz)	2.42 (3H, s)
2c	56	102—105 [26]	2120	2.97 (1H, s)	7.00 (1H, d, J=5.0 Hz) 7.23 (1H, s) 8.37 (1H, d, J=5 Hz)	2.31 (3H, s)
2d	61	97—99 [24]	2125	2.94 (1H, s)	7.3—7.4 (2H, m) 8.2—8.5 (1H, m)	2.33 (3H, s)
2e	51	92—94 [25]	2120	3.00 (1H, s)	7.0—7.7 (3H, m)	2.50 (3H, s)
2f	61	81—82 [3]	2095	3.16 (1H, s)	7.12 (1H, dd, J=8.0, 5.0 Hz) 7.45 (1H, dd, J=8.0, 1.0 Hz) 8.35 (1H, dd, J=5.0, 1.0 Hz)	1.25 (3H, t, J=7.0 Hz) 2.82 (2H, q, J=7.0 Hz)
2g	54	71—73 [3]	2125[a]	3.35 (1H, s)	7.22 (1H, dd, J=8.0, 5.0 Hz) 7.73 (1H, dd, J=8.0, 1.0 Hz) 8.45 (1H, dd, J=5.0, 1.0 Hz)	
2h	50	120—121 [23]	2120	3.33 (1H, s)	7.13 (1H, dd, J=8.0, 5.0 Hz) 7.84 (1H, dd, J=8.0, 1.0 Hz) 8.50 (1H, dd, J=5.0, 1.0 Hz)	

a) $CHCl_3$.

TABLE II. Analytical Data for Ethynylpyridines

Compd. No.	Formula	Analysis (%) Calcd C	Calcd H	Calcd N	Found C	Found H	Found N
2b	C_8H_7N	82.02	6.06	11.96	81.98	6.03	11.89
2c	C_8H_7N	82.02	6.06	11.96	82.52	6.11	12.00
2d	C_8H_7N	82.02	6.06	11.96	81.86	6.10	11.79
2e	C_8H_7N	82.02	6.06	11.96	82.10	6.11	11.74
2f	C_9H_9N	82.40	6.92	10.68	82.08	6.98	10.58
2g	C_7H_4ClN	61.12	2.93	10.18	61.07	2.86	10.23
2h	C_7H_4BrN	46.19	2.21	7.70	46.37	2.15	7.82

2-(1-Propynyl)pyridine (9)——Propyne generated from 1,2-dibromopropane (40 g, 0.2 mol) with KOH (36 g, 0.64 mol) in *n*-BuOH (120 ml) was introduced into a mixture of 2-iodopyridine (4.10 g, 0.02 mol), $Pd(PPh_3)_2Cl_2$ (0.56 g, 0.8 mmol), CuI (0.30 g, 1.6 mmol), and Et_3N (60 ml). The reaction mixture was stirred at room temperature for 24 h, then worked up as described above to give a colorless liquid, bp 113 °C (23 mmHg). Yield 66%. IR (neat): 2215 cm^{-1}. ^{1}H-NMR (CCl_4): 2.08 (3H, s), 6.9—7.7 (3H, m), 8.3—8.6 (1H, m). *Anal.* Calcd for C_8H_7N: C, 82.02; H, 6.02; N, 11.96. Found: C, 82.22; H, 6.08; N, 11.73.

Reductive Amination of Ethynylarenes with $NaBH_3CN$——General Procedure: A mixture of ethynylarene (4 mmol), amine hydrochloride (20 mmol), $NaBH_3CN$ (0.38 g, 6 mmol), and EtOH (5 ml) was refluxed for 24 h. In the case of **9**, after reflux for 24 h, additional $NaBH_3CN$ (0.38 g, 6 mmol) was added, and the mixture was refluxed for a further 24 h. After removal of the EtOH, the reaction mixture was diluted with 3 N NaOH, and extracted with $CHCl_3$. The $CHCl_3$ extract was purified by SiO_2 column chromatography using AcOEt–Et_3N (9 : 1, v/v) as an eluent. Distillation of the product from the AcOEt–Et_3N (9 : 1) eluate afforded the pure aminoethyl compound.

