Concave Reagents, 28[+]

Comparison of Bimacrocyclic, Monomacrocyclic, and Nonmacrocyclic Bis(amidomethyl)pyridines as Catalysts in the Base-Catalyzed Addition of Alcohols to Ketenes

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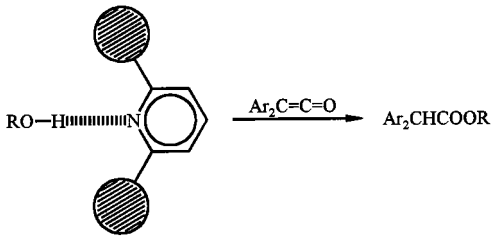
Nineteen new bimacrocyclic, monomacrocyclic, and nonmacrocyclic pyridines **1**–**6** bearing amide functions have been synthesized and utilized in base-catalyzed additions of alcohols (ethanol, 2-propanol) and polyols [propane-1,2-diol (**11a**), butane-1,3-diol (**12a**), methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**13a**)] to diphenylketene. Compounds **4c**, **4d** and **1b** proved to be efficient and selective catalysts; **4c** and **4d** exhibited better results with **11a** and **12a**, and **1b** was the best catalyst for selective 2-*O*-acylation of **13a**.

The esterification of hydroxy groups is a very important reaction, which is widely used for the protection of alcohol functions.[1] Three factors are important in choosing a suitable protecting group: (i) selective introduction, (ii) sufficient stability to allow various transformations of the protected molecule, and (iii) selective deprotection. Requirements (ii) and (iii) are fulfilled by the ester group. In natural products such as carbohydrates, however, more than one hydroxy group is likely to be present. Here, the key requirement is the selective introduction of protecting groups.

Butane-1,3-diol (**12a**) has been widely used as a model compound in studies of the selective acylation of primary and secondary hydroxy groups. Selective acylation of the primary alcohol function has been accomplished in yields of 80−99% with varying primary/secondary selectivities.[2] Good results have been achieved by variation of the leaving group of the acylating reagent and by employing sterically hindered bases.[3]

With carbohydrates, differentiation between various secondary hydroxy groups is often important. These secondary alcohol functions can be oriented axially or equatorially. Many reagents have been tested with the model compound methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**13a**), in which two secondary equatorial hydroxy groups are present. While acyl chlorides in pyridine offer little selectivity and lead to mixtures of **13b**, **13c** and **13d**,[4] other reagents favor acylation at the 2-position and thus selectively furnish **13b**.[5] Using carboxylic acid imidazolides in combination with dibutyltin oxide, a selectivity of 92:1 in favor of **13b** was found.[6] Excellent selectivities have also been realized in enzyme-catalyzed acylations and deacylations.[7] Thus, the use of PFL (*Pseudomonas fluorescens* lipase) leads to the 2-*O*-acylated model compound in 94% yield.[8] Despite these good results, there is still a need for new and improved selective acylation reagents as the applicability of enzymes is often limited by the solvents that can be used.[9] Generally speaking, the substrates have to be hydrophilic.

Steric control seems to be a major factor in determining the aforementioned selectivities. Consequently, the acylation of alcohols and polyols by ketenes, as catalyzed by various sterically demanding bases, including the concave bases **1** and **2**, has been investigated, and selectivities have been measured for a number of model compounds.[10] The ketenes used in these studies were diarylketenes.[11]



The mechanism of the base-catalyzed addition of alcohols to ketenes has been well investigated.[12] Two principal reaction pathways can be envisaged: activation of the alcohol by the base through formation of a hydrogen bond,[12b] or addition of the base to the ketene to form a betaine as a reactive intermediate.[12c] Although ketene−pyridine ylides have been observed in matrices,[13] in the case of sterically shielded pyridines, such as the concave pyridines **1** or **2**, the base cannot react as a nucleophile due to steric hindrance.[10a] Thus, with these bases, the catalysis takes place by formation of a hydrogen bond between the alcohol and the base. This increases the nucleophilicity of the oxygen atom and facilitates nucleophilic attack on the sp-hybridized carbon atom of the ketene. This reaction of the alcohol oxygen atom with the ketene represents the sel-

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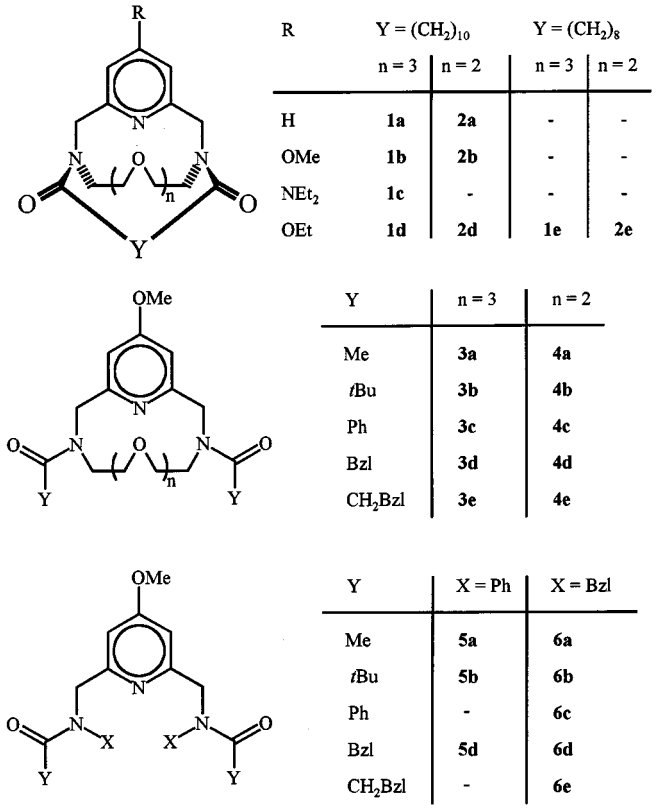
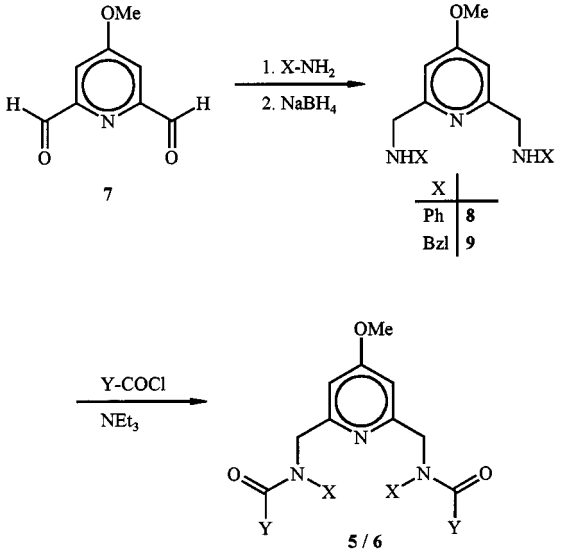


Scheme 1



Scheme 2. Synthesis of bis(amidomethyl)pyridines, as exemplified by the case of the nonmacrocyclic pyridines **5** and **6**; bimacrocyclic or monomacrocyclic analogues **1**−**4** were obtained by using divalent amines or acid chlorides[14]

ectivity-determining step. Steric shielding at both the ketene and the base−alcohol complex changes the activation parameters for the addition and thus has an influence on the selectivity. The outcome of the acylation can thus be influenced by judicious choice of the pyridine catalyst.

