A New Route to N^2- and N^3-Substituted-2,3-diaminopyridines. Synthesis of 1- and 3-Alkoxycarbonyl-*v*-triazolo[4,5-*b*]pyridines

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Selective protection of the 3-amino group of 2,3-diaminopyridine with benzyl chloroformate allows a new synthesis of 3-methylamino- and 3-amino-2-alkylaminopyridines. The preparation of 1- and 3-alkoxycarbonyl-*v*-triazolo[4,5-*b*]pyridines is also reported.

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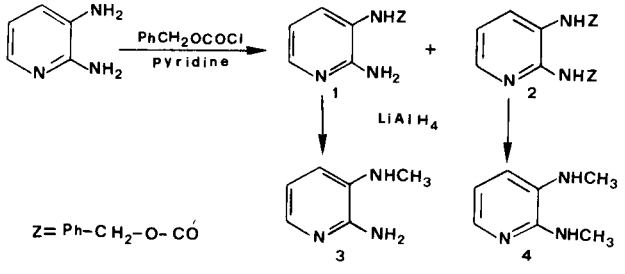
N-substituted-2,3-diaminopyridines are intermediates in the synthesis of some fused heterocyclic systems as imidazo- and triazolo[4,5-*b*]pyridines of biological interest. Although several methods to prepare the monocyclic title compounds are reported [1a-d], 2,3-diaminopyridine (DAP) has never utilized as starting material.

In the course of our systematic investigation on the reactivity of DAP toward acid chlorides and anhydrides, we found that treatment of DAP with benzyl chloroformate in tetrahydrofuran in presence of pyridine gave N^3-benzyloxycarbonyl-2,3-diaminopyridine (**1**) as the main product. The expected [2a-c] selective protection of 3-NH_2 group allows, as a first application of the key intermediate **1**, a simple preparation of N^3-methyl-2,3-diaminopyridine (**3**) by reduction with lithium aluminium hydride (LAH).

Scheme 1



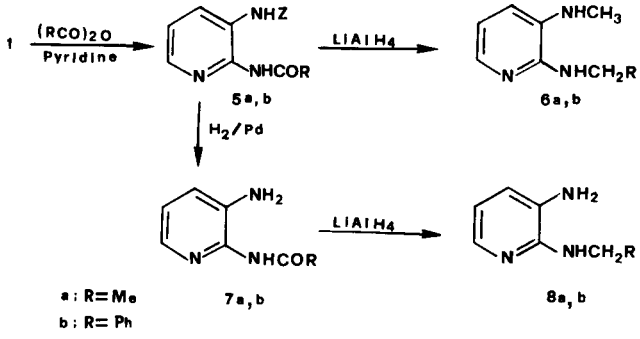
Similar treatment of dicarbamate **2** (the side product of the previous acylation) afforded N^2,N^3-dimethyl-2,3-diaminopyridine (**4**).

Oyama and Stewart [2b] reported that methylation of DAP with methyl iodide was solvent dependent and led to mixtures of ring and N^3-methylated derivatives.

As shown in Scheme 2, N^2-acyl-N^3-benzyloxycarbonyl-2,3-diaminopyridines **5a,b** were then readily obtained from **1** and the appropriate anhydrides in basic medium. The corresponding acid chlorides which lead to complex mixtures cannot be conveniently used. Reduction of **5a,b** with LAH in ether gave N^2-alkyl-N^3-methyl-2,3-diaminopyridines **6a,b** as the only discernible reaction products.