Ethyl Methyl-2-pyridineacetates (5b—e)——General Procedure: A 15% hexane solution of *n*-BuLi (42.7 g, 0.1 mol) was added to a dry THF (150 ml) solution of 2,X-dimethylpyridine (**6**) (10.72 g, 0.1 mol) at room temperature for **6b**, **d**, **e** or at −60 °C for **6c** with stirring in an N_2 atmosphere. Then, a dry THF (50 ml) solution of diethyl carbonate (11.81 g, 0.1 mol) was added to the mixture at −60 °C. After the reaction mixture had reached room

TABLE III. Aminoethylarenes

Compd. No.	Yield[a] (%)	bp (°C) [mmHg]	–NH–	^{1}H-NMR (CCl_4) δ (ppm)		
				$-CH_2CH_2N$	Ring protons	Other protons
3b	71 [47]	110—114 [24]	1.23 (1H, s)	2.86 (4H, s)	6.8—7.5 (2H, m) 8.23 (1H, s)	2.28 (3H, s) 2.37 (3H, s)
3c	64 [85]	128—134 [28]	1.69 (1H, s)	2.87 (4H, s)	6.95 (1H, d, J=5.0 Hz) 6.98 (1H, s) 8.25 (1H, d, J=5.0 Hz)	2.31 (3H, s) 2.38 (3H, s)
3d	39 [39]	112 [25]	1.15 (1H, s)	2.83 (4H, s)	6.9—7.5 (2H, m) 8.24 (1H, s)	2.28 (3H, s) 2.35 (3H, s)
3e	76 [61]	114—116 [28]	1.21 (1H, s)	2.83 (4H, s)	6.8—7.5 (3H, m)	2.35 (3H, s) 2.45 (3H, s)
3f	67	130 [25]	1.33 (1H, s)	2.87 (4H, s)	6.93 (1H, dd, J=8.0, 5.0 Hz) 7.30 (1H, dd, J=8.0, 2.0 Hz) 8.24 (1H, dd, J=5.0, 2.0 Hz)	1.21 (3H, t, J=7.0 Hz) 2.36 (3H, s) 2.65 (2H, q, J=7.0 Hz)
3g	67	121—122 [23]	1.08 (1H, s)	2.9—3.3 (4H, m)	7.00 (1H, dd, J=8.0, 5.0 Hz) 7.55 (1H, dd, J=8.0, 1.0 Hz) 8.33 (1H, dd, J=5.0, 1.0 Hz)	2.40 (3H, s)
3h	73	94—97 [3]	3.06 (1H, s)	2.9—3.4 (4H, m)	6.97 (1H, dd, J=8.0, 5.0 Hz) 7.75 (1H, dd, J=8.0, 1.0 Hz) 8.41 (1H, dd, J=5.0, 1.0 Hz)	2.42 (3H, s)
7	93	102—104 [23][b]		2.4—3.3 (4H, m)	6.9—7.7 (3H, m) 8.3—8.7 (1H, m)	2.21 (6H, s)
8	40	154 [3][c]	3.7—4.5 (1H, b)	2.8—3.1 (2H, m) 3.3—3.7 (2H, m)	6.3—6.7 (3H, m) 6.8—7.3 (4H, m) 7.3—7.7 (1H, m) 8.4—8.7 (1H, m)	
11	41	102 [21]		2.6—3.3 (3H, m)	6.7—7.6 (3H, m) 8.3—8.6 (1H, m)	0.91 (1H, d, J=7.0 Hz) 2.22 (6H, s)
13	18	108 [21][d]		2.3—3.0 (4H, m)	6.9—7.6 (2H, m) 8.3—8.6 (2H, m)	2.17 (6H, s)
15	15	133—135 [25]		2.3—2.9 (4H, m)	8.17 (1H, s)	2.21 (6H, s) 2.41 (3H, s) 2.53 (3H, s)
18	94	130—132 [3][e]		2.4—3.0 (4H, m)	7.32 (2H, d, J=8.0 Hz) 8.06 (2H, d, J=8.0 Hz)	2.20 (6H, s)

a) Yields in brackets show the yields from **4**. *b*) Lit.[6] bp 101—103 °C (17 mmHg). *c*) Lit.[7] bp 167—168 °C (2.5 mmHg).
d) Lit.[8] bp 96—97 °C (10 mmHg). *e*) Picrate (EtOH), mp 157—160 °C; lit.[9] mp 162 °C.