Syntheses of the Catalysts 1−6

The syntheses of the catalysts **1**−**6** were carried out in analogy to literature procedures.[10b,14] Nineteen new compounds have been fully characterized. All syntheses started from pyridine-2,6-dicarbaldehydes.[10b,14] In the first step, Schiff bases were formed by reaction with primary mono- or diamines. The resulting diimides were then reduced with sodium tetrahydroborate to give monomacrocyclic secondary diamines[10b,14] and nonmacrocyclic secondary diamines **8** and **9**. In the second reaction step, these secondary diamines were acylated using mono- or diacid chlorides to give bimacrocyclic (**1** and **2**), monomacrocyclic (**3** and **4**), and nonmacrocyclic (**5** and **6**) pyridinebis(lactams) (**1** and **2**) and -diamides (**3**−**6**, see Scheme 2). The basicities of the products in ethanol solution were measured using an established photometric titration against thymol blue,[15] which gives relative basicities lg *K*. Due to the amide functions, all pyridines **1**−**6** exist as mixtures of conformers (*EE*, *EZ*, *ZZ*). The yields, basicities, and conformer distributions are listed in Table 1.

Compared to the bimacrocyclic pyridinebis(lactams) **1** and **2**, the monomacrocycles **3** and **4** were obtained in better yields as no second macrocycle had to be built-up and thus high-dilution conditions were unnecessary. Compounds **3** and **4** exhibit simpler NMR spectra than **1** and **2**, despite the fact that they also exist as mixtures of conformers. In fact, the monomacrocycles **3** and **4** possess higher symmetry than the bimacrocycles **1** and **2** (time averaged, the molecules are planar). Diphenylketene was synthesized as described previously.[18]

Selectivity Measurements

The various catalysts **1**−**6** were subsequently tested in the acylation of hydroxy groups with diphenylketene. Table 2 lists the selectivities achieved with these pyridine catalysts in four model reactions using diphenylketene as the acylating agent. The four model reactions[10] were (i) an intermolecular competition between the primary alcohol ethanol and the secondary alcohol 2-propanol, (ii) and (iii) two intramolecular competitions between primary and secondary hydroxy groups in propane-1,2-diol (**11a**) and butane-1,3-diol (**12a**), and (iv) an intramolecular competition between two secondary equatorial hydroxy groups in the glucose derivative **13a**.

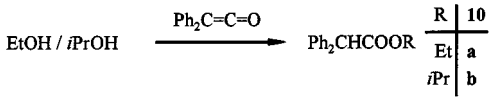
The reaction mixtures were analyzed by GC in the case of the ethyl and isopropyl esters **10a** and **10b**, as were the product mixtures **11b/11c** and **12b/12c**, after derivatization of the remaining alcohol functions with trimethylsilyl chloride. The carbohydrate mixtures **13a**−**13d** were analyzed by ^{1}H-NMR spectroscopy.

Besides the concave pyridines **1** and **2**, some of the mono- and nonmacrocyclic pyridines **3**−**6** also selectively catalyzed

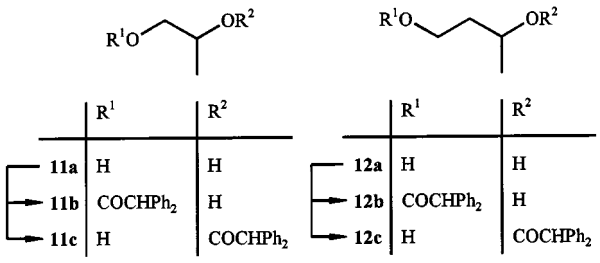
Table 1. Yields, basicities (listed as lg *K* values[15]), and conformer distributions of the pyridinebis(lactams) **1**–**6**

	R	polyether chain or X	Y	yield (%)	lg *K*	*ZZ*/*EZ*/*EE*
1a	H	$CH_2[CH_2OCH_2]_3CH_2$	$[CH_2]_{10}$	48[14]	−0.30[14]	75:ca. 23:< 5[14]
1b	OMe	$CH_2[CH_2OCH_2]_3CH_2$	$[CH_2]_{10}$	45[14]	1.00[14]	68:27:5[14]
1c	NEt_2	$CH_2[CH_2OCH_2]_3CH_2$	$[CH_2]_{10}$	20[16]	ca. 4.0[16]	71:23:6[16]
1d	OEt	$CH_2[CH_2OCH_2]_3CH_2$	$[CH_2]_{10}$	46[10b]	1.30	68:27:5[10b]
1e	OEt	$CH_2[CH_2OCH_2]_3CH_2$	$[CH_2]_8$	44	1.10	60:34:6
2a	H	$CH_2[CH_2OCH_2]_2CH_2$	$[CH_2]_{10}$	56[17]	0.60[14]	63:25:12[14]
2b	OMe	$CH_2[CH_2OCH_2]_2CH_2$	$[CH_2]_{10}$	44[14]	> 1.40[14]	54:28:18[14]
2d	OEt	$CH_2[CH_2OCH_2]_2CH_2$	$[CH_2]_{10}$	46[10b]	2.20	34:46:20
2e	OEt	$CH_2[CH_2OCH_2]_2CH_2$	$[CH_2]_8$	24	ca. 2.5	18:69:13
3a	OMe	$CH_2[CH_2OCH_2]_3CH_2$	Me	86	0.60	18:60:22
3b	OMe	$CH_2[CH_2OCH_2]_3CH_2$	*t*Bu	76	1.10	–[a]
3c	OMe	$CH_2[CH_2OCH_2]_3CH_2$	Ph	49	0.40	–[a]
3d	OMe	$CH_2[CH_2OCH_2]_3CH_2$	Bzl	39	0.45	20:60:20
3e	OMe	$CH_2[CH_2OCH_2]_3CH_2$	CH_2Bzl	42	0.75	20:60:20
4a	OMe	$CH_2[CH_2OCH_2]_2CH_2$	Me	60	1.30	25:50:25
4b	OMe	$CH_2[CH_2OCH_2]_2CH_2$	*t*Bu	61[10b]	1.70	–[a]
4c	OMe	$CH_2[CH_2OCH_2]_2CH_2$	Ph	66	1.20	–[a]
4d	OMe	$CH_2[CH_2OCH_2]_2CH_2$	Bzl	44	1.40	25:50:25
4e	OMe	$CH_2[CH_2OCH_2]_2CH_2$	CH_2Bzl	75	1.50	25:50:25
5a	OMe	Ph	Me	22	ca. −0.45	–[a]
5b	OMe	Ph	*t*Bu	17	ca. 0.45	–[a]
5d	OMe	Ph	Bzl	28	ca. 1.10	–[a]
6a	OMe	Bzl	Me	52	−0.40	25:50:25
6b	OMe	Bzl	*t*Bu	67	−0.20	–[a]
6c	OMe	Bzl	Ph	61	−0.70	50:00:50
6d	OMe	Bzl	Bzl	55	−0.60	20:60:20
6e	OMe	Bzl	CH_2Bzl	50	−0.50	20:60:20

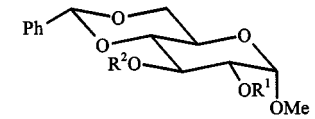
[a] Conformer distributions could not be determined (broad signals).