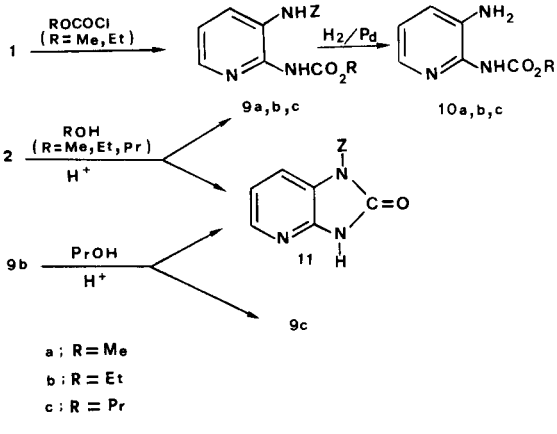
Furthermore, preliminary deprotection of 3-amino group of **5a,b** by hydrogenolysis on 5% Pd on alumina afforded N^2-acyl-2,3-diaminopyridines **7a,b**, which were then converted into N^2-alkyl-2,3-diaminopyridines **8a,b** by the usual hydride treatment.

Scheme 2



Following an analogous synthetic pathway N^2-alkoxycarbonyl-2,3-diaminopyridines **10a,b** can be easily prepared from **1** (Scheme 3). Methyl and ethyl chloroformates were used to introduce the alkoxycarbonyl group and yield **9a,b** (method A). Another interesting route to the intermediates **9** involves a site-selective exchange of alcohol moiety of the N^2-urethane group of **2**. In fact this compound

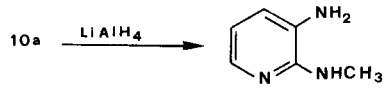
Scheme 3



can be converted to dicarbamates **9a,b,c** by refluxing in the appropriate alcohol, containing catalytic amounts of acetic acid (method B). A similar reactivity at the N^2-position was observed when **9b** was heated with 1-propanol to yield **9c**. 1-Benzyloxycarbonyl-1,3-dihydro-2*H*-imidazo-[4,5-*b*]pyridin-2-one (**11**) was also isolated as side product of these latter transformations. The structure of this cyclization product was assigned on the basis of analytical and spectroscopic data.

Reduction of **10a** with LAH provided N^2-methyl-2,3-diaminopyridine (**12**) isomeric to **3**.

Scheme 4



12

It is known that *N*-acyltriazoles and imidazoles can be used as acylating reagents and utility of mesoionic triazolopyridines concerned with the peptide synthesis has been recently investigated [3]. Epoxidation of inert alkenes and Baeyer-Villiger oxidation of aldehydes using the 1-alkoxycarbonyl-1,2,4-triazoles/hydrogen peroxide system were also reported [4].

Therefore, in order to examine the influence of the urethane group position on their reactivity, we decided to prepare both 1- and 3-alkoxycarbonyl-*v*-triazolo[4,5-*b*]pyridines. Cyclization of **10a,b,c** with isoamyl nitrite in refluxing THF, containing acetic acid, afforded in quantitative yields 3-alkoxycarbonyl-3*H*-*v*-triazolo[4,5-*b*]pyridines **13a,b,c**. Analogous treatment of N^3-ethoxycarbonyl-2,3-diaminopyridine (**14**) [1b] gave 1-ethoxycarbonyl-1*H*-*v*-triazolo[4,5-*b*]pyridine (**15b**). On other hand direct acylation of unsubstituted *v*-triazolo[4,5-*b*]pyridine [5] with alkyl

Table I

Physical and Analytical Data of N^2-Acyl-N^3-benzyloxycarbonyl-2,3-diaminopyridines **5a,b** and **9a-c**

Compound	Yield % [a]	Mp, °C Crystallization Solvent [b]	Formula	Analyses % Calcd./Found C	H	N
5a	100	148-149	$C_{15}H_{15}N_3O_3$	63.15	5.30	14.73
		E		63.08	5.32	14.69
5b	100	124-125	$C_{20}H_{17}N_3O_3$	69.15	4.93	12.10
		E		69.04	4.78	11.96
9a	80 (58) [c]	117-118	$C_{15}H_{15}N_3O_4$	59.79	5.02	13.95
		D-E		59.65	4.96	13.80
9b	85 (89) [c]	97-98	$C_{16}H_{17}N_3O_4$	60.94	5.43	13.33
		EA-H		61.01	5.50	13.29
9c	(70) [c]	97-98	$C_{17}H_{19}N_3O_4$	61.99	5.82	12.76
		E-LP		62.03	5.90	12.84

[a] The values in parentheses refer to method B. [b] Crystallization solvents: E = ether; D = dichloromethane; EA = ethyl acetate; LP = light petroleum; H = *n*-hexane. [c] The preparations of **9a**, **9b**, and **9c**, following method B, were performed in 24, 8, and 4 hours respectively.

