74. Selective Synthesis of Polyamine Derivatives: Efficient Derivatization of the Secondary Amino Group of *N*-Monosubstituted 1,3-Diamines

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Dedicated to Professor *Klaus Schreiber* on the occasion of his 70th birthday

(9.I.97)

N-Monosubstituted 1,3-diamines were selectively functionalized at the secondary N-atom *via* 2-Ph-substituted hexahydropyrimidine intermediates. Reaction of the diamines with benzaldehyde, followed by treatment with an electrophile and hydrolysis, provided the desired products with excellent selectivity and in high yields. N^4,N^9-bis[3-phenylprop-2-enoyl]spermine (**4a**), which was further converted to N^1,N^{12}-bis[3-phenylprop-2-enoyl]spermine (**15**) by a transamidation reaction, was prepared by this way in 82% yield from spermine (**1**). Compound **4a** was alternatively synthesized in 83% yield, equally from **1**, by a sequence involving intermediary protection of the terminal amino groups.

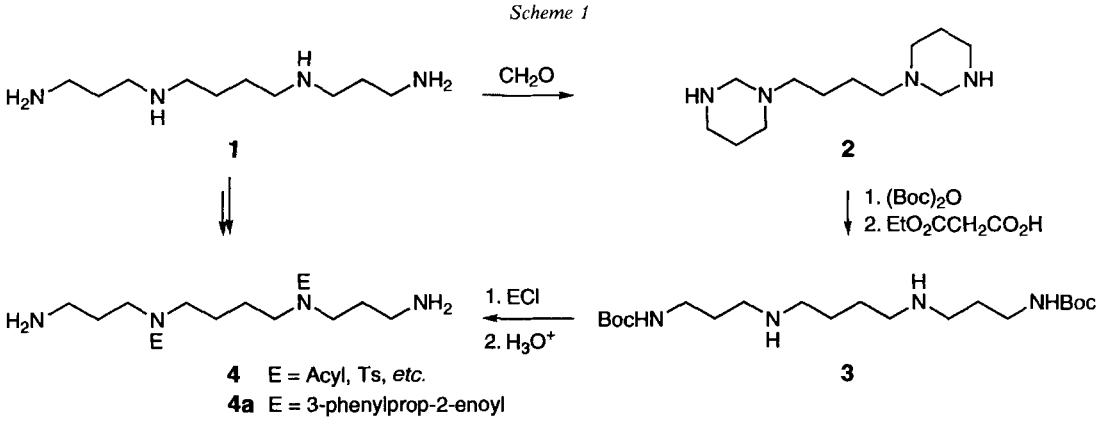
Introduction. – Linear biogenic polyamines, particularly putrescine, spermidine, and spermine (**1**), are ubiquitous in living cells, playing important roles for several cell functions. It is not surprising, therefore, that derivatives of polyamines – alkylated or acylated conjugates with sugars, steroids, carboxylic acids, and peptides – exhibit notable and diverse physiological properties [1]. In recent years, a renewed and increased interest in neurotoxic polyamine derivatives arose [2–4]. Such compounds allow the study of specific neurologically important subtypes of ionotropic glutamate receptors, and they are considered as lead structures for potential drugs for the treatment of *Alzheimer*, *Parkinson* and other brain diseases.

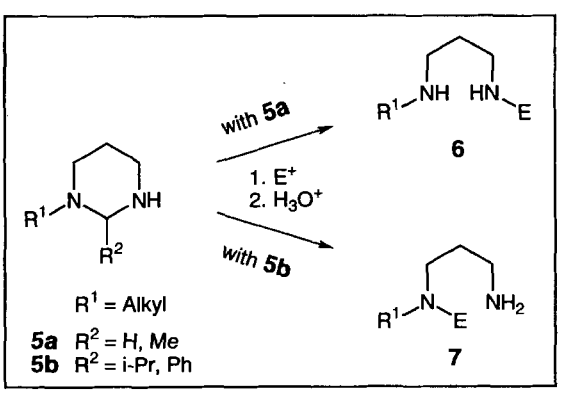
Since the access to physiologically interesting polyamine derivatives from natural sources is rather limited, the quest for efficient syntheses for such compounds has been intensified over the last decade. So far, the specific derivatization of the several amino groups in polyamine precursors turned out to be the major problem: whereas the selective functionalization of the terminal primary amines was often possible due to their slightly higher reactivity, the direct and selective derivatization of the internal secondary amine functions without prior blocking of the NH_2 groups was not possible. Usually, elaborate protective group strategies had to be used in such cases. For instance, N^4,N^9-diacylspermines **4** were prepared on several routes, but always by intermediary block of the primary amine functions [5–10]. In one example, the hexahydropyrimidine intermediate **2** was elegantly used for the introduction of the respective protecting groups (*Scheme 1*) [10]. The selective reaction of hexahydropyrimidines of the type **5a** at the less

[1]) Part of the diploma thesis of *R. H.* and of the planned Ph.D. thesis of *C. J.*

substituted amino group, leading to compounds of the type **6**, is well-known and was already used earlier [1] [11] [12]. It was, thus, rather interesting to learn that 1,2-disubstituted hexahydropyrimidines **5b** behave differently. *Parrinello* and *Mülhaupt* [13] have recently shown that compounds of the type **5b** can react with isocyanates also at the higher substituted N-atom, yielding derivatives of the type **7**. Depending on the size and the electronic nature of the substituents R^2, partial or complete derivatization at N(1) occurred. Hence, the question arose, whether 2-substituted hexahydropyrimidines of the type **5b** – complementary to 2-unsubstituted analogs **5a** – could generally be used for the straightforward preparation of *N*-derivatized *N*-monosubstituted 1,3-diamine moieties in polyamines, *e.g.*, for the synthesis of N^4,N^9-bis[3-phenylprop-2-enoyl]spermine (**4a**).

