2,6-Disubstituted 4-Aminopyridines from 1,3-Dialkoxy-2-azapropenylium Salts and *N*-Methyl-4-piperidone Enamines☆

Richard Schleimer and Ernst-Ulrich Würthwein*

Organisch-Chemisches Institut der Universität Münster,
Corrensstraße 40, D-48149 Münster, Germany

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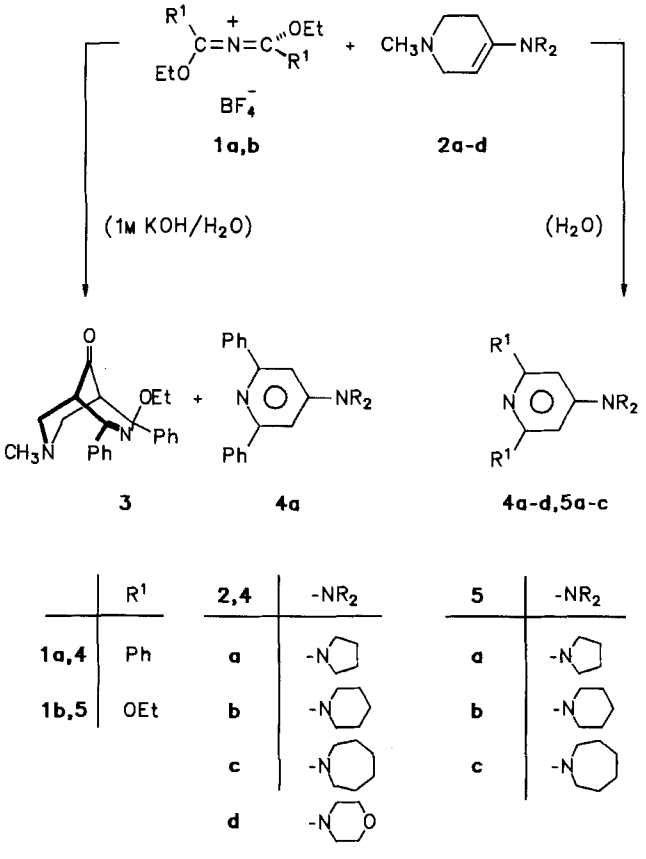
1,3-Dialkoxy-2-azapropenylium salts **1** react with enamines **2** of *N*-methyl-4-piperidone at room temperature to give 2,6-disubstituted 4-aminopyridines **4**, **5** in low to moderate yield after hydrolysis. Intermediates of the reaction of **1a** with **2** are the bicyclic iminium salts **6** and **7**, which may be detected ^{1}H-NMR spectroscopically prior to hydrolysis. Hydrolysis of the mixture obtained from the reaction of **1a** with **2a** under basic conditions furnishes the bicyclic ketone **3** as the major product. A "retro-Mannich"-type reaction is suggested to explain the degradation of the bicyclic intermediates **6**, **7** with the formation of the pyridines **4**, **5**.

Syntheses and structural properties of alkoxy-substituted 2-azapropenylium salts **1** have been recently reported from our laboratory[1]; we are currently investigating synthetic applications of these polyfunctional cationic C–N–C building blocks in heterocyclic and acyclic chemistry. Enamines[2] of cyclic ketones (with β′-CH groups) as „hidden" bisnucleophiles have been established as interesting reaction partners for the new biselectrophilic salts **1**. They lead via intermediate iminium salts after aqueous workup in good overall yield to differently substituted 3-azabicyclic ketones with variable ring sizes[3].

In addition to our previous paper[3] on the formation of 3-azabicyclic ketones from 1,3-dialkoxy-2-azapropenylium salts **1** and enamines of cyclic ketones we now report on a surprising and unexpected side reaction, which occurs if the salts **1** are treated with enamines **2** of *N*-methyl-4-piperidone at room temperature. The tetrafluoroborates **1** are easily accessible by oxonium salt alkylation of the appropriate *N*-acylimidate[4] (for **1a** see ref.[1c,e]) and the *N*-(dialkoxymethylene)carbamate[5] (for **1b** see ref.[1h]), resp. When a solution of the salt **1a** is stirred in the presence of a 4% excess of enamine **2a**, the typical intense C=N=C$^+$ cumulene IR absorption band disappears within several minutes. After hydrolytic workup under basic conditions (2M KOH, 12h) two compounds are isolated by fractional crystallization from the organic residue. Spectroscopic evidence clearly indicates the bicyclic ketone **3**[3,6] as the major product (80–90% crude yield; due to decomposition during the isolation only 28% yield of pure material). The less soluble material proves to be 2,6-diphenyl-4-pyrrolidinopyridine (**4a**), which is isolated in 6% yield. This surprising observation has prompted us to investigate the formation of such pyridines more deeply.