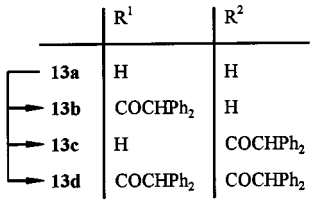


Scheme 3



Scheme 4





Scheme 5

acylation of the primary hydroxy groups in the ethanol/2-propanol mixture (intermolecular competition) and in the diols **11a** and **12a** (intramolecular competition). The most promising catalysts **1**–**6** were then employed in the acylation of the sugar derivative **13a** with diphenylketene.

Compared to the bimacrocycles **1** and **2** as well as to regular pyridines, the results in Table 2 show that in the intermolecular competition between ethanol and 2-propanol, the monomacrocycles **3** are the most selective catalysts of all the pyridines investigated. The nonmacrocyclic pyridines **5** and **6** produced comparable or lower selectivities than the bimacrocycles **1** and **2**.

In the intramolecular competitions (acylation of the diols **11a** and **12a**), the monomacrocycles **3** and **4** again proved to be selective catalysts. The 15-membered ring systems **3** gave rise to **11b**/**11c** selectivities of 20 to 28, while the larger macrocycles **4** led to favored formation of the primary ester by factors of 11.5 to 14.

With the carbohydrate **13a**, some monomacrocycles led to favored formation of the 2-*O* derivative **13b** over the 3-*O* derivative **13c** with selectivities comparable to those achieved with the most effective bimacrocycle **1b**. A comparison of catalysts **1b**, **4c** and **4d** reveals a better conversion with the monomacrocycles **4c** and **4d** (100% and 93%) than with **1b** (85%), but the monomacrocycles allow the formation of some 3-*O*-acyl derivative **13c**. While the starting ma-

Table 2. Selectivities achieved in base-catalyzed acylations of different hydroxy groups with diphenylketene in four sets of experiments: intermolecular competition: EtOH/*i*PrOH; intramolecular competition: **11a**, **12a** and **13a** (reaction time 15 h)

catalyst	product ratios			product ratio			
	10a/10b	**11b/11c**	**12b/12c**	**13a/13b/13c/13d**			
without catalyst	3.4	2.7	2.5	74	18	8	–
pyridine	4.7	6.3	8.7	36	45	12	7
2-picoline	4.9	9.7	–	–	–	–	–
2,6-lutidine	7.1	–	22.0	34	20	32	14
2,4,6-collidine	9.1	24.0	40.0	26[a]	24	31	19
1a	7.9	10.3	–	–	–	–	–
1b	10.0	13.0	23.0	15[b]	85	–	–
1c	12.0	–	–	–	–	–	–
1d	10.5	13.2	–	43	57	–	–
1e	6.3	7.5	–	78	22	trace	–
2a	3.5	4.0	–	–	–	–	–
2b	4.1	4.5	4.2	68	24	8	–
2d	4.0	5.0	–	–	–	–	–
2e	3.5	4.0	–	–	–	–	–
3a	14	13	–	56[c]	40	4	–
3b	15	11.5	–	52[c]	33	15	–
3c	13	12	–	35[c]	55	10	–
3d	13	12	–	17[c]	74	9	–
3e	13	14	–	33[c]	63	4	–
4a	11.2	23	16	42[c]	51	7	–
4b	12.8	24	21	36[c]	53	11	–
4c	8.6	20	16	–[c]	93	7	–
4d	11.2	24	21	7[c]	89	4	–
4e	13.9	28	–	18[c]	76	6	–
5a	9.9	9.1	–	–	–	–	–
5b	12.9	10.2	–	–	–	–	–
5d	8.5	11.5	–	–	–	–	–
6a	6.3	12.5	–	–	–	–	–
6b	6.3	14.5	–	–	–	–	–
6c	4.4	14.2	–	–	–	–	–
6d	4.6	10.5	–	–	–	–	–
6e	5.2	13.3	–	–	–	–	–

[a] 10 equiv. of base. – [b] 0.02 equiv. of base. – [c] 1.50 equiv. of diphenylketene.

terial **13a** can easily be removed from the 2-*O*-acyl derivative **13b** by chromatography, the separation of **13b** and **13c** is tedious. Therefore, it is advisable to aim for selectivity rather than for maximum conversion. Formation of the diacyl derivative **13d** was not observed with any of the bi- or monomacrocycles **1**–**4**.

Conclusions

Three different types of 2,6-disubstituted pyridines bearing amidomethyl substituents have been investigated as catalysts. For the acylation of polyols, efficient and selective catalysts have only been found among the monomacrocycles and bimacrocycles (**4c**, **4d** and **1b**). Among the monomacrocycles, a 15-membered ring (**4** in contrast to **3**) is essential for selectivity, while the bimacrocycles require one additional ethylene oxide moiety between the two amide nitrogen atoms (**1**). As with enzymes, there is no single optimal catalyst for all substrates; the best catalyst for each substrate may vary and has to be found in each specific case.

Experimental Section

General Remarks: See refs.[10b,10c] The selectivity measurements were carried out as described in ref.[10c]

Syntheses of Pyridinediamines 8 and 9. – General Procedure: One equivalent of 4-methoxypyridine-2,6-dicarbaldehyde (**7**)[14] (3.0–9.1 mmol) was dissolved in 150 mL of dry methanol. Under nitrogen, 2.2 equivalents of aniline or benzylamine, dissolved in 30 mL of dry methanol, were added over a period of ca. 30 min. The reddish-brown mixture was stirred for 1 h at room temperature and was then heated under reflux for several hours until no further reaction could be detected by TLC (reaction time 2.5–4 h). After cooling to 0°C, sodium tetrahydroborate (18.2–54.6 mmol) was added in small portions. The resulting mixture was stirred for 15 h at room temperature, 50 mL of water was added, and stirring was continued for a further 6 h. The mixture was then concentrated to a volume of 100 mL, whereupon it became very turbid owing to the precipitation of borates. After filtration, the dark-brown solution was extracted four times with 100 mL of dichloromethane. The combined organic extracts were dried with $MgSO_4$ and filtered. The solvents were evaporated and the residue was dried in vacuo.

4-Methoxy-2,6-bis(phenylaminomethyl)pyridine (8): Starting materials: 1.00 g (3.6 mmol) of 4-methoxypyridine-2,6-dicarbaldehyde[14] (**7**), 0.62 g (6.7 mmol) of aniline, 0.69 g (18.2 mmol) of sodium tetrahydroborate. Yield: 0.84 g (87%), brown oil. – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.77 (s, 3 H), 4.41 (s, 4 H), 4.67 (br. s, ca. 2 H, exchangeable with D_2O), 6.6–6.8 (m, ca. 8 H), 7.1–7.3 (m, ca. 4 H). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 53.5 (t), 54.6 (t), 55.1 (q), 106.5 (d), 127.0 (d), 128.3 (d), 128.4 (d), 140.2 (s), 161.0 (s), 166.7 (s). – IR (KBr): $\tilde{\nu}$ = 3400 cm^{-1} (br., NH), 1603 (arom.), 1573 (arom.). – MS (EI, 70 eV); *m/z* (%): 319 (100) [M^+], 318 (31), 226 (44). – MS (CI, isobutane); *m/z* (%): 320 (100) [M^+ + H], 319

(15) [M^+]. − HR MS: $C_{20}H_{21}N_3O$: calcd. 319.1685; found 319.1684. $C_{19}{}^{13}CH_{21}N_3O$: calcd. 320.1718; found 320.1718.