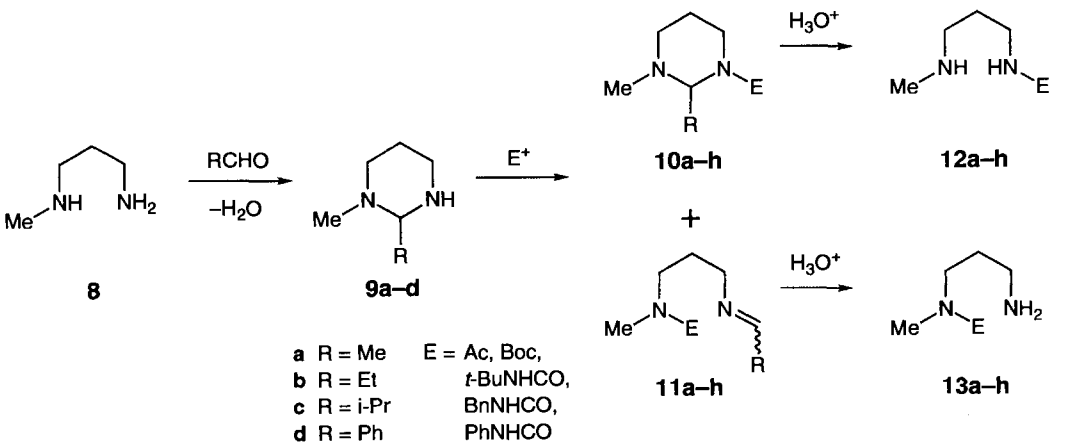
Scheme 1





Results and Discussion. – The four hexahydropyrimidine derivatives **9a–d** used as model compounds in our investigation were almost quantitatively formed from diamine **8** and the corresponding parent aldehydes (*Scheme 2*). The two reactants condensed readily at low temperature, and the transformation was brought to completion by trapping the reaction H_2O with molecular sieves (3 Å), Na_2CO_3, or K_2CO_3. After removal of the solids by filtration, followed by evaporation, the products were obtained sufficiently pure for further transformations.

Scheme 2



The reactions of the hexahydropyrimidine derivatives **9a–d** with several electrophiles led, as expected, to products of the type **10** and **11**, or, after hydrolysis, to **12** and **13** (*Table*). As already observed in the earlier investigations of *Parrinello* and *Mülhaupt* [13], the ratio of the compounds **10**/**11** or **12**/**13**, depends mostly on the bulkiness of the substituents at C(2) of the starting **9**. The chemoselectivity of the reaction is less dependent on the nature or the size of the electrophiles. Best results with in respect to the formation of the desired compounds of the type **11** or **13** were obtained with **9c** and **9d** possessing the Ph or the i-Pr group, respectively, at C(2). Their reactions with Ac_2O, $(Boc)_2O$, and isocyanates provided high yields of **11c–e** or **13f–h**, respectively (*Entries 3–5*, *12–17*, *Table*). Much to our surprise, the Me and Et derivatives **9a** and **9b**, which have not been investigated previously, gave almost completely products of the type **10** or **12** (*Entries 1*, *2*, and *6–11*). Obviously, only with the step from the Et to the i-Pr group, the critical steric demand for directing the reaction towards products of the type **11**/**13** was reached.

The chemoselectivities of the derivatizations of compounds of the type **9** is only slightly dependent on the nature and the size of the electrophiles. In connection with the aforementioned influence of the bulkiness of substituents at C(2) on the chemical outcome of these reactions, the latter is rather astonishing [14]. The acetylation and *tert*-butoxycarbonylation reactions proceeded a trifle more selectively than the transformations with the isocyanates.

The selective formation of the compounds of the type **10** or **11** is explained by means of the mechanism outlined in *Scheme 3*. It is assumed that the hexahydropyrimidines **9** are in a rapid equilibrium with the open-chain forms **9′** [14] [15], even though no evidence for the presence of species of the type **9′** was found in the NMR spectra[2]). In treatment of the mixture of **9** and **9′** with an electrophile, the reagent would react with both compounds at the less hindered and more reactive N-atom. This would lead to

[2]) Evidence for fast equilibria between hexahydropyrimidines and open-chain forms is found for *N*-unsubstituted compounds, though [14].

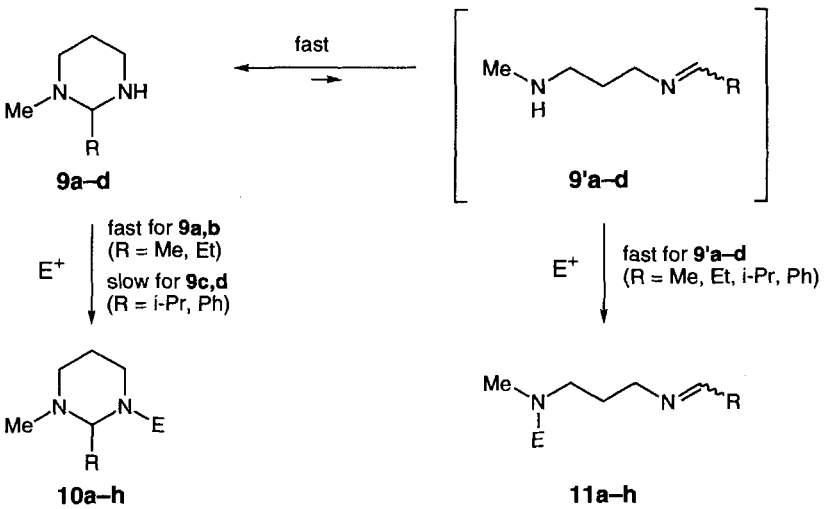
Table. *Formation of Compounds* **10a–e**, **11a–e**, **12f–h**, *and* **13f–h** *from Hexahydropyrimidines* **9a–d**

Entry	Educt		Conditions[a])	Product			
	No.	R		No.	E	Yield [%]	Ratio
1	**9a**	Me	*A*	**10a**	Ac	63	98:2
				11a	Ac		
2	**9b**	Et	*A*	**10b**	Ac	83	96:4
				11b	Ac		
3	**9c**	i-Pr	*A*	**10c**	Ac	83	7:93
				11c	Ac		
4	**9d**	Ph	*A*	**10d**	Ac	95	5:95
				11d	Ac		
5	**9d**	Ph	*B*	**10e**	Boc	95	0:100
				11e	Boc		
6	**9a**	Me	*C*	**12f**	*t*-BuNHCO	90	100:0
				13f	*t*-BuNHCO		
7	**9a**	Me	*C*	**12g**	BnNHCO	90	100:0
				13g	BnNHCO		
8	**9a**	Me	*C*	**12h**	PhNHCO	86	100:0
				13h	PhNHCO		
9	**9b**	Et	*C*	**12f**	*t*-BuNHCO	84	100:0
				13f	*t*-BuNHCO		
10	**9b**	Et	*C*	**12g**	BnNHCO	82	94:6
				13g	BnNHCO		
11	**9b**	Et	*C*	**12h**	PhNHCO	87	100:0
				13h	PhNHCO		
12	**9c**	i-Pr	*C*	**12f**	*t*-BuNHCO	85	7:93
				13f	*t*-BuNHCO		
13	**9c**	i-Pr	*C*	**12g**	BnNHCO	83	3:97
				13g	BnNHCO		
14	**9c**	i-Pr	*C*	**12h**	PhNHCO	86	18:82
				13h	PhNHCO		
15	**9d**	Ph	*C*	**12f**	*t*-BuNHCO	84	57:43
				13f	*t*-BuNHCO		
16	**9d**	Ph	*C*	**12g**	BnNHCO	98	12:88
				13g	BnNHCO		
17	**9d**	Ph	*C*	**12h**	PhNHCO	87	7:93
				13h	PhNHCO		