	R^1	2,4	$-NR_2$	5	$-NR_2$
1a,4	Ph	a	-N	a	-N
1b,5	OEt	b	-N	b	-N
		c	-N	c	-N
		d	-N O		

Additional experiments involving reaction of **1a** with the enamines **2b–d** have been carried out by using acidic conditions (1M HCl) for the hydrolysis. Thus, the 2,6-diphenyl-4-aminopyridines **4b–d** are easily isolated by crystallization in low to moderate yield (Table 1). Prior to hydrolysis, the characteristic signals of bicyclic iminium salts (like **6**,**7**) are

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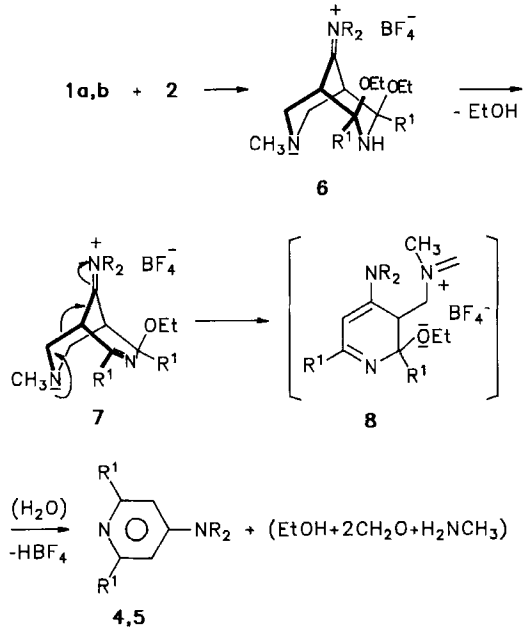
Table 1. Substitution patterns, yields, and physical properties of the pyridines **4**, **5**

	R^1	R_2	From	Hydrolysis	Yield (%)	mp. [°C] bp. [°C/Torr]
4a	Ph	$[CH_2]_4$	**1a, 2a**	1M KOH 1M HCl	6 34[a]	233
4b	Ph	$[CH_2]_5$	**1a, 2b**	1M HCl	21	208
4c	Ph	$[CH_2]_6$	**1a, 2c**	1M HCl	10	131-132
4d	Ph	$C_2H_4OC_2H_4$	**1a, 2d**	1M HCl	43	215
5a	OEt	$[CH_2]_4$	**1b, 2a**	$NaHCO_3$	30	27-34 90-120/0.6[b]
5b	OEt	$[CH_2]_5$	**1b, 2b**	$NaHCO_3$	19	80-120/0.4[b]
5c	OEt	$[CH_2]_6$	**1b, 2c**	$NaHCO_3$	26	90-130/0.05[b]
5d	OEt	$C_2H_4OC_2H_4$	**1b, 2d**	$NaHCO_3$	0	—

[a] Determined by ^{1}H-NMR integration. – [b] Bath temperature.

observed in the NMR spectra of the crude reaction mixtures.

Similarly, the reactions of the tetraalkoxy-2-azapropenylium salt **1b** with the enamines **2a–c** lead to the 2,6-dialkoxy-4-aminopyridines **5a–c**. In these cases hydrolysis with a satd. $NaHCO_3$ solution has proven to be the method of choice. Spectroscopic indications of the formation of bicyclic products (like **6**,**7**) prior to or after aqueous workup have not been obtained. In the case of the enamine **2d** the expected pyridine has not been found. The only product obtained is ethyl *N*-(diethoxymethylene)carbamate, which results from dealkylation of the salt **1b**, presumably by alkyl transfer to the enamine **2d**.