Table II

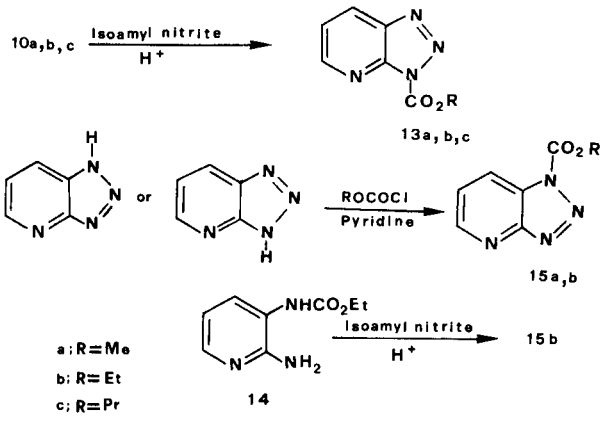
Spectral Data for N^2-Acyl-N^3-benzyloxycarbonyl-2,3-diaminopyridines **5a,b** and **9a-c**

	^{1}H-NMR (δ)				
	Pyridine Protons [a]				
Compound	α-H	β-H	γ-H	Other Signals	IR, cm^{-1}
5a	8.06	7.18	8.33	2.15 (3H, s, OCH_3), 5.19 (2H, s, OCH_2-Ph), 7.27-7.53 (5H, m, aromatic), 8.71 and 10.29 (2H, two s, two NH)	3200, 1730, 1635
5b	8.00	7.12	8.33	5.18 (2H, s, OCH_2), 7.25-7.58 (8H, m, aromatic), 8.73 and 9.81 (2H, two s, two NH)	3231, 1720, 1662, 1611
9a	8.13	7.17	8.31	3.81 (3H, s, OCH_3), 5.23 (2H, s, OCH_2-Ph), 7.23-7.51 (5H, m, aromatic), 8.61 and 9.33 (2H, two s, two NH)	3188, 1735, 1714, 1607
9b	8.19	7.17	8.31	1.27 (3H, t, J = 7.5 Hz, CH_2-CH_3), 4.25 (2H, q, J = 7.5 Hz, CH_2-CH_3), 5.21 (2H, s, OCH_2-Ph), 7.28-7.53 (5H, m, aromatic), 8.68 and 9.47 (2H, two s, two NH)	3170, 1732, 1712, 1605
9c	8.20	7.17	8.33	0.92 (3H, t, J = 7.5 Hz, CH_2-CH_3), 1.67 (2H, m, CH_2-CH_3), 4.17 (2H, t, J = 6 Hz, OCH_2-CH_2), 5.20 (2H, s, OCH_2-Ph), 7.30-7.56 (5H, m, aromatic), 8.73 and 9.50 (2H, two s, two NH)	3181, 1729, 1713, 1605

[a] *Ortho* (α-H), *meta* (β-H) and *para* (γ-H) protons occur as double doublets ($J_{\alpha,\beta}$ = 5 Hz, $J_{\beta,\gamma}$ = 8.5 Hz, $J_{\alpha,\gamma}$ = 1.5 Hz); the poorly resolved α-H signal of **9a-c** appears as a broad doublet; the α-H signal is superimposed on two aromatics in **5b**.

chloroformates or corresponding anhydrides gave, as largely predominant isomers, 1-substituted triazolides **15** (Scheme 5).