Table IV. Analytical Data for Aminoethylarenes

Compd. No.	Formula	Analysis (%) Calcd C	H	N	Found C	H	N
3b	$C_{21}H_{20}N_8O_{14}$ (dipicrate)[a]	41.45	3.31	18.42	41.47	3.29	18.40
3c	$C_{21}H_{20}N_8O_{14}$ (dipicrate)[b]	41.45	3.31	18.42	41.18	3.26	18.47
3d	$C_{21}H_{20}N_8O_{14}$ (dipicrate)[c]	41.45	3.31	18.42	41.67	3.28	18.47
3e	$C_{21}H_{20}N_8O_{14}$ (dipicrate)[d]	41.45	3.31	18.42	41.37	3.42	18.31
3f	$C_{10}H_{16}N_2$	73.12	9.82	17.06	72.97	9.34	17.01
3g	$C_8H_{11}ClN_2$	56.31	6.50	16.41	56.57	6.56	16.14
3h	$C_{20}H_{17}BrN_8O_{14}$ (dipicrate)[e]	35.68	2.55	16.64	35.76	2.41	16.61
11	$C_{10}H_{16}N_2$	73.12	9.82	17.06	72.96	10.10	17.00
15	$C_{10}H_{17}N_3$	41.45	3.64	19.77	41.33	3.61	19.64

a) mp 206—207 °C. *b*) mp 175—176 °C. *c*) mp 196—198 °C.
d) mp 193—194 °C. *e*) mp 160 °C.

Table V. Spectral Data for Ethyl Methylpyridineacetates

Compd. No.	IR ($CHCl_3$) cm^{-1} C=O	^{1}H-NMR (CCl_4) δ (ppm) OCH_2CH_3	OCH_2CH_3	CH_3	CH_2CO	Ring protons
5b	1720	1.25 (3H, t, J=7.0 Hz)	4.04 (2H, q, J=7.0 Hz)	2.20 (3H, s)	3.66 (2H, s)	6.8—7.5 (2H, m) 8.23 (1H, d, J=5.0 Hz)
5c	1730	1.23 (3H, t, J=7.0 Hz)	4.10 (2H, q, J=7.0 Hz)	2.32 (3H, s)	3.64 (2H, s)	6.89 (1H, d, J=5.0 Hz) 7.01 (1H, s) 8.25 (1H, d, J=5.0 Hz)
5'c	1730	1.23 (3H, t, J=7.0 Hz)	4.11 (2H, q, J=7.0 Hz)	2.48 (3H, s)	3.45 (2H, s)	6.90 (1H, d, J=5.0 Hz) 6.97 (1H, s) 8.33 (1H, d, J=5.0 Hz)
5d	1730	1.22 (3H, t, J=7.0 Hz)	4.07 (2H, q, J=7.0 Hz)	2.27 (3H, s)	3.64 (2H, s)	7.0—7.5 (2H, m) 8.23 (1H, s)
5e	1730	1.25 (3H, t, J=7.0 Hz)	4.10 (2H, q, J=7.0 Hz)	2.48 (3H, s)	3.65 (2H, s)	6.8—7.7 (3H, m)