Inspection of the substitution patterns of the compounds **4**,**5** clearly reveals that the C2–N–C6 part of the pyridines has formerly been the 2-azapropenylium salt **1**, whereas the C3–C4–C5 chain of the pyridines originates from the enamines **2**. Therefore, the formation of **4**,**5** is mechanistically best described by a multistep process involving first a double electrophilic attack of the salt **1** in β and β′ position of the enamine leading to a 3-azabicyclic iminium salt **6** (compare ref.[3]). The detection of the ketone **3** as the product of *basic* hydrolysis of such an iminium salt **6** in the reaction mixture confirms this hypothesis. Furthermore, our results are best explained by the assumption that **6** or its ethanol elimination product **7** is subject to a rapid "retro-Mannich"-type reaction, opening the former piperidone ring. This possibly leads to an intermediate like **8**, which collapses to the stable pyridines **4**,**5**, accompanied by hydrolytic degradation of the remaining C–N(CH_3)–C unit. The NMR spectra of the crude reaction mixtures obtained by the reaction of **1a** with **2** clearly show the presence of such intermediates. For the reaction of **1a** with **2a** giving **4a** variations of the workup conditions have been studied. The pH of the solution used for the hydrolysis shows a significant influence on the yield of the pyridines **4**. Under basic conditions, rather low yields of pyridine **4a** (6–12%), but substantial amounts of ketone **3** (63–90%) are detected by ^{1}H-NMR spectroscopy. This indicates a preferred nucleophilic attack by OH^- at the iminium moiety of **6** or **7** leading to **3**. Acidic hydrolysis gives higher yields of the pyridine **4a** (25–34%) but no bicyclic product.

The intermediates **6** and **7** (R^1 = OEt) resulting from the salt **1b** are much less stable, even in the absence of water; NMR-spectroscopic indications of their existence prior to or after hydrolysis have not been obtained.

The formation of pyridines from *N*,*N*′-dichloro-3,7-diazabicyclo[3.3.1]nonanes under strong basic conditions is described by Quast and Müller[7]; a similar "retro-Mannich" mechanism as in our case may have been operative.

In conclusion, the unexpected formation of the pyridines **4**,**5** seems to be the consequence of several equilibria leading to the pyridines as the thermodynamically most stable products via bicyclic intermediates like **6–8**. The inherent instability of the intermediate iminium salts **6**,**7** (iminium analogous of Mannich bases) is a prerequisite for the degradation process, which has not been observed with enamines of cyclic ketones[3], but exclusively with enamines of 4-piperidone.

4-Aminopyridines have found use as very active acylation catalysts in organic synthesis[8] and have been investigated for their use as complexones[9] as well as for their properties in non-coordinating buffer solutions[10].

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Experimental

IR: Perkin-Elmer PE 298. – ^{1}H NMR: Bruker WM 300 (300 MHz), internal reference tetramethylsilane. – ^{13}C NMR: Bruker WM 300 (75.47 MHz), internal reference the corresponding solvent. – MS: Finnigan MAT C 312. – CHN analyses: Perkin Elmer CHN Analysator 240. – Melting points are not corrected. – All solvents are carefully purified and dried by standard methods. All experiments are carried out with the exclusion of moisture (Ar).

For the synthesis of the 2-azapropenylium salts **1a**, see ref.[1c,e], for that of **1b** see ref.[1h]. For the synthesis of the enamines **2a** see ref.[11], for **2b,d**[12] see ref.[13] (azeotropic distillation according to Stork et al.).

4-(1-Azepanyl)-1,2,3,6-tetrahydro-1-methylpyridine (**2c**): 7.71 g (50 mmol) of *N*-Methyl-4-piperidinone and 7.44 g (75 mmol) of azepane are dissolved in toluene (30 ml); the solution is refluxed for 10 h by using a Dean-Stark trap. After removal of the toluene in vacuo and distillation of the residue under reduced pressure a colorless oil is obtained. Yield 7.42 g (76%), b.p. 98°C/0.6 Torr. – ^{1}H NMR ($CDCl_3$): δ = 1.53 (m, 4H), 1.63 (m, 4H, azepanyl-3-H_2/4-H_2/5-H_2/6-H_2), 2.32 (m, 5H, CH_3N, HC=CCH_2), 2.55 (m, 2H), 2.99 (m, 2H, CH_3NCH_2), 3.16 (m, 4H, CH_2NCH_2), 4.23 (t, ^3J = 3.6 Hz, 1H, HC=C). – ^{13}C NMR ($CDCl_3$): δ = 26.77 (azepanyl-C-4/-5), 27.04 (HC=CCH_2), 28.56 (azepanyl-C-3/-6), 45.45 (CH_3N), 48.51 (CH_2NCH_2), 52.46, 54.42 (CH_3N-CH_2), 88.98 (HC=C), 140.61 (HC=*C*). – IR (Film): ṽ = 3040 (w) cm^{-1}, 2910, 2845, 2775 (s), 2670 (m, C–H, aliph.), 1640 (s, C=N), 1465, 1445 (s), 1425 (m), 1405, 1375 (s), 1335 (m). – MS, *m/z* (%): 195 (5) [M^+ + H], 194 (21) [M^+], 193 (100) [M^+ – H], 179 (3), 150 (4), 136 (5), 108 (6), 97 (6), 96 (40). – $C_{12}H_{22}N_2$ (194.3): calcd. C 74.17, H 11.41, N 14.42; found C 74.06, H 11.61, N 14.50.