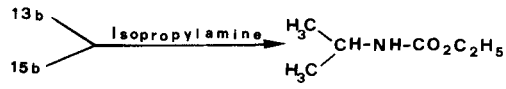
Scheme 5



Isomers **13** and **15** can be distinguished by nmr on the basis of the characteristic chemical shifts of their pyridinic protons. The 5-H and 6-H signals of the 1-derivatives occur respectively at slightly higher and lower field than those of 3-isomers.

The nearly complete conversion of **13b** to the more stable isomer **15b** under the usual acylation conditions (equimolar amount of ethyl chloroformate was in this case employed) suggests a thermodynamic control on the product distribution. Hence, an initial attack of the reagent at the 3-*N* atom of triazole ring cannot be ruled out. In two preliminary experiments **13b** and **15b** were added to deuteriochloroform solutions of isopropylamine and the reaction outcomes monitored by ^{1}H nmr. Although both isomers were found active as acylating reagents, **13b** led to ethyl *N*-isopropylcarbamate faster. This different reactivity agrees with the previous observation on the stability of the condensed triazolides **13** and **15**.

Scheme 6



Further investigations on the properties of this class of compounds are in progress.

Table III

Physical and Analytical Data of N^2-Acyl-2,3-diaminopyridines **7a,b** and **10a-c**

Compound	Time [a]	Mp, °C Crystallization Solvent [b]	Formula	Analyses % Calcd./Found C	H	N
7a	5	142-143	$C_7H_9N_3O$	55.61	6.00	27.80
		EA		55.49	6.01	27.89
7b	24	179-180	$C_{12}H_{11}N_3O$	67.59	5.20	19.71
		EA		67.65	5.29	19.80
10a	3	113	$C_7H_9N_3O_2$	50.29	5.43	25.14
		E		50.02	5.43	24.83
10b	0.5	136-137	$C_8H_{11}N_3O_2$	53.03	6.12	23.19
		EA		52.93	6.10	23.19
10c	3	105-106	$C_9H_{13}N_3O_2$	55.37	6.71	21.53
		E		55.19	6.64	21.49

[a] Hours required for complete remotion of benzyloxycarbonyl group. [b] Crystallization solvents: EA = ethyl acetate; E = ether.

Table IV

Spectral Data for N^2-Acyl-2,3-diaminopyridines **7a,b** and **10a-c**

	^{1}H-NMR (δ) [a] Pyridine Protons [b]				
Compound	α-H	β-H	γ-H	Other Signals	IR, cm^{-1}
7a	7.79	7.19		2.15 (3H, s, OCH_3)	3220, 1675
7b	7.79	7.18		7.47-7.69 (3H, m, aromatic), 8.10 (2H, m, aromatic)	3147, 1648, 1602
10a	7.87	7.07		3.77 (3H, s, OCH_3)	3420, 1711, 1616
10b	7.73	7.16		1.27 (3H, t, J = 7 Hz, CH_2-CH_3), 4.22 (2H, q, J = 7 Hz, CH_2-CH_3)	3420, 1690, 1622
10c	7.92	7.06		0.93 (3H, t, J = 7 Hz, CH_2-CH_3), 1.69 (2H, m, CH_2-CH_3), 4.13 (2H, t, J = 6.5 Hz, O-CH_2)	3429, 1698, 1620

[a] Methanol-d_4 solutions for **7a** and **10b**; DMSO-d_6 solution for **7b**. [b] α-H appears as double doublet; β-H resonates at slightly higher field than γ-H, and the mid point of the resulting 8 lines system is given.