[a]) *A*: AcCl (1 equiv.), CH_2Cl_2, −20 to 23°, 1 h. *B*: $(Boc)_2O$ (1 equiv.), CH_2Cl_2, 23°, 5 min, *C*: 1. Isocyanate (1 equiv.), THF, < 30 to 23°, 1 h. 2. 1N aq. HCl soln., reflux, 30 min.

compounds of the type **10** from **9** and **11** from **9′**. Depending on the nature and the size of the substituent at C(2), the reaction with **9** could now be either fast (for small R groups), so that the chemical outcome reflects more or less the relative concentrations of the species **9** and **9′** in solution. The attack of the electrophile could, however, be retarded due to steric hindrance in compounds with bulky R groups. In this case, the minor but more reactive open-chain tautomer **9′**, which is constantly refurnished from

Scheme 3



9, could react preferentially. The overall process would then mainly lead to compounds **11**. The drastic substituent effect, observed when the R group in **9** is changed from Me or Et to i-Pr or Ph, is explained by model considerations: in case of aryl or α-branched substituents at C(2), the NH function of the hexahydropyrimidine moiety in both chair-like structures of **9** would be sterically strongly shielded (see below)[3]), which could avoid immediate attack by an electrophile. In the case of **9a** or **9b**, a H-atom instead of a Me group can be placed in the labelled synclinal position to the NH group. This would allow a more or less unhindered access to the free electron pair of the N-atom for these compounds. The proposed reaction course also accounts for the electronic influence of the substituents R as described by *Parrinello* and *Mülhaupt* [13]: when 2-phenyl- and 2-(4-nitrophenyl)-substituted compounds of the type **9** were reacted with BuNCO or PhNCO, the nitro derivatives delivered in both cases lower selectivities in favor of compounds of the type **11**. Since the 4-NO_2 group does destabilize an imino species of the type **9'**, the open-chain tautomer is in this case less efficiently refurnished from the corresponding hexahydropyrimidine precursors **9**. Hence, the heterocycles **9** can react to a higher degree to **10**, which is manifested by the observed drop of selectivity.

In accordance with the above discussed preparation of 3-(methylamino)propan-1-amine derivatives **13** *via* hexahydropyrimidines **9**, the spermine derivative **4a** was prepared in virtually a one-pot procedure, requiring negligible intermediary workup (*Scheme 4*): treatment of spermine (**1**) with 2 equiv. of PhCHO in toluene, followed by

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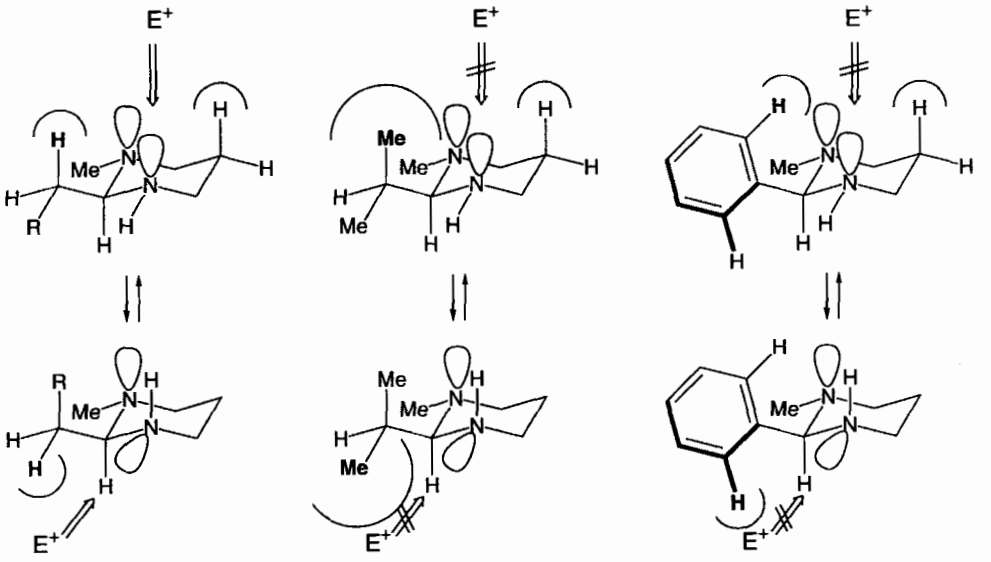
[3]) It was established on the basis of spectral data that hexahydropyrimidines **9b–d** (as **9a** [16]) prefer a chair-like conformation [17] with the Me group at N(2), the R group at C(2), and the lone pair at N(1) in equatorial positions. The nitrogen inversion is rather rapid ($\Delta G^{\ddagger} \ll 45$ kJmol^{-1}), though; considerably faster than the ring inversion ($\Delta G^{\ddagger} \approx 45$ kJmol^{-1}) [17] [18]. Consequently, the thermodynamically preferred structures of **9a–d** are not necessarily the most important ones with respect to their reactivity towards electrophiles or other reagents. Therefore, both geometrical structures of compounds of the type **9** have to be taken into account.

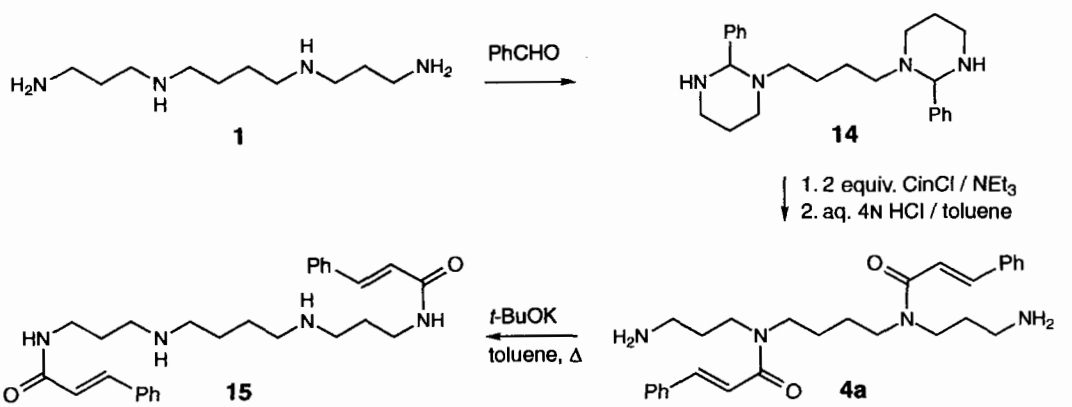


9a R = H
9b R = Me

9c **9d**

reaction of the intermediary bis[hexahydropyrimidine] **14** with 2 equiv. of 3-phenylprop-2-enoyl chloride (cinnamoyl chloride, CinCl) in CH_2Cl_2, hydrolysis with aqueous HCl solution/toluene, and purification, delivered the desired product **4a** in overall 82% yield. Previously published alternative routes gave rise to similar products with *ca.* 50% yields at their best.