(1a,4a,5a)-4-Ethoxy-7-methyl-2,4-diphenyl-3,7-diazabicyclo-[3.3.1]non-2-en-9-one (**3**) *and 2,6-diphenyl-4-pyrrolidinopyridine* (**4a**): A solution of 3.69 g (10 mmol) of **1a** in 1,2-dichloroethane (20 ml) is cooled to –35°C and treated with 1.75 g (10.5 mmol) of **2a** with stirring. After 10 min the reaction mixture is allowed to warm up to room temp. and then stirred for additional 30 min. It is subsequently hydrolyzed by addition of 20 ml of 2 M KOH with stirring for 12 h. After addition of 100 ml of water the layers are separated. The aqueous layer is extracted with dichloromethane. The combined organic layers are dried with $MgSO_4$. After removal of the solvent repeated fractional crystallization of the residue from acetone gives **4a** as a less soluble yellow solid; yield 0.19 g (0.63 mmol, 6%), m.p. 233°C. – The main product (28%) of this reaction is **3**; for its physical and spectroscopic data, see **10d** in ref.[3]. If 1 M HCl instead of 2 M KOH is used for the hydrolysis **4a** is isolated in 34% yield as the sole product. **4a**: ^{1}H NMR ($CDCl_3$): δ = 2.04 (m, 4H, pyrrolidine-3-H_2/4-H_2), 3.42 (m, 4H, CH_2NCH_2), 6.78 (s, 2H, pyridine-H), 7.32–7.51 (m, 6H, *m*-, *p*-H), 8.09 (m, 4H, *o*-H). – ^{13}C NMR (CD_3NO_2): δ = 25.72 (pyrrolidine-C-3/-4), 47.66 (CH_2NCH_2), 102.71 (pyridine-*C*H), 127.34, 128.79 (*o*-, *m*-C), 128.79 (*p*-C), 141.15 (*i*-C), 153.83 (pyridine-C-4), 157.22 (pyridine-C-2/-6). – IR (KBr): ṽ = 3045 (w, C–H arom.) cm^{-1}, 2955, 2845 (m, C–H aliph.), 1615, 1610 (s), 1595, 1575 (m), 1530 (s, C=C, C=N arom.), 1495 (m), 1480 (w), 1450, 1435, 1425, 1355 (m), 1265, 1235, 1175, 1155, 1120, 1075 (w), 1030, 1000 (m). – MS, *m/z* (%): 301 (32) [M^+ + H], 300 (100) [M^+], 299 (58) [M^+ – H], 273 (19), 272 (83) [M^+ – C_2H_4], 271 (82) [M^+ – C_2H_5], 245 (36), 231 (48), 230 (22) [M^+ – pyrrolidine], 195 (10), 167 (12), 150 (29), 149 (23), 129 (25), 127 (74), 115 (35), 114 (22), 77 (40). – $C_{21}H_{20}N_2$ (300.4): calcd. C 83.96, H 6.71, N 9.32; found C 83.90, H 6.60, N 9.21.

Synthesis of the 4-Amino-2,6-diphenylpyridines **4b–d**. – *General Procedure:* To a solution of 1.85 g (5 mmol) of salt **1a** in 20 ml of dichloromethane 5.2 mmol of enamine **2** is added at room temp. with vigorous stirring by means of a syringe. After 8 h the reaction mixture is hydrolyzed with stirring with 10 ml of 1 N HCl for 10 min. The aqueous layer is adjusted to weakly basic pH by dropwise addition of 1 N NaOH and a satd. $NaHCO_3$ solution. After addition of 50 ml of water the organic layer is separated and washed with dichloromethane. The combined organic layers are dried with $MgSO_4$.