4-Methoxy-2,6-bis(benzylaminomethyl)pyridine (9): Starting materials: 1.50 g (3.6 mmol) of 4-methoxypyridine-2,6-dicarbaldehyde[14] (**7**), 2.14 g (20.0 mmol) of benzylamine, 2.06 g (54.6 mmol) of sodium tetrahydroborate. Yield: 2.34 g (73%), brown oil. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.50 (br. s, ca. 2 H, exchangeable with D_2O), 3.83 (s, 8 H), 3.86 (s, 3 H), 6.75 (s, 2 H), 7.2−7.4 (m, 10 H). − IR (KBr): $\tilde{\nu}$ = 3300 cm^{-1} (br., NH), 1598 (arom.), 1574 (arom.). − MS (EI, 70 eV); *m/z* (%): 347 (1) [M^+], 242 (100). − MS (CI, isobutane); *m/z* (%): 348 (100) [M^+ + H], 242 (11).

27-Ethoxy-4,7,10-trioxa-1,13,31-triazatricyclo[11.10.7.1^{25,29}]hentriaconta-25(31),26,28-triene-14,23-dione (1e): Synthetic procedure see ref.[14]; amounts used: 2.10 g (6.2 mmol) of 19-ethoxy-6,9,12-trioxa-3,15,21-triazabicyclo[15.3.1]heneicosa-1(20),17(21),18-triene,[10c] 1.48 g (6.2 mmol) of sebacoyl dichloride, 3.76 g (37.2 mmol) of NEt_3. Yield: 1.37 g (44%), colorless needles, m.p. 118−119°C. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.0−1.7 (m, ca. 19 H), 2.1−2.6 (m, ca. 4 H), 3.1−4.3 (m, ca. 14 H), 4.4−5.3 (m, ca. 4 H), 6.52 (s, 1.2 H, PyH_{ZZ}), 6.52 (d, *J* = 2.2 Hz, ca. 0.34 H, PyH_{EZ}), 6.76 (d, *J* = 2.2 Hz, ca. 0.34 H, PyH_{EZ}), 6.90 (s, 0.12 H, PyH_{EE}). − IR (KBr): $\tilde{\nu}$ = 1649 cm^{-1} (C=O), 1600 (arom.), 1572 (arom.). − MS (EI, 70 eV); *m/z* (%): 505 (100) [M^+], 475 (32), 416 (38). − MS (CI, isobutane); *m/z* (%): 506 (100) [M^+ + H], 505 (6) [M^+]. − $C_{27}H_{43}N_3O_6$ (505.3): calcd. C 64.13, H 8.57, N 8.31; found C 64.42, H 8.78, N 7.80.

24-Ethoxy-15,18-dioxa-1,12,28-triazatricyclo[10.8.7.1^{22,26}]octacosa-22(28),23,25-triene-2,11-dione (2e): Synthetic procedure see ref.[14]; amounts used: 1.74 g (5.9 mmol) of 16-ethoxy-6,9-dioxa-3,12,18-triazabicyclo[12.3.1]octadeca-1(17),14(18),15-triene,[10c] 1.26 g (5.9 mmol) of sebacoyl dichloride, 3.58 g (35.4 mmol) of NEt_3. Yield: 0.65 g (24%), colorless oil, slowly crystallizing, m.p. 104−107°C. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.8−1.8 (m, ca. 19 H), 1.8−2.5 (m, ca. 4 H), 3.0−4.4 (m, ca. 10 H), 4.7−5.4 (m, ca. 4 H), 6.57 (s, 0.36 H, PyH_{ZZ}), 6.59 (d, *J* = 2.0 Hz, 0.69 H, PyH_{ZE}), 6.81 (d, *J* = 2.0 Hz, 0.69 H, PyH_{ZE}), 6.87 (s, 0.26 H, PyH_{EE}). − IR (KBr): $\tilde{\nu}$ = 1636 cm^{-1} (C=O), 1596 (arom.), 1571 (arom.). − MS (EI, 70 eV); *m/z* (%): 461 (88) [M^+], 431 (64), 416 (50), 151 (100). − $C_{25}H_{39}N_3O_6$ (461.3): calcd. C 65.05, H 8.52, N 9.10; found C 65.22, H 8.56, N 8.86.

Syntheses of Pyridinebis(lactams) 3, 4, 5 and 6. − General Procedure: One equivalent of the appropriate pyridinediamine[14] (1.6−5.6 mmol) and six equivalents of triethylamine were dissolved in 100 mL of dry dichloromethane. To this, 2.1 equivalents of the appropriate acid chloride, dissolved in 25 mL of dry dichloromethane, were added over a period of 1 h. The resulting mixture was stirred for 15 h at room temperature, then concentrated to a volume of 50 mL, and washed with 50 mL of 2 N NaOH solution. The aqueous layer was extracted three times with 100 mL of dichloromethane. The combined organic phases were dried with $MgSO_4$ and filtered. After evaporation of the solvent, the remaining oil was purified by column chromatography (silica gel, 100 g, diameter 4 cm, dichloromethane/ethanol, 10:1) and radial chromatography (Chromatotron, dichloromethane).

3,15-Diacetyl-19-methoxy-6,9,12-trioxa-3,15,21-triazabicyclo-[15.3.1]heneicosa-1(20),17(21),18-triene (3a): Starting materials: 0.82 g (2.5 mmol) of 19-methoxy-6,9,12-trioxa-3,15,21-triazabicyclo[15.3.1]heneicosa-1(20),17(21),18-triene,[14] 0.42 g (5.3 mmol) of acetyl chloride, 1.54 g (15.3 mmol) of NEt_3. Yield: 0.90 g (86%), m.p. 72−74°C. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.13 (s, ca. 3 H), 2.17 (s, ca. 3 H), 3.4−3.8 (m, ca. 16 H), 3.81 (s, ca. 0.75 H), 3.83 (s, ca. 1.65 H), 3.84 (s, ca. 0.6 H), 4.62 (s, ca. 1.2 H), 4.70 (s, ca. 0.9 H), 4.72 (s, ca. 0.7 H), 4.76 (s, 1.2 H), 6.53 (d, *J* = 2.2 Hz, 0.6 H, PyH_{EZ}), 6.58 (s, 0.36 H, PyH_{ZZ}), 6.76 (s, 0.44 H, PyH_{EE}), 6.80 (d, *J* = 2.2 Hz, 0.6 H, PyH_{EZ}). − ^{1}H NMR (200 MHz, $CDCl_3$, 7.8 equiv. of picric acid): δ = 2.11 (br. s, ca. 1.3 H), 2.22 (br. s, ca. 1.3 H), 2.24 (br. s, ca. 3.4 H), 3.3−3.8 (m, ca. 16 H), 4.08 (s, ca. 1 H), 4.09 (s, ca. 2 H), 4.91 (s, ca. 2.72 H), 4.93 (s, ca. 0.64 H), 5.07 (s, ca. 0.64 H), 6.96 (d, *J* = 2.0 Hz, 0.35 H, PyH_{EZ}), 7.06 (d, *J* = 2.0 Hz, 0.35 H, PyH_{EZ}), 7.15 (s, 1.30 H), 9.13 (br. s, ca. 15.6 H, picric acid). − IR (KBr): $\tilde{\nu}$ = 1624 cm^{-1} (C=O), 1576 (arom.). − MS (EI, 70 eV); *m/z* (%): 409 (55) [M^+], 366 (86) [M^+ − $COCH_3$], 320 (35), 291 (39), 281 (48), 248 (60), 220 (97), 137 (100). − MS (CI, isobutane); *m/z* (%): 410 (100) [M^+ + H], 409 (4) [M^+]. − $C_{20}H_{31}N_3O_6$ (409.2): calcd. C 58.67, H 7.63, N 10.26; found C 58.48, H 7.57, N 10.19.