Table V

Physical and Analytical Data of Alkylaminopyridines **3**, **4**, **6a**, **6b**, **8a**, **8b**, and **12**

Compound	Yield %	Mp, °C [a] Crystallization Solvent [b]	Formula	Analyses % Calcd./Found C	H	N
3	91	120-121 (124-125) [c] E				
4	83	93-94 (97.5-98.5) [d] B-LP				
6a	98	115 E-LP	$C_8H_{13}N_3$	63.54 63.51	8.67 8.66	27.79 27.70
6b	92	68-70 E-LP	$C_{13}H_{15}N_3$	73.21 73.24	7.09 7.17	19.70 19.69
8a	91 [e]	98-99 (106-107) [f] LP (bp 60-80°)				
8b	90 [e]	84-86 (89.5-90.5) [g] H				
12	91 [e]	97 (101) [h] LP (bp 60-80°)				

[a] The values in parentheses refer to determination with a Kofler hot stage apparatus. [b] Crystallization solvents: E = ether; B = benzene; LP = light petroleum; H = *n*-hexane. [c] Lit [1b] mp 124-125°. [d] Lit [2b] mp 97.8-98.2°. [e] Yields calculated from weights of nearly homogeneous (tlc and nmr) residues. [f] Lit [6] mp 103-106°. [g] Lit [6] mp 87-90°. [h] Lit [1a] mp 100-101°.

Table VI

Spectral Data for Alkylaminopyridines **3**, **4**, **6a**, **6b**, **8a**, **8b** and **12**

	^{1}H-NMR (δ) [a]				
	Pyridine Protons [b]				
Compound	α-H	β-H	γ-H	Other Signals	IR, cm^{-1}
3	7.37	6.70		2.77 (3H, s, CH_3)	3317, 1614, 1448
4	7.77	6.70		2.78 and 2.98 (6H, two s, two CH_3)	3383, 1613, 1406,
6a	7.75	6.69		1.19 (3H, t, J = 7.5 Hz, $CH_2C\mathit{H}_3$), 2.77 (3H, s, NH-CH_3), 3.45 (2H, q, J = 7.5 Hz, CH_2-CH_3)	3358, 1617, 1461
6b	7.77	6.73		2.73 (3H, s, NH-CH_3), 4.60 (2H, s, CH_2-Ph), 7.21-7.43 (5H, m, aromatic)	3417, 1603, 1413
8a	7.78	6.49	6.82	1.21 (3H, t, J = 7.5 Hz, CH_2-CH_3), 3.48 (2H, q, J = 7.5 Hz, CH_2-CH_3)	3378, 1606, 1468
8b	7.82	6.55	6.85	4.64 (2H, br s, CH_2-Ph), 7.25-7.65 (5H, m, aromatic)	3335, 1608, 1513
12	7.83	6.53	6.86	2.97 (3H, s, NH-CH_3)	3373, 1612, 1414

[a] Methanol-d_4 solution for **3**. [b] Signals for **8a**, **8b** and **12** appear as double doublets; compounds **3**, **4**, **6a**, and **6b** show resonance patterns similar to those reported in Table IV.

Table VII

Physical and Analytical Data of 3- and 1-Alkoxycarbonyl-*v*-triazolo[4,5-*b*]pyridines **13a-c** and **15a,b**

Compound	Mp, °C Crystallization Solvent [a]	Formula	Analyses % Calcd./Found C	H	N
13a	127-128	$C_7H_6N_4O_2$	47.19 47.20	3.39 3.43	31.45 31.58
13b	120-121	$C_8H_8N_4O_2$	49.99 49.89	4.20 4.25	29.16 29.11
13c	57-58	$C_9H_{10}N_4O_2$	52.42 52.24	4.89 4.92	27.17 27.05
15a	112-114	$C_7H_6N_4O_2$	47.19 47.00	3.39 3.39	31.45 31.24
15b	104-105	$C_8H_8N_4O_2$	49.99 49.95	4.20 4.26	29.16 29.05

[a] All the products were crystallized from ether.