Scheme 4



For chemical and spectroscopic comparison, isomeric N^1,N^{12}-bis[3-phenylprop-2-enoyl]spermine (**15**) was also prepared from **4a** by the transamidation reaction [19–23]. Treatment of **4a** with *t*-BuOK in toluene under reflux for 4 h afforded **15** in high yield. The structure of **15** is secured by an independent synthesis [24].

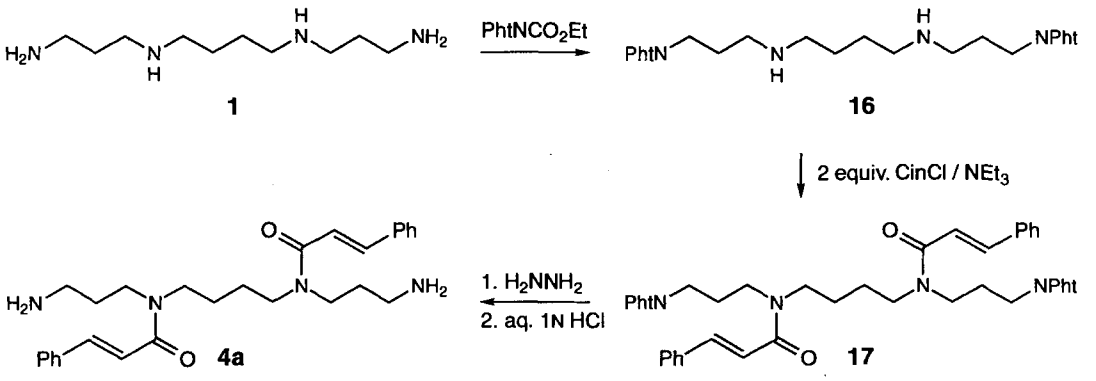
Compounds **4a** and **15** differ from each other in their chemical and spectroscopic behavior. For instance, the terminal bis-amide **15**, in contrast to the internal bis[3-phenylprop-2-enoyl] derivative **4a**, does not show reaction with *Fluram*® [25]. This indicates the absence of any primary amine function in **15**. As a matter of fact, the *Fluram*® reaction, which is very sensitive and reliable for the detection of primary amines, was used to follow the progress of the rearrangement of **4a** to **15** by TLC. The compounds **4a** and **15** differ characteristically in their IR spectra: the internally acylated compound **4a** shows a single and strong absorption band at 1645 cm^{-1} for the *N*,*N*-disubstituted amide function, whereas the terminally acylated compound **15** manifests two strong amide bands at 1655 cm^{-1} (amide I) and 1540 cm^{-1} (amide II), usually observed for open-chain *N*-monosubstituted amides. Also the NMR spectroscopic differences of **4a** and **15** are striking: The ^{1}H-NMR spectrum of **4a** exhibits solely some poorly resolved multiplets, and the ^{13}C-NMR spectrum indicates the presence of a number of isomers. In contrast to this, the signals in the ^{1}H-NMR of **15** are well resolved, giving clearly evidence for only two isomeric components of **15** in a ratio of *ca.* 4:1. The same information is obtained from the ^{13}C-NMR spectrum of **15**. The isomers of **4a** and **15** arise probably due to the restricted rotations around the amidic C–N bonds. Since *N*-monosubstituted amides usually prefer the (s-*cis*)-conformation, **15** most probably exists predominantly in the (s-*cis*,s-*cis*)-form; minor amounts of the (s-*trans*,s-*cis*)-isomer (*ca.* 20%) might be detected, but the amounts of (s-*trans*,s-*trans*)-configured products would be expected to be negligible. For compound **4a**, the situation is quite different: because of the similar rests on the *N*-atoms, the *N*,*N*-disubstituted amides **4a** should not prefer a specific conformation. This ought to be manifested by the presence of approximately equivalent amounts of the three isomeric compounds in the mixture of **4**. The situation is even more complicated when the samples are aged. By the action of day-light, the C=C bonds of the 3-phenylprop-2-enoyl moieties can isomerize [26], giving rise to even more isomeric species. Similar effects as with **4a** and **15** were observed with internally and terminally acylated spermidine [27] [28].

It would be presumptuous to claim that the preparation of selectively functionalized diamines of the type **13** *via* hexahydropyrimidine intermediates is always superior to the classic sequence using intermediary protection of the terminal amines. Lately, the direct terminal bis-protection of spermine and related compounds has been highly improved. For instance, treatment of polyamines with (benzyloxycarbonyl)carbonitrile (Z–CN) in $CHCl_3$ or their reaction with *Nefkens* reagent [29] [30] gave rise to high yields of N^1,N^{12}-bis-protected compounds that were ready for acylation at the free amine functions [8], [31], [32]. Whereas the Z-protective group is not suitable for the synthesis of N^4,N^9-bis[3-phenylprop-2-enoyl]spermine (**4a**), the reaction course *via* bis[phthaloyl]-protected spermine **16** proved to be competitive to the hexahydropyrimidine strategy (*Scheme 5*). Treatment of **16** with CinCl gave **17** and, after hydrazinolysis, the N^4,N^9-bis-acylated product **4a** in as high as 83% yield (starting from **1**).

Conclusion. – We have shown with the preparation of the propane-1,3-diamine derivatives **11** and **13** and the bis[3-phenylprop-2-enoyl]spermine derivative **4a** that hexahydropyrimidines of the type **9** can efficiently be used for the selective functionalization of the secondary N-atom of *N*-monosubstituted 1,3-diamines. The reactions are high-yielding, easily performed, and readily worked-up. The use of intermediary 2-Ph-substituted hexahydropyrimidines is complementary to the use of 2-unsubstituted analogs, which deliver the opposite regioisomers, and it is competitive to strategies where N^a,N^ω-bis-protected polyamines are involved.

We thank the members of our analytical laboratories for their excellent services and the *Swiss National Science Foundation* for generous financial support.