3,15-Bis(2,2-dimethylpropionyl)-19-methoxy-6,9,12-trioxa-3,15,21-triazabicyclo[15.3.1]heneicosa-1(20),17(21),18-triene (3b): Starting materials: 1.08 g (3.3 mmol) of 19-methoxy-6,9,12-trioxa-3,15,21-triazabicyclo[15.3.1]heneicosa-1(20),17(21),18-triene,[14] 0.88 g (7.3 mmol) of pivaloyl chloride, 2.02 g (20.0 mmol) of NEt_3. Yield: 1.25 g (76%), pale-yellow oil. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.32 (s, ca. 18 H), 3.5−3.8 (m, ca. 16 H), 3.79 (s, 3 H), 4.88 (br. s, 4 H), 6.61 (s, 2 H). − IR (KBr): $\tilde{\nu}$ = 1633 cm^{-1} (C=O), 1574 (arom.). − MS (EI, 70 eV); *m/z* (%): 493 (23) [M^+], 436 (54) [M^+ − C_4H_9], 408 (100) [M^+ − $COC(CH_3)_3$], 367 (30), 137 (60). − MS (CI, isobutane); *m/z* (%): 493 (100) [M^+ + H], 492 (6) [M^+]. − HR MS: $C_{26}H_{43}N_3O_6$: calcd. 493.3152; found 493.3152. $C_{25}{}^{13}CH_{43}N_3O_6$: calcd. 494.3185; found 494.3184. − $C_{26}H_{43}N_3O_6$ (493.2): calcd. C 63.26, H 8.78, N 8.51; found C 63.92, H 8.97, N 8.53.

3,15-Dibenzoyl-19-methoxy-6,9,12-trioxa-3,15,21-triazabicyclo-[15.3.1]heneicosa-1(20),17(21),18-triene (3c): Starting materials: 1.30 g (4.0 mmol) of 19-methoxy-6,9,12-trioxa-3,15,21-triazabicyclo[15.3.1]heneicosa-1(20),17(21),18-triene,[14] 1.24 g (8.8 mmol) of benzoyl chloride, 2.42 g (24.0 mmol) of NEt_3. Yield: 1.04 g (49%), pale-yellow oil. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.4−3.9 (m, ca. 19 H), 4.7−5.1 (m, ca. 4 H), 6.5−6.7 (m, ca. 1 H), 6.8−7.0 (m, ca. 1 H), 7.40 (m_c, ca. 10 H). − IR (KBr): $\tilde{\nu}$ = 1636 cm^{-1} (C=O), 1599 (arom.), 1575 (arom.). − MS (EI, 70 eV); *m/z* (%): 533 (16) [M^+], 428 (23) [M^+ − COPh], 105 (100) [$C_7H_5O^+$]. − MS (CI, isobutane); *m/z* (%): 534 (100) [M^+ + H], 533 (5) [M^+]. − HR MS: $C_{30}H_{35}N_3O_6$: calcd. 533.2526; found 533.2523. $C_{29}{}^{13}CH_{35}N_3O_6$: calcd. 534.2559; found 534.2558. − $C_{30}H_{35}N_3O_6$ (533.3): calcd. C 67.53, H 6.61, N 7.87; found C 66.26, H 6.47, N 7.61.

19-Methoxy-3,15-bis(phenylacetyl)-6,9,12-trioxa-3,15,21-triazabicyclo[15.3.1]heneicosa-1(20),17(21),18-triene (3d): Starting materials: 1.82 g (5.6 mmol) of 19-methoxy-6,9,12-trioxa-3,15,21-triazabicyclo[15.3.1]heneicosa-1(20),17(21),18-triene,[14] 1.90 g (12.3 mmol) of phenylacetyl chloride, 3.39 g (33.6 mmol) of NEt_3. Yield: 1.21 g (39%), pale-yellow oil. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.50 (br. s, 1 H, H_2O), 3.4−3.8 (m, ca. 19 H), 4.65 (s, 1.2 H), 4.71 (s, 0.8 H), 4.74 (s, 0.8 H), 4.80 (s, 1.2 H), 6.35 (d, *J* = 2.4 Hz, 0.6 H, PyH_{EZ}), 6.37 (s, 0.4 H, PyH_{ZZ}), 6.67 (s, 0.4 H, PyH_{EE}), 6.72 (d, *J* = 2.4 Hz, 0.6 H, PyH_{EZ}), 7.2−7.4 (m, 10 H). − IR (KBr): $\tilde{\nu}$ = 1644 cm^{-1} (C=O), 1599 (arom.), 1574 (arom.). − MS (EI, 70 eV); *m/z* (%): 561 (32) [M^+], 470 (19) [M^+ − C_7H_7], 442 (28) [M^+ − $COCH_2Ph$], 324 (17), 137 (48), 91 (100) [$C_7H_7^+$]. − MS (CI, isobutane); *m/z* (%): 562 (100) [M^+ + H], 561 (5) [M^+]. − HR MS: $C_{32}H_{39}N_3O_6$: calcd. 561.2839; found 561.2836. $C_{31}{}^{13}CH_{39}N_3O_6$: calcd. 562.2872; found 562.2870. − $C_{32}H_{39}N_3O_6 \cdot 0.5\ H_2O$ (561.3 + 9.0): calcd. C 67.35, H 7.07, N 7.36; found C 67.59, H 7.12, N 7.19.

19-Methoxy-3,15-bis(3-phenylpropionyl)-6,9,12-trioxa-3,15,21-triazabicyclo[15.3.1]heneicosa-1(20),17(21),18-triene (3e): Starting ma-

terials: 1.44 g (4.4 mmol) of 19-methoxy-6,9,12-trioxa-3,15,21-triazabicyclo[15.3.1]heneicosa-1(20),17(21),18-triene,[14] 1.64 g (9.8 mmol) of 3-phenylpropionyl chloride, 2.68 g (26.6 mmol) of NEt_3. Yield: 1.11 g (42%), yellow oil. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.6−2.8 (m, 4 H), 2.9−3.1 (m, 4 H), 3.4−3.8 (m, ca. 19 H), 4.59 (s, 1.2 H), 4.64 (s, 0.8 H), 4.69 (s, 0.8 H), 4.74 (s, 1.2 H), 6.43 (d, J = 2.2 Hz, 0.6 H, PyH_{EZ}), 6.45 (s, 0.4 H, PyH_{ZZ}), 6.73 (s, 0.4 H, PyH_{EE}), 6.76 (d, J = 2.2 Hz, 0.6 H, PyH_{EZ}), 7.1−7.3 (m, ca. 10 H). − IR (KBr): $\tilde{\nu}$ = 1644 cm^{-1} (C=O), 1599 (arom.), 1574 (arom.). − MS (EI, 70 eV); *m/z* (%): 589 (35) [M$^+$], 484 (5) [M$^+$ − C_8H_9], 456 (28) [M$^+$ − $COCH_2CH_2Ph$], 105 (62) [$C_8H_9^+$], 91 (100) [$C_7H_7^+$]. − MS (CI, isobutane); *m/z* (%): 590 (100) [M$^+$ + H], 589 (6) [M$^+$]. − HR MS: $C_{34}H_{43}N_3O_6$: calcd. 589.3152; found 589.3152. $C_{33}{}^{13}CH_{43}N_3O_6$: calcd. 590.3185; found 590.3185. − $C_{34}H_{43}N_3O_6$ (589.3): calcd. C 69.25, H 7.35, N 7.13; found C 68.70, H 7.36, N 6.86.