Table VIII

Spectral Data for 3- and 1-Alkoxycarbonyl-*v*-triazolo[4,5-*b*]pyridines **13a-c** and **15a,b**

	^{1}H-NMR (δ)				
	Pyridine Protons [a]				
Compound	α-H	β-H	γ-H	Other Signals	IR, cm^{-1}
13a	8.95	7.54	8.54	4.28 (3H, s, OCH_3)	1772, 1589
13b	8.95	7.54	8.54	1.56 (3H, t, J = 7.5 Hz, CH_2-CH_3), 4.77 (2H, q, J = 7.5 Hz, CH_2-CH_3)	1768, 1596, 1586
13c	8.95	7.54	8.54	1.08 (3H, t, J = 7.5 Hz, CH_2-CH_3), 1.96 (2H, m, CH_2-CH_3), 4.63 (2H, t, J = 6.5 Hz, O-CH_2)	1760, 1596, 1589
15a	8.88	7.67	8.53	4.28 (3H, s, OCH_3)	1780, 1593, 1583
15b	8.88	7.67	8.53	1.57 (3H, t, J = 7.5 Hz, CH_2-CH_3), 4.74 (2H, q, J = 7.5 Hz, CH_2-CH_3)	1755, 1592, 1582

[a] All these signals appear as double doublets.

EXPERIMENTAL

Melting points were determined with a Büchi oil bath apparatus and are uncorrected. Infrared spectra (potassium bromide) were recorded with Perkin-Elmer 521 and 983 spectrophotometers. The ^{1}H nmr spectra were measured with a Varian EM-390 spectrometer using, unless otherwise specified, deuteriochloroform as the solvent (TMS as the internal standard). The coupling constants of resolved pyridinic signals for all described compounds are those reported at footnote of Table II. Mass spectra were obtained using a Hewlett-Packard 5890A spectrometer at 70 eV, m/e (M^+) of all the reported compounds were in satisfactory agreement with the assigned structures. Merck silica gel 60 (230-400 mesh) was used for column chromatography; preparative layer chromatography (plc) was carried out with Merck F_{254} silica gel (layers 0.5 mm thick). Light petroleum refers to the 40-60° bp fraction, unless otherwise specified. The drying agent used was sodium sulfate. Dry pyridine and tetrahydrofuran (THF) were used.

Reaction of DAP with Benzyl Chloroformate.

To a stirred suspension of DAP (0.44 g, 4 mmoles) in THF (10 ml) and pyridine (1 ml), cooled at 0°, benzyl chloroformate (1 ml, 7 mmoles) was added dropwise. After stirring at 0° for 15 minutes and at room temperature for 3 hours, ethyl acetate was added in excess. The organic solution was washed with water, dried and evaporated under vacuum. The residue was chromatographed on a column of silica (1:50). Elution with dichloromethane-ethyl acetate (9:1 and 7:3) gave 0.23 g (15%) of N^2,N^3-dibenzyloxycarbonyl-2,3-diaminopyridine (**2**), mp 127-128° (ether); ir: 3323, 1732, 1709, 1605 cm^{-1}; nmr: δ 5.20 (4H, s, two O-CH_2-Ph), 7.07 (1H, dd, 5-H), 7.33-7.50 (10H, m, aromatic), 8.03 (1H, br d, 6-H), 8.26 (1H, dd, 4-H), 8.59 and 9.38 (2H, two s, two NH).

Anal. Calcd. for $C_{21}H_{19}N_3O_4$: C, 66.83; H, 5.07; N, 11.14. Found: C, 66.59; H, 5.05; N, 11.19.

Further elution with dichloromethane-ethyl acetate (1:2) afforded 0.58 g (60%) of N^3-benzoyloxycarbonyl-2,3-diaminopyridine (**1**), mp 182-183° (ethyl acetate); ir: 3457, 3309, 1703, 1624 cm^{-1}; nmr (DMSO-d_6): δ 5.16 (2H, s, O-CH_2-Ph), 6.57 (1H, dd, 5-H), 7.33-7.57 (5H, m, aromatic), 7.67 (1H, dd, 4-H), 7.79 (1H, dd, 6-H), 8.86 (1H, s, NH-COO).

Anal. Calcd. for $C_{13}H_{13}N_3O_2$: C, 64.18; H, 5.39; N, 17.28. Found: C, 64.31; H, 5.39; N, 17.17.