Scheme 5



Experimental Part

1. *General.* Unless otherwise stated, all org. solvents were distilled prior to use. For the reactions, THF was dried over Na in presence of diphenylketyl; CH_2Cl_2 was dried over molecular sieves (3 Å). All reactions were carried out under an Ar atmosphere. Soln. of salts and acids for workup procedures were prepared in deionized H_2O. Extracts were dried (Na_2SO_4) and evaporated *in vacuo*. Chromatography: silica gel *Merck 60* (40–63 μm). M.p.: *Mettler FP-5/FP-52*. IR Spectra (neat): *Perkin-Elmer 781*; data in $1/\lambda$ [cm^{-1}], absorptions > 1400 cm^{-1} (without fingerprint). ^{1}H-NMR: at 300 MHz in $CDCl_3$; *Bruker AC-300* or *Bruker ARX-300*, δ in ppm rel. to $CHCl_3$ (= 7.26 ppm), J in Hz. ^{13}C-NMR: at 75.6 MHz (*Bruker ARX-300*); or at 131.2 MHz (*Bruker AMX-600*) in $CDCl_3$; δ in ppm rel. to $CDCl_3$ (= 77.0 ppm); multiplicities from DEPT experiments. EI-MS: at 70 eV and CI-MS: with NH_3 as the reactant gas; *Finnigan SSQ 700* or *Varian MAT 90*; ESI-MS: *Finnigan TSQ 700*; data in *m/z*.

2. *Preparation of Hexahydropyrimidines.* 2.1. *1,2-Dimethylhexahydropyrimidine* (**9a**). A soln. of MeCHO (2.5 g, 56.8 mmol) in CH_2Cl_2 (10 ml) was added dropwise at −78° to a soln. of *3-(methylamino)propan-1-amine* (**8**; 5.0 g, 56.8 mmol) in CH_2Cl_2 (10 ml). The cooling was interrupted, and after the temp. reached 23°, K_2CO_3 (5.6 g, 56.8 mmol) was added, and it was stirred for 1 h. Filtration and evaporation of the volatiles gave **9a** (4.8 g, 74%). Colorless oil. IR: 3270*m*, 2970*m*, 2980*m*, 2930*s*, 2840*m*, 2700*w*, 2635*w*, 1460*m*, 1445*m*. ^{1}H-NMR: 2.98–2.92 (*dm*, J = 13.0, H_{eq}–C(4)); 2.85–2.81 (*dm*, J = 11.8, H_{eq}–C(6)); 2.78 (*q*, J = 5.9, H–C(2)); 2.53 (*td*, J = 12.9, 3.2, H_{ax}–C(4)); 2.14 (*td*, J = 11.8, 3.1, H_{ax}–C(6)); 2.11 (*s*, MeN); 1.69–1.54 (*m*, H_{ax}–C(5)); 1.46–1.40 (*dm*, J = 13.0, H_{eq}–C(5)); 1.12 (*d*, J = 5.9, Me–C(2)). ^{13}C-NMR: 74.4 (*d*, C(2)); 56.1 (*t*, C(6)); 45.2 (*t*, C(4)); 41.9 (*q*, MeN); 27.6 (*t*, C(5)); 20.8 (*q*, Me–C(2)). EI-MS: 114 (3, $M^{+\cdot}$), 113 (14, $[M - H]^+$), 99 (100, $[M - Me]^+$), 84(10), 71(15), 70(29), 58(37), 57(38), 56(57).

2.2. *2-Ethyl-1-methylhexahydropyrimidine* (**9b**). Analogously to *2.1*, **8** (5.0 g, 56.8 mmol) reacted with $MeCH_2CHO$ (3.3 g, 56.8 mmol) to give **9b** (7.0 g, 96%). Colorless oil. IR: 3270*m*, 2930*s*, 2880*w*, 2860*w*, 2840*w*, 2770*m*, 2700*w*, 1460*m*, 1430*w*. ^{1}H-NMR: 3.04–2.97 (*dm*, J = 13.3, H_{eq}–C(4)); 2.89–2.83 (*dm*, J = 11.7, H_{eq}–C(6)); 2.68 (*dd*, J = 7.2, 3.3, H–C(2)); 2.56 (*td*, J = 12.8, 3.2, H_{ax}–C(4)); 2.21 (*td*, J = 12.0, 3.1, H_{ax}–C(6)); 2.11 (*s*, MeN); 1.67–1.58 (*m*, H_{ax}–C(5), $MeCH_2$); 1.33–1.27 (*m*, H_{eq}–C(5), NH); 0.84 (*t*, J = 7.5, $MeCH_2$). ^{13}C-NMR: 79.2 (*d*, C(2)); 56.3 (*t*, C(6)); 45.4 (*t*, C(4)); 41.0 (*q*, MeN); 27.0 (*t*, C(5)); 26.0 (*t*, $MeCH_2$); 8.8 (*q*, $MeCH_2$). EI-MS: 128 (1, $M^{+\cdot}$), 127 (2, $[M - H]^+$), 113(31), 99 (100, $[M - Et]^+$), 84(10), 71(26), 70(39), 58(18), 57(13), 56(24).

2.3. *2-Isopropyl-1-methylhexahydropyrimidine* (**9c**). Analogously to *2.1*, **8** (5.0 g, 56.8 mmol) reacted with 2-methylpropanal (4.1 g, 56.8 mmol) to give **9c** (8.0 g, 99%). Colorless oil. IR: 3300*w*, 2940*s*, 2870*w*, 2840*w*, 2770*m*, 2710*w*, 1470*m*, 1432*w*. ^{1}H-NMR: 3.15–3.09 (*dm*, J = 13.3, H_{eq}–C(4)); 2.99–2.93 (*dm*, J = 11.7, H_{eq}–C(6)); 2.64 (*d*, J = 3.8, H–C(2)); 2.59 (*td*, J = 12.8, 3.1, H_{ax}–C(4)); 2.32 (*td*, J = 12.0, 3.0, H_{ax}–C(6));

2.18 (*s*, MeN); 2.10–2.01 (*m*, Me_2CH); 1.77–1.62 (*m*, H_{ax}–C(5)); 1.50–1.45 (*dm*, J = 13.8, H_{eq}–C(5)); 0.95, 0.87 (2*d*, J = 7.0, 7.0, Me_2CH). ^{13}C-NMR: 83.1 (*d*, C(2)); 56.8 (*t*, C(6)); 45.7 (*t*, C(4)); 40.8 (*q*, MeN); 28.0 (*dq*, C(7)); 27.0 (*t*, C(5)); 19.7, 14.6 (2*q*, Me_2CH). EI-MS: 143 (2, $[M + H]^+$), 141 (3, $[M - H]^+$), 99 (100, $[M - (i\text{-}Pr)]^+$), 84(7), 71(8), 70(39), 58(7), 57(3), 56(14).