Table VI. *N*,X-Dimethyl-2-pyridineacetamide

Compd. No.	Yield (%)	bp (°C) [mmHg]	IR ($CHCl_3$) cm^{-1} -NH-	C=O	^{1}H-NMR (CCl_4) δ (ppm) CH_3	CH_2	Ring protons and NH
4b	58	140—142 [5]	3500—3100	1645	2.34 (3H, s) 2.70 (3H, s)	3.60 (2H, s)	6.8—7.6 (3H, m) 8.20 (1H, d, J=5.0 Hz)
4c	81	140—143 [3]	3400—3160	1660	2.30 (3H, s) 2.69 (3H, s)	3.54 (2H, s)	6.89 (1H, d, J=5.0 Hz) 7.10 (1H, s), 7.3—7.8 (1H, b) 8.24 (1H, d, J=5.0 Hz)
4d	59	143 [5]	3400—3200	1660	2.31 (3H, s) 2.76 (3H, s)	3.66 (2H, s)	6.9—7.7 (3H, m) 8.35 (1H, s)
4e	74	144—145 [2]	3400—3200	1665	2.46 (3H, s) 2.68 (3H, s)	3.53 (2H, s)	6.8—7.7 (4H, m)

temperature, the mixture was acidified with 3 N HCl, and the THF was evaporated off. The residual aq. layer was washed with C_6H_6, made alkaline with K_2CO_3, salted out with NaCl, and extracted with $CHCl_3$. The extract was evaporated to dryness, and distillation of the residue gave a yellow liquid.

TABLE VII. Analytical Data for Picrates of *N*,X-Dimethyl-2-pyridineacetamide

Compd. No.	mp (°C)	Formula	Analysis (%) Calcd			Found		
			C	H	N	C	H	N
4b	145—147	$C_{15}H_{15}N_5O_8$	45.80	3.84	17.81	45.60	3.95	17.77
4c	158—159	$C_{15}H_{15}N_5O_8$	45.80	3.84	17.81	46.03	3.69	17.92
4d	176—178	$C_{15}H_{15}N_5O_8$	45.80	3.84	17.81	45.58	3.73	17.63
4e	164—166	$C_{15}H_{15}N_5O_8$	45.80	3.84	17.81	45.77	3.80	17.80

Ethyl 3-Methyl-2-pyridineacetate (**5b**): bp 115—116 °C (5 mmHg) (lit.[10] bp 141—145 °C (18 mmHg)). Yield 25%.

Ethyl 4-Methyl-2-pyridineacetate (**5c**): bp 103—105 °C (5 mmHg) (lit.[10] bp 142—146 °C (17 mmHg)). Yield 21%.

Ethyl 5-Methyl-2-pyridineacetate (**5d**): bp 122—124 °C (8 mmHg) (lit.[10] bp 100—105 °C (2 mmHg)). Yield 24%.

Ethyl 6-Methyl-2-pyridineacetate (**5e**): bp 95—97 °C (5 mmHg) (lit.[10] bp 130—132 °C (15 mmHg)). Yield 17%.

Ethyl 2-methyl-4-pyridineacetate (**5'c**) was obtained according to the general procedure for **6b**, **d**, **e**, as a yellow liquid, bp 110 °C (1 mmHg). Yield 32%. *Anal.* Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 67.14; H, 7.26; N, 7.71.

***N*,X-Dimethyl-2-pyridineacetamides (4b—e)**——General Procedure: A mixture of **5** (10 mmol) and 40% aq. solution of $MeNH_2$ (5 ml) was heated in a sealed tube at 120 °C for 24 h. The mixture was diluted with water, salted out with K_2CO_3, and extracted with $CHCl_3$. The residue obtained from the $CHCl_3$ extract was distilled to afford a pale yellow liquid or solid.

***N*-Methyl-2-(X-methyl-2-pyridinyl)ethylamines (3)**——General Procedure: A dry THF (20 ml) solution of **4** was added to a dry THF solution of B_2H_6, which was prepared by addition of $BF_3 \cdot Et_2O$ (8.52 g, 6 mmol) to a suspension of $NaBH_4$ (1.70 g, 45 mmol) in dry THF (20 ml). After being refluxed for 1 h, the reaction mixture was acidified with 3 N HCl, and the THF was distilled off under ordinary pressure. The residue was made alkaline with K_2CO_3 and extracted with $CHCl_3$. Distillation of the $CHCl_3$ extract gave a colorless liquid.

References and Notes

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