3,12-Diacetyl-16-methoxy-6,9-dioxa-3,12,18-triazabicyclo-[12.3.1]octadeca-1(17),14(18),15-triene (4a): Starting materials: 1.25 g (4.5 mmol) of 16-methoxy-6,9-dioxa-3,12,18-triazabicyclo[12.3.1]octadeca-1(17),14(18),15-triene,[14] 0.77 g (9.8 mmol) of acetyl chloride, 2.70 g (26.7 mmol) of NEt_3. Yield: 0.97 g (60%), yellow oil, slowly crystallizing, m.p. 70−74°C. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.17 (s, ca. 3.0 H), 2.25 (s, ca. 1.50 H), 2.27 (s, ca. 1.75 H), 3.0−3.8 (m, 12 H), 4.60 (s, 1 H), 4.65 (s, 1 H), 4.68 (s, 2 H), 6.58 (s, 0.5 H, PyH_{ZZ}), 6.59 (d, J = 2.3 Hz, 0.5 H, PyH_{EZ}), 6.82 (s, 0.5 H, PyH_{EE}), 6.88 (d, J = 2.3 Hz, 0.5 H, PyH_{EZ}). − ^{1}H NMR (200 MHz, $CDCl_3$, 6.1 equiv. of picric acid): δ = 2.18 (br. s, ca. 1.5 H), 2.25 (br. s, ca. 4.5 H), 3.20 (br. s, 4 H), 3.4−3.9 (m, ca. 8 H), 4.08 (s, ca. 0.75 H), 4.10 (s, ca. 2.25 H), 4.90 (br. s, ca. 4 H), 6.91 (d, J = 2.3 Hz, 0.10 H, PyH_{EZ}), 7.30 (s, 1.8 H), 7.34 (d, J = 2.3 Hz, 0.10 H, PyH_{EZ}), 9.13 (br. s, ca. 12.2 H, picric acid). − IR (KBr): $\tilde{\nu}$ = 1633 cm^{-1} (C=O), 1598 (arom.), 1571 (arom.). − MS (EI, 70 eV); *m/z* (%): 365 (70) [M$^+$], 335 (29), 322 (77) [M$^+$ − $COCH_3$]. − MS (CI, isobutane); *m/z* (%): 366 (100) [M$^+$ + H], 365 (4) [M$^+$]. − HR MS: $C_{18}H_{27}N_3O_5$: calcd. 365.1951; found 365.1947. $C_{17}{}^{13}CH_{27}N_3O_5$: calcd. 366.1984; found 366.1983. − $C_{18}H_{27}N_3O_5$ (365.2): calcd. C 59.16, H 7.45, N 11.50; found C 59.15, H 7.50, N 11.42.

3,12-Dibenzoyl-16-methoxy-6,9-dioxa-3,12,18-triazabicyclo[12.3.1]-octadeca-1(17),14(18),15-triene (4c): Starting materials: 1.00 g (3.6 mmol) of 16-methoxy-6,9-dioxa-3,12,18-triazabicyclo[12.3.1]octadeca-1(17),14(18),15-triene,[14] 1.10 g (7.8 mmol) of benzoyl chloride, 2.16 g (21.4 mmol) of NEt_3. Yield: 1.16 g (66%), m.p. 55−58°C. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.1−3.9 (m, ca. 15 H), 4.64 (br. s, 1.8 H), 4.91 (br. s, 2.2 H), 6.55 (br. s, 0.9 H), 6.9−7.0 (m, 1.1 H), 7.3−7.7 (m, ca. 10 H). − ^{1}H NMR (200 MHz, $CDCl_3$, 5.5 equiv. of picric acid): δ = 3.19 (br. s, ca. 4 H), 3.40 (br. s, 4 H), 3.76 (br. s, 4 H), 4.15 (br. s, 3 H), 5.11 (br. s, 4 H), 7.3−7.5 (m, ca. 12 H), 9.11 (br. s, ca. 11.0 H, picric acid). − IR (KBr): $\tilde{\nu}$ = 1629 cm^{-1} (C=O), 1600 (arom.), 1576 (arom.). − MS (EI, 70 eV); *m/z* (%): 489 (13) [M$^+$], 384 (23) [M$^+$ − COPh], 105 (100) [$C_7H_5O^+$]. − MS (CI, isobutane); *m/z* (%): 490 (100) [M$^+$ + H], 489 (5) [M$^+$]. − HR MS: $C_{28}H_{31}N_3O_5$: calcd. 489.2264; found 489.2259. $C_{27}{}^{13}CH_{31}N_3O_5$: calcd. 490.2297; found 490.2297. − $C_{28}H_{31}N_3O_5$ (489.2): calcd. C 68.70, H 6.38, N 8.58; found C 67.98, H 6.30, N 8.46.

16-Methoxy-3,12-bis(phenylacetyl)-6,9-dioxa-3,12,18-triazabicyclo-[12.3.1]octadeca-1(17),14(18),15-triene (4d): Starting materials: 1.00 g (3.6 mmol) of 16-methoxy-6,9-dioxa-3,12,18-triazabicyclo[12.3.1]octadeca-1(17),14(18),15-triene,[14] 1.21 g (7.9 mmol) of phenylacetyl chloride, 2.16 g (21.4 mmol) of NEt_3. Yield: 0.81 g (44%), m.p. 103−105°C. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.1−3.9 (m, ca. 19 H), 4.7−4.8 (m, 4 H), 6.22 (d, J = 2.2 Hz, 0.5 H, PyH_{EZ}), 6.28 (s, 0.5 H, PyH_{ZZ}), 6.62 (s, 0.5 H, PyH_{EE}), 6.67 (d, J = 2.2 Hz, 0.5 H, PyH_{EZ}), 7.2−7.4 (m, ca. 10 H). − ^{1}H NMR (200 MHz, $CDCl_3$, 9.1 equiv. of picric acid): δ = 3.15 (s, 4 H), 3.3−3.9 (m, 12 H), 4.03 (s, 3 H), 4.89 (s, 4 H), 7.1−7.4 (m, ca. 12 H), 9.15 (br. s, ca. 18.2 H, picric acid). − IR (KBr): $\tilde{\nu}$ = 1644 cm^{-1} (C=O), 1599 (arom.), 1574 (arom.). − MS (EI, 70 eV); *m/z* (%): 517 (48) [M$^+$], 426 (32) [M$^+$ − C_7H_7], 398 (38) [M$^+$ − $COCH_2Ph$], 91 (100) [$C_7H_7^+$]. − MS (CI, isobutane); *m/z* (%): 518 (100) [M$^+$ + H], 517 (7) [M$^+$]. − HR MS: $C_{30}H_{35}N_3O_5$: calcd. 517.2577; found 517.2575. $C_{29}{}^{13}CH_{35}N_3O_5$: calcd. 518.2611; found 518.2609. − $C_{30}H_{35}N_3O_5$ (517.3): calcd. C 69.61, H 6.82, N 8.12; found C 69.14, H 6.78, N 8.04.