Acylation of **1** with Acetic or Benzoic Anhydride.

A mixture of **1** (1 mmole) and acetic anhydride (10 mmoles) in pyridine (4 ml) was stirred overnight at room temperature. The resulting solution was poured into crushed ice and ethyl acetate was added. The organic phase was washed with water to neutrality, dried and evaporated under *vacuum* to yield pure N^2-acetyl-N^3-benzyloxycarbonyl-2,3-diaminopyridine (**5a**). In the case of benzoyl derivative **5b** the acylation of **1** was performed at 50° with 3 mmoles of benzoic anhydride, and the ethyl acetate solution was washed with saturated aqueous sodium carbonate and water. Column chromatography on silica (1:50) [dichloromethane-ether (9:1) as eluant] allowed the separation of pure **5b** from residual benzoic anhydride.

Syntheses of N^2-Alkoxycarbonyl-N^3-benzyloxycarbonyl-2,3-diaminopyridines **9a,b,c**.

Method A.

To a stirred suspension of **1** (0.5 mmole) in THF (3 ml) and pyridine (0.32 ml), cooled at 0°, methyl chloroformate (2 mmoles) was added dropwise. After stirring at 0° for 2 hours, ethyl acetate was added and the organic phase was washed with water, dried and evaporated under *vacuum*. The residue was chromatographed on a column of silica (1:50). Elution with dichloromethane-ether (9:1) afforded pure N^3-benzyloxycarbonyl-N^2-methoxycarbonyl-2,3-diaminopyridine (**9a**). In the case of **9b**, 1 mmole of **1**, 5 ml of THF, 0.24 ml of pyridine and 1.5 mmoles of ethyl chloroformate were used. The mixture was stirred at 0° for 15 minutes and at room temperature for 3 hours, and then worked up as above.

Method B.

Compound **2** (0.2 mmole) in dry ethanol or 1-propanol (6 ml) and acetic acid (0.12 ml) was refluxed for the appropriate period and evaporated under *vacuum* (2 ml of methanol and 0.04 ml of acetic acid were employed to yield **9a**). The residue arising from *n*-propanol treatment was chromatographed on silica column (1:50), eluting with dichloromethane-ether (9:1) to yield pure **9c**, and with dichloromethane-ether (7:3) to separate 1-benzyloxycarbonyl-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-one (**11**) (17%), mp 186-187° (methanol); ir: 3011, 1783, 1727, 1614 cm^{-1}; nmr (DMSO-d_6): δ 5.46 (2H, s, O-CH_2-Ph), 7.10 (1H, dd, 6-H), 7.36-7.66 (5H, m, aromatic), 7.93 (1H, dd, 7-H), 8.10 (1H, dd, 5-H).

Anal. Calcd. for $C_{14}H_{11}N_3O_3$: C, 62.45; H, 4.12; N, 15.61. Found: C, 62.35; H, 4.22; N, 15.47.

Chromatography of the residues on plc [dichloromethane-ether (8:2) as eluant] allowed the purification of **9a** and **9b**. In both the cases cyclization product **11** was not isolated, but detected by nmr in the more polar fractions.

Conversion of **9b** to **9c** was performed in the conditions employed for the **2** into **9c** transformation. Usual column chromatography afforded **9c** (70%) and **11** (24%).

Hydrogenolyses of N^3-Benzyloxycarbonyl-2,3-diaminopyridine Derivatives **5a,b** and **9a-c**.

A solution of the benzyl carbamate (0.2 g) in dichloromethane (8 ml) (dry ethanol in the case of **9b**) was subjected to catalytic hydrogenolysis, using 5% Pd on alumina as catalyst (0.05 g), for the appropriate period under standard conditions. Catalyst was removed by filtration through Celite. All the hydrogenolyzed compounds were obtained in quantitative yield, except for **7b** (90%).

Hydride Reduction of 2,3-Diaminopyridine Derivatives **1,2,5a,b**.