2,6-Diphenyl-4-piperidinopyridine (**4b**): From **1a** and **2b** (0.94 g, 5.2 mmol). Recrystallization from acetone yields **4b** as a colorless solid. Yield 0.33 g (1.1 mmol, 21%), m.p. 208°C. – ^{1}H NMR ($CDCl_3$): δ = 1.69 (s, 6H, piperidine-3-H_2/4-H_2/5-H_2), 3.46 (s, 4H, CH_2NCH_2), 7.09 (s, 2H, pyridine-H), 7.35–7.53 (m, 6H, *m*-, *p*-H), 8.07 (m, 4H, *o*-H). – ^{13}C NMR ($CDCl_3$): δ = 24.33 (piperidine-C-4), 25.18 (piperidine-C-3/-5), 47.77 (CH_2NCH_2), 104.20 (pyridine-*C*H), 127.05, 128.37, 128.42 (*o*-, *m*-, *p*-C), 140.70 (*i*-C), 156.81 (pyridine-C-4), 157.83 (pyridine-C-2/-6). – IR (KBr): ṽ = 3040 (vw, C–H arom.) cm^{-1}, 2930, 2910, 2840 (w, C–H aliph.), 1600, 1590 (s), 1570, 1525 (m, C=C, C=N arom.), 1490, 1445, 1420, 1380, 1355, 1235, 1175 (m), 1150 (w), 1125, 1070, 1025 (m). – MS, *m/z* (%): 315 (40) [M^+ + H], 314 (94) [M^+], 313 (99) [M^+ – H], 286 (31) [M^+ – C_2H_4], 285 (50) [M^+ – C_2H_5], 259 (57), 231 (81), 230 (36), 160 (38), 149 (77), 147 (35), 127 (100), 81 (53), 78 (28). – $C_{22}H_{22}N_2$ (314.4): calcd. C 84.04, H 7.05, N 8.91; found C 83.77, H 7.05, N 8.93.

4-(1-Azepanyl)-2,6-diphenylpyridine (**4c**): From **1a** and **2c** (1.10 g, 5.2 mmol). Recrystallization from acetone yields **4c** as a light yellow solid. Yield 0.16 g (0.49 mmol, 10%), m.p. 131–132°C. – ^{1}H NMR ($CDCl_3$): δ = 1.59 (m, 4H, azepanyl-4-H_2/5-H_2), 1.86 (s, br., 4H, azepanyl-3-H_2/6-H_2), 3.60 (m, 4H, CH_2NCH_2), 6.92 (s, 2H, pyridine-H), 7.36–7.51 (m, 6H, *m*-, *p*-H), 8.07 (m, 4H, *o*-H). – ^{13}C NMR ($CDCl_3$): δ = 26.81, 27.30 (azepanyl-C-3/-4/-5/-6), 48.97 (CH_2NCH_2), 101.86 (pyridine-*C*H), 127.17, 128.35, 128.37 (*o*-, *m*-, *p*-C), 140.99 (*i*-C), 154.66 (pyridine-C-4), 157.70 (pyridine-C-2/-6). – IR (KBr): ṽ = 3040 (w, C–H arom.) cm^{-1}, 2900, 2840 (m, C–H aliph.), 1600, 1590 (s), 1570, 1525 (m, C=C, C=N arom.), 1490, 1425, 1385 (m), 1285 (w), 1255, 1235, 1190, 1170 (m), 1150, 1130, 1100 (w), 1070, 1020 (m), 1000 (w). – MS, *m/z* (%): 329 (81) [M^+ + H], 328 (100) [M^+], 327 (75) [M^+ – H], 313 (65), 299 (89) [M^+ – C_2H_5], 285 (91), 272 (77), 259 (80), 231 (81), 230 (75), 196 (66), 149 (71), 128 (78), 127 (98), 115 (74), 104 (80), 77 (83). – $C_{21}H_{20}N_2O$ (328.5): calcd. C 84.11, H 7.36, N 8.53; found C 83.99, H 7.34, N 8.47.