16-Methoxy-3,12-bis(3-phenylpropionyl)-6,9-dioxa-3,12,18-triazabicyclo[12.3.1]octadeca-1(17),14(18),15-triene (4e): Starting materials: 1.00 g (3.6 mmol) of 16-methoxy-6,9-dioxa-3,12,18-triazabicyclo[12.3.1]octadeca-1(17),14(18),15-triene,[14] 1.32 g (7.8 mmol) of 3-phenylpropionyl chloride, 2.16 g (21.4 mmol) of NEt_3. Yield: 1.48 g (75%), pale-yellow oil. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.6−2.9 (m, ca. 4 H), 2.9−3.1 (m, ca. 4 H), 3.1−3.8 (m, ca. 15 H), 4.51 (s, 1 H), 4.59 (s, 1 H), 4.66 (s, 1 H), 4.69 (s, 1 H), 6.47 (s, 0.5 H, PyH_{ZZ}), 6.50 (d, J = 2.2 Hz, 0.5 H, PyH_{EZ}), 6.81 (s, 0.5 H, PyH_{EE}), 6.86 (d, J = 2.2 Hz, 0.5 H, PyH_{ZZ}), 7.1−7.4 (m, ca. 10 H). − ^{1}H NMR (200 MHz, $CDCl_3$, 9.1 equiv. of picric acid): δ = 2.6−2.8 (m, ca. 4 H), 2.9−3.1 (m, ca. 4 H), 3.1−3.2 (m, ca. 4 H), 3.3−3.5 (m, ca. 4 H), 3.6−3.8 (m, ca. 4 H), 3.92 (s, 0.60 H), 4.03 (s, 2.40 H), 4.80 (s, 0.60 H), 4.88 (s, 3.40 H), 7.1−7.4 (m, ca. 12 H), 9.15 (br. s, ca. 18.2 H, picric acid). − IR (KBr): $\tilde{\nu}$ = 1644 cm^{-1} (C=O), 1600 (arom.), 1574 (arom.). − MS (EI, 70 eV); *m/z* (%): 545 (100) [M$^+$], 440 (8) [M$^+$ − C_8H_9], 412 (83) [M$^+$ − $COCH_2CH_2Ph$], 137 (94). − MS (CI, isobutane); *m/z* (%): 546 (100) [M$^+$ + H], 545 (11) [M$^+$]. − HR MS: $C_{32}H_{39}N_3O_5$: calcd. 545.2890; found 545.2887. $C_{31}{}^{13}CH_{39}N_3O_5$: calcd. 546.2923; found 546.2920. − $C_{32}H_{39}N_3O_5$ (545.3): calcd. C 70.44, H 7.20, N 7.70; found C 70.28, H 7.31, N 7.60.

2,6-Bis[(*N*-acetyl-*N*-phenylamino)methyl]-4-methoxypyridine (5a): Starting materials: 0.94 g (2.9 mmol) of 4-methoxy-2,6-bis(phenylaminomethyl)pyridine (**8**), 0.94 g (2.9 mmol) of acetyl chloride, 1.79 g (17.7 mmol) of NEt_3. Yield: 0.35 g (22%), pale-yellow oil. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.92 (s, ca. 5.27 H), 2.06 (s, ca. 0.73 H), 3.82 (s, ca. 2.3 H), 3.90 (s, ca. 0.7 H), 4.89 (m_c, ca. 4 H), 6.75 (br. s, 2 H), 7.0−7.4 (m, ca. 10 H). − ^{1}H NMR (200 MHz, $CDCl_3$, 9.7 equiv. of picric acid): δ = 1.89 (s, ca. 4.5 H), 2.04 (s, ca. 1.5 H), 4.11 (s, 2.25 H), 4.26 (s, 0.75 H), 5.1−5.3 (m, ca. 4 H), 7.0−7.4 (m, ca. 12 H), 9.14 (br. s, ca. 19.4 H, picric acid). − IR (KBr): $\tilde{\nu}$ = 1660 cm^{-1} (C=O), 1596 (arom.). − MS (EI, 70 eV); *m/z* (%): 403 (10) [M$^+$], 360 (63) [M$^+$ − $COCH_3$], 317 (75) [M$^+$ − $COCH_3$ − $COCH_3$], 225 (100). − MS (CI, isobutane); *m/z* (%): 404 (100) [M$^+$ + H], 403 (6) [M$^+$], 361 (17) [M$^+$ + H − $COCH_3$]. − $C_{24}H_{25}N_3O_3$ (403.2): calcd. C 71.45, H 6.25, N 10.41; found. C 70.83, H 6.45, N 9.81.

2,6-Bis{[*N*-(2,2-dimethylpropionyl)-*N*-phenylamino]methyl}-4-methoxypyridine (5b): Starting materials: 1.20 g (3.8 mmol) of 4-methoxy-2,6-bis(phenylaminomethyl)pyridine (**8**), 1.00 g (8.4 mmol) of pivaloyl chloride, 2.30 g (22.8 mmol) of NEt_3. Yield: 0.32 g (17%), pale-yellow oil. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.04 (s, 18 H), 3.83 (s, ca. 3 H), 4.81 (s, ca. 4 H), 6.77 (s, 2 H), 7.1−7.4 (m, 10 H). − IR (KBr): $\tilde{\nu}$ = 1634 cm^{-1} (C=O), 1595 (arom.). − MS (EI, 70 eV); *m/z* (%): 487 (3) [M$^+$], 430 (100) [M$^+$ − $C(CH_3)_3$], 402 (97) [M$^+$ − $COC(CH_3)_3$]. − MS (CI, isobutane); *m/z* (%): 488 (100) [M$^+$ + H]. − $C_{30}H_{37}N_3O_3$ (487.3): calcd. C 73.89, H 7.65, N 8.62; found C 72.67, H 7.57, N 8.90.

2,6-Bis[(*N*-benzoyl-*N*-phenylamino)methyl]-4-methoxypyridine (5d): Starting materials: 1.20 g (3.8 mmol) of 4-methoxy-2,6-bis(phenylaminomethyl)pyridine (**8**), 1.30 g (8.4 mmol) of phenylacetyl chloride, 2.30 g (22.8 mmol) of NEt_3. Yield: 0.58 g (28%), yellow oil. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.5−3.7 (m, ca. 4 H), 3.83 (s, ca. 3 H), 4.7−4.9 (m, ca. 4 H), 6.6−6.8 (m, ca. 2 H), 7.1−7.4 (m, 10 H). − IR (KBr): $\tilde{\nu}$ = 1654 cm^{-1} (C=O), 1602 (arom.). − MS (EI, 70 eV); *m/z* (%): 555 (9) [M^+], 478 (32) [$M^+ - C_6H_5$], 319 (81), 145 (100). − MS (CI, isobutane); *m/z* (%): 556 (4) [$M^+ + H$], 320 (100).