2.4. *1-Methyl-2-phenylhexahydropyrimidine* (**9d**). Analogously to *2.1*, **8** (5.0 g, 56.8 mmol) reacted with PhCHO (6.0 g, 56.8 mmol) to give **9d** (9.6 g, 96%). Colorless oil. IR: 3280*m*, 3080*w*, 3060*m*, 3030*m*, 2980*m*, 2940*s*, 2840*w*, 2790*m*, 2620*w*, 1645*w*, 1605*w*, 1575*w*, 1490*m*, 1450*s*. ^{1}H-NMR: 7.41–7.25 (*m*, 5 arom. H); 3.66 (*s*, H–C(2)); 3.17–3.08 (*m*, H_{eq}–C(4), H_{eq}–C(6)); 2.74 (*td*, J = 13.0, 3.1, H_{ax}–C(4)); 2.29 (*td*, J = 12.0, 2.9, H_{ax}–C(6)); 1.93 (*s*, MeN); 1.90–1.83 (*dm*, J = 12.8, H_{ax}–C(5)); 1.64–1.57 (*dm*, J = 12.9, H_{eq}–C(5)). ^{13}C-NMR: 141.7 (*s*, arom. C); 127.9 (*d*, 2 arom. C); 127.5 (*d*, arom. C); 126.7 (*d*, 2 arom. C); 83.0 (*d*, C(2)); 55.7 (*t*, C(6)); 45.1 (*t*, C(4)); 42.2 (*q*, MeN); 26.8 (*t*, C(5)). EI-MS: 176 (3, $M^{+\cdot}$), 175 (7, $[M - H]^+$), 132(15), 119(30), 118(100), 99(31, $[M - Ph]^+$), 91(18), 78(6), 77(19), 70(6), 58(87), 51(9).

3. *Reactions with Electrophiles.* 3.1. *1-Acetyl-2,3-dimethylhexahydropyrimidine* (**10a**) *and* N-*[3-(Ethylidenamino)propyl]*-N-*methylacetamide* (**11a**). A soln. of Ac_2O (5.79 g, 56.8 mmol) and Et_3N (5.73 g, 56.8 mmol) in CH_2Cl_2 (10 ml) was added at −20° dropwise to a soln. of **9a** (6.47 g, 56.8 mmol) in CH_2Cl_2 (10 ml). It was warmed to 23° and stirred for 1 h before it was quenched by addition of an aq. 1N NaOH soln. (20 ml). Separation of the org. phase, washing with brine until neutral, and evaporation gave a colorless oil (5.58 g, 63%), consisting of **10a** (98%, mixture of conformational isomers) and **11a** (2%), which could not be further separated.

Data of **10a** (relevant NMR signals from the spectra of the mixture **10a**/**11a**): IR: 2940*s*, 2870*m*, 2700*m*, 1645*s*, 1420*s*. ^{1}H-NMR: 5.38, 4.52 (2*q*, J = 6.6, 6.8, H–C(2)); 4.48, 3.61 (2*dd*, J = 14.2, 5.2 and 13.5, 4.6, H_{eq}–C(6)); 3.30, 2.78 (2*td*, J = 13.3, 3.1 and 13.4, 3.8, H_{ax}–C(6)); 3.05 (*td*, J = 13.2, H_{eq}–C(4)); 2.59 (*dd*, J = 13.5, 3.8, H_{ax}–C(4)); 2.40, 2.37 (2*s*, MeN); 2.04, 2.03 (2*s*, MeCON); 1.99–1.77 (*m*, H_{ax}–C(5)); 1.36, 1.24 (2*d*, J = 6.4, 6.6, Me–C(2)); 1.34–1.23 (*m*, H_{eq}–C(5)). ^{13}C-NMR: 168.9, 168.6 (2*s*, CO); 77.8, 77.1 (2*d*, C(2)); 70.3, 64.8 (2*t*, C(4)); 44.9, 40.2 (2*q*, MeN); 41.2 (*d*, C(6)); 34.6, 21.3 (2*q*, *Me*CO); 21.5, 20.5 (2*t*, C(5)); 14.3, 12.7 (2*q*, *Me*–C(2)). EI-MS: 157 (43, $[M + H]^+$), 156 (13, $M^{+\cdot}$), 141(72), 113(10), 100(12), 99(100), 85(5), 72(8), 71(11), 70(13), 58(6), 57(9), 56(26).

3.2. *1-Acetyl-2-ethyl-3-methylhexahydropyrimidine* (**10b**) *and* N-*Methyl*-N-*[3-(propylidenamino)propyl]-acetamide* (**11b**). Analogously to *3.1*, **9b** (7.27 g, 56.8 mmol) reacted with Ac_2O (5.79 g, 56.8 mmol) in the presence of Et_3N (5.73 g, 56.8 mmol) to give a colorless oil (8.01 g, 83%), consisting of **10b** (96%, mixture of conformational isomers) and **11b** (4%), which could not be further separated.

Data of **10b** (relevant NMR signals from the spectra of the mixture **10b**/**11b**): ^{1}H-NMR: 5.10–5.04, 4.17–4.13 (2*m*, H–C(2)); 4.46, 3.55 (2 br. *d*, J = 13.6, 13.6, H_{eq}–C(6)); 3.30–3.15, 2.70–2.60 (2*m*, H_{ax}–C(6)); 3.06 (br. *t*, J = 13.8, H_{eq}–C(4)); 2.51 (br. *d*, J = 13.9, H_{ax}–C(4)); 2.38, 2.37, 2.35, 2.33 (4*s*, MeN); 2.01, 1.99, 1.98 (3*s*, MeCO); 1.96–1.62 (*m*, H_{eq}–C(5), $MeCH_2$); 0.98–0.64 (*m*, H_{ax}–C(5), $MeCH_2$). ^{13}C-NMR: 169.4, 169.2 (2*s*, CO); 76.1, 69.9 (2*d*, C(2)); 45.1, 44.9 (2*t*, C(4)); 41.1 (*q*, MeN); 40.6, 34.9 (*d*, C(6)); 21.3 (*q*, *Me*CO); 21.8, 21.2, 20.9, 19.5 (4*t*, C(5), $MeCH_2$); 10.0, 9.7 (2*q*, $MeCH_2$). EI-MS: 171 (11, $[M + H]^+$), 170 (< 1, $M^{+\cdot}$), 141(62), 100(7), 99(100), 84(5), 71(5), 70(10), 56(7).