4-Morpholino-2,6-diphenylpyridine (**4d**): From **1a** (1.47 g, 4.0 mmol) and **2d** (0.75 g, 4.2 mmol) after stirring for 15 h. Recrystallization from acetone yields **4d** as yellow rods. Yield 0.54 g (1.71 mmol, 43%), m.p. 215°C. – ^{1}H NMR ($CDCl_3$): δ = 3.41 (m, 4H, CH_2NCH_2), 3.89 (m, 4H, CH_2OCH_2), 7.09 (s, 2H, pyridine-H), 7.40–7.49 (m, 6H, *m*-, *p*-H), 8.08 (m, 4H, *o*-H). – ^{13}C NMR ($CDCl_3$): δ = 46.72 (CH_2NCH_2), 68.43 (CH_2OCH_2), 104.08 (pyridine-*C*H), 127.09, 128.47 (*o*-, *m*-C), 128.71 (*p*-C), 140.18 (*i*-C), 157.01 (pyridine-C-4), 157.88 (pyridine-C-2/-6). – IR (KBr): ṽ = 3050 (w, C–H arom.) cm^{-1}, 2980, 2910, 2875 (w, C–H aliph.), 1605, 1595 (s), 1575 (m), 1540 (s, C=C, C=N arom.), 1495, 1445 (m), 1425 (s), 1380, 1370, 1280 (w), 1230 (s), 1175, 1165 (w), 1120 (s), 1080 (s), 1070, 1060 (w), 1030 (m). – MS, *m/z* (%): 317 (36) [M^+ + H], 316 (99) [M^+], 301 (18) [M^+ – CH_3], 286 (40) [M^+ – CH_2O], 285 (26), 260 (16), 259 (57), 258 (45), 232 (32), 231 (100), 230 (54) [M^+ – morpholine], 203 (7), 202 (7), 154 (10), 136 (25), 129 (22), 128 (34), 127 (54), 126 (15), 115 (42), 114 (33), 104 (12), 102 (17), 101 (22), 78 (13), 77 (45). – $C_{21}H_{20}N_2O$ (316.4): calcd. C 79.72, H 6.37, N 8.85; found C 79.50, H 6.39, N 9.12.

Synthesis of the 4-Amino-2,6-diethoxypyridines **5a–c**. – *General Procedure:* To 1.52 g (5.0 mmol) of salt **1b** in 20 ml of dichloromethane 5.2 mmol of the corresponding enamine **2** is added at room temp. with vigorous stirring by means of a syringe. The reaction mixture is stirred for 3 h and afterwards hydrolyzed with 10 ml of a satd. $NaHCO_3$ solution. The aqueous layer is removed after 3 h, and the residue is extracted with dichloromethane. After drying of the combined organic layers with $MgSO_4$, the solvent is removed

in vacuo. The oily residue is dissolved in diethyl ether, and the solution is filtered from basic alumina. The filtrate is concentrated in vacuo. Workup of the residue is continued as indicated.

2,5-Diethoxy-4-pyrrolidinopyridine (**5a**): From **1b** and **2a** (0.86 g, 5.2 mmol). Kugelrohr distillation at 90–120°C (0.6 Torr) yields a colorless liquid, which solidifies after a short period of time to give large, colorless plates. Yield 0.36 g (1.52 mmol, 30%), m.p. 27–34°C. – ^{1}H NMR ($CDCl_3$): δ = 1.36 (t, ^3J = 7.1 Hz, 6H, OCH_2CH_3), 1.97 (m, 4H, pyrrolidine-3-H_2/4-H_2), 3.26 (m, 4H, CH_2NCH_2), 4.27 (q, ^3J = 7.1 Hz, 4H, OCH_2CH_3), 5.48 (s, 2H, pyridine-H). – ^{13}C NMR ($CDCl_3$): δ = 14.73 (OCH_2CH_3), 25.14 (pyrrolidine-C-3/-4), 47.10 (CH_2NCH_2), 61.17 (OCH_2CH_3), 84.39 (pyridine-CH), 156.33 (pyridine-C-4), 163.41 (pyridine-C-2/-6). – IR (KBr): $\tilde{\nu}$ = 1610 (s) cm^{-1}, 1545 (s, C=C, C=N arom.), 1495, 1480, 1375, 1345, 1300, 1285, 1240, 1220, 1170, 1110, 1090, 1060 (s), 1040, 1015 (m). – MS, *m/z* (%): 236 (35) [M^+], 221 (35) [$M^+ - CH_3$], 208 (23) [$M^+ - C_2H_4$], 193 (44), 179 (37), 169 (46), 143 (39), 141 (45), 130 (35), 114 (55), 113 (62), 98 (71), 85 (75), 84 (68), 71 (80), 70 (100). – $C_{13}H_{20}N_2O_2$ (236.3): calcd. C 66.07, H 8.53, N 11.85; found C 66.13, H 8.80, N 12.04.