2,6-Bis[(*N*-acetyl-*N*-benzylamino)methyl]-4-methoxypyridine (6a): Starting materials: 1.17 g (3.4 mmol) of 2,6-bis(benzylaminomethyl)-4-methoxypyridine (**9**), 0.58 g (7.4 mmol) of acetyl chloride, 2.02 g (20.0 mmol) of NEt_3. Yield: 0.76 g (52%), pale-yellow oil. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.19 (s, 1.5 H), 2.21 (s, 4.5 H), 3.75 (s, 0.75 H), 3.79 (s, 1.5 H), 3.81 (s, 0.75 H), 4.42 (d, *J* = 4.2 Hz, 2 H), 4.60 (s, 4 H), 4.6−4.7 (m, 2 H), 6.47 (d, *J* = 2.2 Hz, 0.5 H, PyH_{EZ}), 6.48 (s, 0.5 H, PyH_{ZZ}), 6.71 (s, 0.5 H, PyH_{EE}), 6.72 (d, *J* = 2.2 Hz, 0.5 H, PyH_{EZ}), 7.1−7.4 (m, 10 H, Ar*H*). − ^{1}H NMR (200 MHz, $CDCl_3$, 7.5 equiv. of picric acid): δ = 2.12 (br. s, 1 H), 2.22 (br. s, 5 H), 3.96 (s, 0.5 H), 4.02 (s, 2.5 H), 4.60 (br. s, 4 H), 4.77 (br. s, 4 H), 6.7−7.3 (m, ca. 12 H), 9.10 (br. s, ca. 15 H, picric acid). − IR (KBr): $\tilde{\nu}$ = 1650 cm^{-1} (C=O), 1599 (arom.), 1574 (arom.). − MS (EI, 70 eV); *m/z* (%): 431 (1) [M^+], 388 (2) [$M^+ - COCH_3$], 284 (100). − MS (CI, isobutane); *m/z* (%): 432 (100) [$M^+ + H$]. − $C_{26}H_{29}N_3O_3$ (431.2): calcd. C 72.37, H 6.77, N 9.74; found C 71.62, H 6.92, N 9.49.

2,6-Bis{[*N*-benzyl-*N*-(2,2-dimethylpropionyl)amino]methyl}-4-methoxypyridine (6b): Starting materials: 1.20 g (3.5 mmol) of 2,6-bis(benzylaminomethyl)-4-methoxypyridine (**9**), 0.92 g (7.6 mmol) of pivaloyl chloride, 2.12 g (21.0 mmol) of NEt_3. Yield: 1.24 g (67%), pale-yellow oil. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.33 (s, 18 H), 3.80 (s, 3 H), 4.4−5.0 (m, ca. 8 H), 6.57 (s, 2 H), 7.1−7.4 (m, ca. 10 H). − IR (KBr): $\tilde{\nu}$ = 1632 cm^{-1} (C=O), 1600 (arom.), 1574 (arom.). − MS (EI, 70 eV); *m/z* (%): 430 (3) [$M^+ - COC(CH_3)_3$], 326 (100). − MS (CI, isobutane); *m/z* (%): 516 (100) [$M^+ + H$]. − $C_{32}H_{41}N_3O_3$ (515.3): calcd. C 74.53, H 8.01, N 8.15; found C 74.44, H 8.21, N 7.95.

2,6-Bis[(*N*-benzoyl-*N*-benzylamino)methyl]-4-methoxypyridine (6c): Starting materials: 1.23 g (3.5 mmol) of 2,6-bis(benzylaminomethyl)-4-methoxypyridine (**9**), 1.09 g (7.1 mmol) of benzoyl chloride, 2.15 g (21.3 mmol) of NEt_3. Yield: 0.98 g (61%), colorless oil, slowly crystallizing, m.p. 101−109°C. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.52 (br. s, 1 H, H_2O), 3.82 (br. s, ca. 3 H), 4.3−4.9 (m, ca. 8 H), 6.49 (br. s, ca. 1 H), 6.81 (br. s, ca. 1 H), 7.1−7.6 (m, ca. 20 H). − IR (KBr): $\tilde{\nu}$ = 1633 cm^{-1} (C=O), 1600 (arom.), 1574 (arom.). − MS (EI, 70 eV); *m/z* (%): 450 (3) [M^+ − COPh], 347 (39) [M^+ − COPh − COPh], 346 (100). − MS (CI, isobutane); *m/z* (%): 556 (100) [$M^+ + H$], 346 (23) [M^+ − COPh − COPh]. − $C_{36}H_{33}N_3O_3 \cdot 0.5\,H_2O$ (555.3 + 9.0): calcd. C 76.57, H 6.07, N 7.44; found C 76.77, H 6.13, N 7.30.

2,6-Bis[(*N*-benzyl-*N*-phenylacetylamino)methyl]-4-methoxypyridine (6d): Starting materials: 1.23 g (3.5 mmol) of 2,6-bis(benzylaminomethyl)-4-methoxypyridine (**9**), 1.09 g (7.1 mmol) of phenylacetyl chloride, 2.15 g (21.3 mmol) of NEt_3. Yield: 1.14 g (55%), colorless oil. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.6−3.9 (m, ca. 8 H), 4.3−4.7 (m, ca. 8 H), 6.35 (s, 0.40 H, PyH_{ZZ}), 6.37 (d, *J* = 2.2 Hz, 0.60 H, PyH_{EZ}), 6.56 (s, 0.40 H, PyH_{EE}), 6.61 (d, *J* = 2.2 Hz, 0.60 H, PyH_{EZ}), 7.0−7.4 (m, ca. 20 H). − IR (KBr): $\tilde{\nu}$ = 1644 cm^{-1} (C=O), 1599 (arom.), 1573 (arom.). − MS (EI, 70 eV); *m/z* (%): 583 (5) [M^+], 492 (6) [$M^+ - C_7H_7$], 464 (5) [$M^+ - C_8H_7O$], 360 (100). − MS (CI, isobutane); *m/z* (%): 584 (100) [$M^+ + H$], 583 (6) [M^+]. − $C_{38}H_{37}N_3O_3$ (583.3): calcd. C 78.19, H 6.38, N 7.20; found C 78.15, H 6.46, N 7.13.

2,6-Bis{[*N*-benzyl-*N*-(3-phenylpropionyl)amino]methyl}-4-methoxypyridine (6e): Starting materials: 1.23 g (3.5 mmol) of 2,6-bis(benzylaminomethyl)-4-methoxypyridine (**9**), 1.19 g (7.1 mmol) of 3-phenylpropionyl chloride, 2.15 g (21.3 mmol) of NEt_3. Yield: 1.08 g (50%), yellow oil. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.6−2.8 (m, ca. 4 H), 2.9−3.1 (m, ca. 4 H), 3.65 (s, ca. 0.7 H), 3.74 (s, ca. 1.7 H), 3.79 (s, ca. 0.6 H), 4.3−4.7 (m, ca. 8 H), 6.38 (s, 0.5 H, PyH_{ZZ}), 6.40 (d, *J* = 2.2 Hz, 0.5 H, PyH_{EZ}), 6.69 (s, 0.5 H, PyH_{EE}), 6.70 (d, *J* = 2.2 Hz, 0.5 H, PyH_{EZ}), 7.0−7.4 (m, ca. 20 H). − IR (KBr): $\tilde{\nu}$ = 1650 cm^{-1} (C=O), 1599 (arom.), 1574 (arom.). − MS (EI, 70 eV); *m/z* (%): 611 (5) [M^+], 520 (3) [$M^+ - C_7H_7$], 478 (4) [$M^+ - C_9H_9O$], 374 (100). − MS (CI, isobutane); *m/z* (%): 612 (100) [$M^+ + H$], 611 (8) [M^+]. − $C_{40}H_{41}N_3O_3$ (611.3): calcd. C 78.53, H 6.75, N 6.87; found C 77.81, H 6.87, N 6.58.

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