3.3. *1-Acetyl-2-isopropyl-3-methylhexahydropyrimidine* (**10c**) *and* N-*Methyl*-N-*{[3-(2-methylpropylidene)-amino]propyl}acetamide* (**11c**). Analogously to *3.1*, **9c** (8.07 g, 56.8 mmol) reacted with Ac_2O (5.8 g, 56.79 mmol) in the presence of Et_3N (5.73 g, 56.8 mmol) to give a colorless oil (8.67 g, 83%), consisting of **10c** (7%, mixture of conformational isomers) and **11c** (93%), which could not be further separated.

Data of **11c** (relevant NMR signals from the spectra of the mixture **10c**/**11c**): IR: 2960*s*, 2930*s*, 2870*m*, 2740*m*, 1640*s*, 1485*m*, 1475*m*, 1445*m*, 1400*s*. ^{1}H-NMR: 7.46–7.38 (*m*, HC=N); 3.27–3.19 (*m*, 2 NCH_2); 2.87, 2.86, 2.79, 2.78 (4*s*, MeN); 2.32–2.25 (*m*, Me_2CH); 2.12–1.96 (*m*, $CH_2CH_2CH_2$); 1.97, 1.96, 1.94 (3*s*, MeCO); 0.96–0.91 (*m*, Me_2CH). ^{13}C-NMR: 177.6, 177.4 (2*s*, CO); 170.5, 170.4 (2*d*, CHO); 58.5, 57.7 (2*t*, $MeCONCH_2$); 48.5, 45.4 (2*t*, $HC{=}NCH_2$); 36.0, 33.0 (2*q*, MeN); 33.7 (*d*, Me_2CH); 29.4, 28.3 (2*t*, $CH_2CH_2CH_2$); 21.8, 21.1 (2*q*, *Me*CO); 19.25, 19.18 (2*q*, Me_2CH). EI-MS 185 (14, $[M + H]^+$), 184 (5, $M^{+\cdot}$), 141(28), 114(28), 112(9), 111(52), 99(31), 98(100), 70(79).

3.4. *1-Acetyl-3-methyl-2-phenylhexahydropyrimidine* (**10d**) *and* N-*[3-(Benzylidenamino)propyl]*-N-*methyl-acetamide* (**11d**). Analogously to *3.1*, **9d** (10.0 g, 56.8 mmol) reacted with Ac_2O (5.79 g, 56.8 mmol) in the presence of Et_3N (5.73 g, 56.8 mmol) to give a slighly yellow oil (11.76 g, 95%), consisting of **10d** (5%, mixture of conformational isomers) and **11d** (95%), which could not be further separated.

Data of **11d** (relevant NMR signals from the spectra of the mixture **10d**/**11d**): IR: 3060*w*, 3030*w*, 3000*w*, 2930*s*, 1700*w*, 1645*s*, 1580*m*, 1495*m*, 1450*m*, 1400*s*. ^{1}H-NMR: 8.26–8.24 (*m*, HC=N); 7.78–7.66 (*m*, 2 arom. H); 7.39–7.36 (*m*, 3 arom. H); 3.60–3.55, 3.45–3.36 (2*m*, 2 NCH_2); 2.96, 2.95, 2.90. 2.89 (4*s*, MeN); 2.08, 2.07, 2.00, 1.99 (4*s*, MeCO); 1.93–1.86 (*m*, $CH_2CH_2CH_2$). ^{13}C-NMR: 170.5, 170.3 (2*s*, CO); 161.6, 161.3 (2*d*, HC=N);

136.1, 135.9 (2*s*, arom. C); 130.7, 130.5 (2*d*, arom. C); 128.6, 128.5 (2*d*, 2 arom. C); 127.9 (*d*, 2 arom. C); 59.0, 57.9 (2*t*, MeCONCH_2); 48.5, 45.5 (2*t*, HC=NCH_2); 36.1, 33.1 (2*q*, MeN); 29.6, 28.4 (2*t*, $CH_2CH_2CH_2$); 21.8, 21.2 (2*q*, *Me*CO). EI-MS: 218 (3, $M^{+\cdot}$), 146(16), 145(80), 132(90), 118(100), 99(7), 91(34), 77(12).

3.5. *1-(*tert*-Butoxycarbonyl)-3-methyl-2-phenylhexahydropyrimidine* (**10e**) *and* tert*-Butyl* N*-[3-(Benzylidene-amino)propyl]-*N*-methylcarbamate* (**11e**). A soln. of $(Boc)_2O$ (2.92 g, 13.4 mmol) in CH_2Cl_2 (20 ml) was added at 23° dropwise to a soln. of **9d** (2.36 g, 13.4 mmol) in CH_2Cl_2 (20 ml). After 5 min, the volatiles were evaporated to give **11e** (3.51 g, 95%), a colorless oil, as the only product. IR: 2980*m*, 2930*m*, 1820*w*, 1760*w*, 1700*s*, 1650*m*, 1590*w*, 1480*m*, 1450*m*. ^{1}H-NMR: 8.28 (*s*, HC=N); 7.72–7.69 (*m*, 2 arom. H); 7.41–7.3 (*m*, 3 arom. H); 3.60, 3.31 (2*t*, J = 6.9, 7.0, 2 NCH_2); 2.86 (*s*, MeN); 1.9 (*quint.*, J = 7.0, $CH_2CH_2CH_2$); 1.43 (*s*, *t*-Bu). ^{13}C-NMR: 161.2 (*d*, HC=N); 155.8 (*s*, CO); 136.1 (*s*, arom. C); 130.5 (*d*, arom. C); 128.9, 128.5 (2*d*, 2 × 2 arom. C); 79.2 (*s*, Me_3C); 59.0 (*t*, BocNCH_2); 48.1 (*t*, HC=NCH_2); 34.2 (*q*, MeN); 28.9 (*t*, $CH_2CH_2CH_2$); 28.4 (*q*, Me_3C). EI-MS: 277 (3, $[M + H]^+$), 276 (< 1, $M^{+\cdot}$), 219(1), 203(3), 175(2), 159(1), 145(17), 133(17), 132(26), 119(15), 118(34), 105(6), 104(7), 91(25), 88(5), 77(7), 70(7), 58(13), 57(100).