2,5-Diethoxy-4-piperidinopyridine (**5b**): From **1b** and **2b** (0.94 g, 5.2 mmol). Kugelrohr distillation at 80–120°C (0.4 Torr) yields a light yellow oil (0.36 g). Preparative HPLC (eluent *n*-hexane/ethyl acetate, 5:1) gives pure **5b** (colorless oil). Yield 0.24 g (0.95 mmol, 19%), t_R = 4.5–6 min (*n*-hexane/ethyl acetate, 5:1; flow rate 10 ml/min). – ^{1}H NMR ($CDCl_3$): δ = 1.35 (t, ^3J = 7.1 Hz, 6H, OCH_2CH_3), 1.66 (m, 6H, piperidine-3-H_2/4-H_2/5-H_2), 3.26 (m, 4H, CH_2NCH_2), 4.26 (q, ^3J = 7.1 Hz, 4H, OCH_2CH_3), 5.74 (s, 2H, pyridine-H). – ^{13}C NMR ($CDCl_3$): δ = 14.77 (OCH_2CH_3), 24.44 (piperidine-C-4), 25.03 (piperidine-C-3/-5), 47.93 (CH_2NCH_2), 61.28 (OCH_2CH_3), 86.25 (pyridine-CH), 159.85 (pyridine-C-4), 163.99 (pyridine-C-2/-6). – IR (Film): $\tilde{\nu}$ = 2965 cm^{-1}, 2920, 2840, 2800 (s, C–H aliph.), 1605 (s), 1540 (s, C=C, C=N arom.), 1425, 1375, 1345, 1300, 1225, 1200, 1120, 1090, 1060, 1020 (s). – MS: *m/z* (%): 251 (44) [M^+ + H], 250 (100) [M^+], 249 (40) [M^+ – H], 235 (97) [$M^+ - CH_3$], 222 (62) [$M^+ - C_2H_4$], 221 (45) [$M^+ - C_2H_5$], 207 (88), 193 (95), 122 (51), 110 (52), 97 (57), 84 (99), 70 (83). – $C_{14}H_{22}N_2O_2$ (250.3): calcd. C 67.17, H 8.86, N 11.19; found C 66.99, H 8.91, N 11.48.

4-(1-Azepanyl)-2,5-diethoxypyridine (**5c**): From **1b** and **2c** (1.01 g, 5.2 mmol). Distillation at an oil bath temp. of 90–130°C (0.05 Torr) gives **5c** in pure form. Colorless oil; yield: 0.34 g (1.29 mmol, 26%). – ^{1}H NMR ($CDCl_3$): δ = 1.36 (t, ^3J = 7.1 Hz, 6H, OCH_2CH_3), 1.52 (m, 4H, azepanyl-4-H_2/5-H_2), 1.74 (m, 4H, azepanyl-3-H_2/6-H_2), 3.39 (m, 4H, CH_2NCH_2), 4.27 (q, ^3J = 7.1 Hz, 4H, OCH_2CH_3), 5.59 (s, 2H, pyridine-H). – ^{13}C NMR ($CDCl_3$): δ = 14.66 (OCH_2CH_3), 26.60, 27.16 (azepanyl-C-3/-4/-5/-6), 48.94 (CH_2NCH_2), 60.99 (OCH_2CH_3), 83.73 (pyridine-CH), 157.62 (pyridine-C-4), 163.72 (pyridine-C-2/-6). – IR (Film): $\tilde{\nu}$ = 2985 cm^{-1}, 2920, 2845 (m, C–H aliph.), 1610 (s), 1540 (s, C=C, C=N arom.), 1495, 1430, 1380, 1310, 1260, 1230, 1205, 1150, 1110, 1090, 1065, 1030 (s). – MS, *m/z* (%): 265 (33) [M^+ + H], 264 (55) [M^+], 263 (59) [M^+ – H], 250 (46), 249 (60) [$M^+ - CH_3$], 236 (51) [$M^+ - C_2H_4$], 235 (65) [$M^+ - C_2H_5$], 221 (68), 207 (62), 149 (78), 135 (62), 98 (67), 97 (80), 85 (63), 84 (76), 70 (98), 69 (100). – $C_{15}H_{24}N_2O_2$ (264.4): calcd. C 68.15, H 9.15, N 10.60; found C 68.10, H 9.10, N 11.39.