To a stirred suspension of a title compound (0.5 mmole) in dry ether (10 ml), cooled at 0°, LAH (4 mmoles) was carefully added. After stirring at room temperature for 2 hours, the excess of hydride was decomposed with the minimum amount of ethyl acetate and ice, cooling at 0°. The organic solution was separated by filtration, washing the solid residue with ethyl acetate. The monocarbamate **1** was treated with 2 mmoles of hydride, stirring for 3 hours. The alkylaminopyridines **3** [1b] and **6b** were separated from benzyl alcohol by the following work up. The filtered organic solution was extracted with 2*N* hydrochloric acid and then solid sodium carbonate was added to the collected aqueous layers, cooling at 0°. The basic aqueous phase was finally extracted with ethyl acetate to give pure **3** or **6b** after evaporation.

The alkylaminopyridines **4** [2b] and **6a** were isolated by plc [dichloromethane-methanol (95:5) as eluant] of the residues arising from filtered organic solutions.

Hydride Reduction of N^2-Acyl-2,3-diaminopyridines **7a,b** and **10a**.

To a stirred solution of N^2-acylaminopyridine (0.5 mmole) in dry THF (10 ml) LAH (2 mmoles) was carefully added, cooling at 0°. After refluxing for 30 minutes, the mixture was hydrolyzed as above. The filtered organic solutions were washed with water, dried and evaporated to yield nearly pure (tlc, nmr) N^2-alkylaminopyridines **8a,b** [6] or **12** [1a].

3-Alkoxycarbonyl-3*H*-*v*-triazolo[4,5-*b*]pyridines **13a-c**.

A suspension of N^2-alkoxycarbonyl-2,3-diaminopyridine **10a-c** (1 mmole) in THF (5 ml), acetic acid (0.05 ml) and isoamyl nitrite (1.5 mmoles) was refluxed for 2 hours and evaporated under *vacuum* to give pure title compound in quantitative yield.

1-Alkoxycarbonyl-1*H*-*v*-triazolo[4,5-*b*]pyridines **15a,b**.

To a stirred suspension of unsubstituted *v*-triazolo[4,5-*b*]pyridine [5b] (1 mmole) in THF (4 ml) and pyridine (0.4 ml), cooled at 0°, 2 mmoles of the appropriate acylating agent (methyl and ethyl chloroformate or corresponding anhydrides) were added. After stirring at 0° for 30 minutes and at room temperature for 1.5 hours, ethyl acetate was added in excess. The organic phase was washed with water, dried and evaporated under *vacuum*. All the acylations were quantitative, and afforded the title compounds **15a, b** containing traces of 3-*H* isomers, which were removed by crystallization. Compound **15b** was also obtained in quantitative yield from N^3-ethoxycarbonyl-2,3-diaminopyridine (**14**) [1b] *via* isoamyl nitrite as above.

Isomerization of **13b** to **15b**.

To a stirred solution of **13b** (0.2 mmole) in THF (0.8 ml) and pyridine (0.08 ml), cooled at 0°, ethyl chloroformate (0.2 mmole) was added. After stirring and working up as for triazolopyridine acylations, complete conversion to 1-substituted derivative **15b** was observed by ^{1}H nmr.

Reaction of Isomeric Ethoxycarbonyl-*v*-triazolo[4,5-*b*]pyridines **13b** and **15b** with Isopropylamine.

A solution of **13b** (0.2 mmole) and isopropylamine (0.02 ml) in deuteriochloroform (1 ml), containing a few drops of TMS, was stirred for 10 minutes at room temperature in a sealed flask and then filtered into a nmr tube. The spectrum of the reaction mixture, determined after 15 minutes *ab initio*, provided evidence for both the ethyl *N*-isopropylcarbamate formation (signals identical with those of an authentic sample [7], and the disappearance of the acylating agent. An analogous experiment, carried out with **15b**, gave similar results after 1 hour.

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