Reaction of **1b** *with Enamine* **2d**: From **1b** and **2d** (0.95 g, 5.2 mmol). Even after a reaction period of 24 h no pyridine compound is detectable (^{1}H-NMR analysis) in the crude reaction mixture. After removal of the solvent the crude oil (0.57 g) is distilled (oil bath temp. up to 80°C, 0.05 Torr) to furnish ethyl *N*-(diethoxymethylene)carbamate as a colorless oil. Yield 0.37 g (2.00 mmol, 39%). – ^{1}H NMR ($CDCl_3$): δ = 1.30 (t, ^3J = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.33 [t, ^3J = 7.1 Hz, 6H, $C(OCH_2CH_3)_2$], 4.19 (q, ^3J = 7.1 Hz, 2H, $CO_2CH_2CH_3$), 4.26 [q, ^3J = 7.1 Hz, 4H, $C(OCH_2CH_3)_2$]. For a complete set of spectroscopic data, see ref.[5].

☆ Dedicated to Prof. D. Dr. *Ernst Würthwein* on the occasion of his 85th birthday.

[1] [1a] R. Kupfer, E.-U. Würthwein, *Tetrahedron Lett.* **1985**, *26*, 3547–3550. – [1b] R. Kupfer, E.-U. Würthwein, M. Nagel, R. Allmann, *Chem. Ber.* **1985**, *118*, 643–652. – [1c] E.-U. Würthwein, R. Kupfer, R. Allmann, M. Nagel, *Chem. Ber.* **1985**, *116*, 3632–3642. – [1d] R. Kupfer, E.-U. Würthwein, *Chem. Ber.* **1986**, *119*, 857–871. – [1e] E.-U. Würthwein, R. Kupfer, *Chem. Ber.* **1986**, *119*, 1557–1568. – [1f] M. Krestel, R. Kupfer, R. Allmann, E.-U. Würthwein, *Chem. Ber.* **1987**, *120*, 1271–1279. – [1g] R. Kupfer, M. Krestel, R. Allmann, E.-U. Würthwein, *Chem. Ber.* **1988**, *121*, 1657–1664. – [1h] R. Kupfer, S. Meier, E.-U. Würthwein, *Chem. Ber.* **1992**, *125*, 2487–2492.

[2] A. G. Cook, *Enamines: Synthesis, Structure, and Reactions*, 2nd Ed., Marcel Dekker, Inc., New York, **1988**; P. W. Hickmott, P. J. Cox, G. A. Sim, *J. Chem. Soc., Perkin Trans. 1*, **1974**, 2544–2548; P. W. Hickmott, J. R. Hargreaves, *Tetrahedron* **1967**, *23*, 3151–3159; P. W. Hickmott, G. J. Miles, G. Sheppard, R. Urbani, C. T. Yoxall, *J. Chem. Soc., Perkin Trans. 1*, **1973**, 1514–1519; P. W. Hickmott, M. G. Ahmed, S. A. Ahmed, S. Wood, M. Kapon, *ibid.* **1985**, 2559–2571.

[3] R. Schleimer, K. Hornig, M. H. Möller, E.-U. Würthwein, *Chem. Ber.* **1993**, *126*, 133–141.

[4] R. Allmann, R. Kupfer, M. Nagel, E.-U. Würthwein, *Chem. Ber.* **1984**, *117*, 1597–1605.

[5] R. Kupfer, E.-U. Würthwein, M. Krestel, R. Allmann, *Chem. Ber.* **1986**, *119*, 3236–3246.

[6] R. Schleimer, Dissertation, Universität Münster, **1991**.

[7] H. Quast, B. Müller, *Chem. Ber.* **1983**, *116*, 3931–3946.

[8] G. Höfle, W. Steglich, H. Vorbrüggen, *Angew. Chem.* **1978**, *90*, 602–615; *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 569.

[9] F. Vögtle, C. Ohm, *Chem. Ber.* **1984**, *117*, 948.

[10] E. Deutsch, N. K. V. Cheung, *J. Org. Chem.* **1973**, *38*, 1123–1126; K. T. Potts, P. A. Winslow, *Synthesis* **1987**, 839.

[11] S. Danishefsky, R. Cavanaugh, *J. Org. Chem.* **1968**, *33*, 2959–2962.

[12] S. A. Vartanynan, E. A. Abgaryan, *Arm. Khim. Zh.* **1984**, *37*, 316–323; *Chem. Abstr.* **1985**, *102*, 24435 w.

[13] G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, R. Terrell, *J. Am. Chem. Soc.* **1963**, *85*, 207–222.

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