3.6. N*-(*tert*-Butyl)-*N*′-[(3-methylamino)propyl]urea* (**12f**) *and* N*-(3-Aminopropyl)-*N*′-(*tert*-butyl)-*N*-methylurea* (**13f**). With **9a** (*Entry 6*). A soln. of *t*-BuNCO (317 mg, 3.20 mmol) in THF (10 ml) was added dropwise to a soln. of **9a** (365 mg, 3.20 mmol) in THF (10 ml), while the temp. was kept below 30°. After 1 h, the volatiles were evaporated *in vacuo*, and the residue was treated with an aq. 1N HCl soln. (20 ml) at reflux for 30 min. The neutral components were extracted with CH_2Cl_2 and discharged, the aq. soln. brought to pH 14 by addition of KOH, extensively extracted with CH_2Cl_2, and evaporated to give **12f** (539 mg, 90%), a colorless oil, as the only product. *With* **9b** (*Entry 9*): Analogously to above, **9b** (1.00 g, 7.81 mmol) reacted with *t*-BuNCO (773 mg, 7.81 mmol) to give **12f** (1.31 g, 89%) as the only product. With **9c** (*Entry 12*): Analogously to above, **9c** (1.20 g, 8.45 mmol) reacted with *t*-BuNCO (837 mg, 8.45 mmol) to give a colorless oil (1.34 g, 85%) consisting of **12f** (7%) and **13f** (93%). *With* **9d** (*Entry 15*): Analogously to above, **9d** (1.49 g, 8.45 mmol) reacted with *t*-BuNCO (837 mg, 8.45 mmol) to give a colorless oil (1.32 g, 84%) consisting of **12f** (57%) and **13f** (43%).

Data of **12f**: IR: 3320*s*, 3020*w*, 2960*s*, 2930*m*, 2870*m*, 2700*w*, 1640*s*, 1565*s*. ^{1}H-NMR: 5.23, 4.88 (2 br. *s*, 2 NH, exchanged with D_2O); 3.16 (*td*, J = 6.4, 6.2, with D_2O: *t*, J = 6.4, CONHCH_2); 2.95 (*t*, J = 6.3, MeNHCH_2); 2.35 (*s*, MeN); 1.81 (br. *s*, NH, exchanged with D_2O); 1.60 (*quint.*, J = 6.3, $CH_2CH_2CH_2$); 1.29 (*s*, *t*-Bu). ^{13}C-NMR: 158.4 (*s*, CO); 50.1 (*s*, Me_3C); 49.3 (*t*, CONHCH_2); 38.5 (*t*, MeNHCH_2); 36.1 (*q*, MeN); 29.7 (*t*, $CH_2CH_2CH_2$); 29.5 (*q*, Me_3C). EI-MS: 188 (100, $[M + H]^+$), 187 (17, $M^{+\cdot}$), 144(6), 129(13), 115(32), 101(5), 99(10), 89(5), 87(6), 74(11), 73(5), 72(5), 71(14), 70(13), 61(9), 58(77), 57(25), 56(19).

Data of **13f** (from mixture): IR (KBr): 3350*s*, 3280*s*, 1645*s*, 1530*s*. ^{1}H-NMR: 5.57 (br. *s*, NH, exchanged with D_2O); 3.30 (*t*, J = 6.3, MeNCH_2); 2.79 (*s*, MeN); 2.68 (*t*, J = 6.2, NH_2CH_2); 1.59 (*quint.*, J = 6.3, $CH_2CH_2CH_2$); 1.32 (br. *s*, NH_2, exchanged with D_2O); 1.31 (*s*, *t*-Bu). ^{13}C-NMR: 158.4 (*s*, CO); 50.3 (*s*, Me_3C); 45.0 (*t*, MeNCH_2); 37.6 (*t*, NH_2CH_2); 33.8 (*q*, MeN); 30.2 (*t*, $CH_2CH_2CH_2$); 29.4 (*q*, Me_3C). EI-MS: 188 (26, $[M + H]^+$), 187 (11, $M^{+\cdot}$), 170(5), 158(5), 131(7), 129(8), 115(16), 89(16), 88(11), 87(37), 75(8), 72(11), 71(40), 70(13), 59(7), 58(100), 57(54), 56(37).

3.7. N*-Benzyl-*N*′-[3-(methylamino)propyl]urea* (**12g**) *and* N*-(3-Aminopropyl)-*N*′-benzyl-*N*-methylurea* (**13g**). With **9a** (*Entry 7*): Analogously to 3.6, **9a** (365 mg, 3.20 mmol) reacted with $PhCH_2NCO$ (426 mg, 3.20 mmol) to **12g** (636 mg, 90%), a colorless solidifying oil, as the only product. *With* **9b** (*Entry 10*): **9b** (1.00 g, 7.81 mmol) reacted likewise with $PhCH_2NCO$ (1.04 g, 7.81 mmol) to **12g** (1.42 g, 82%) as the only product. *With* **9c** (*Entry 13*): **9c** (1.00 g, 7.04 mmol) reacted with $PhCH_2NCO$ (0.937 g, 7.04 mmol) to a solid (1.30 g, 83%), consisting of **12g** (3%) and **13g** (97%), which could not be further separated. *With* **9d** (*Entry 16*): likewise, **9d** (1.00 g, 5.68 mmol) reacted with $PhCH_2NCO$ (0.756 g, 5.68 mmol) to a mixture (1.24 g, 98%) of **12g** (12%) and **13g** (88%).

Data of **12g**: IR: 3220*s*, 3090*w*, 3060*w*, 3030*w*, 2940*m*, 2860*w*, 2760*w*, 2700*w*, 1640*s*, 1565*s*. ^{1}H-NMR: 7.45–7.22 (*m*, 5 arom. H); 6.16, 5.72 (2 br. *s*, 2 NH, exchanged with D_2O); 4.33 (*d*, J = 5.7, with D_2O: *s*, $PhCH_2$); 3.22 (*td*, J = 6.2, 6.0, with D_2O: *t*, J = 6.2, CONHCH_2); 2.73 (br. *s*, NH, exchanged with D_2O); 2.62 (*t*, J = 6.3, MeNHCH_2); 2.31 (*s*, MeN); 1.63 (*quint.*, J = 6.3, $CH_2CH_2CH_2$). ^{13}C-NMR: 159.4 (*s*, CO); 139.7 (*s*, arom. C); 128.1, 126.7 (2*d*, 2 × 2 arom. C); 126.5 (*d*, arom. C); 48.5 (*t*, CONHCH_2); 43.6 (*t*, PhCH_2); 37.7 (*t*, MeNHCH_2); 35.6 (*q*, MeN); 29.6 (*t*, $CH_2CH_2CH_2$). EI-MS: 222 (27, $[M + H]^+$), 221 (25, $M^{+\cdot}$), 178(48), 149(10), 142(18), 115(23), 107(19), 106(71), 105(8), 104(12), 99(36), 92(9), 91(100), 89(12), 87(12), 79(13), 77(19), 71(37), 70(33), 65(26), 59(7), 58(89), 57(32), 56(43), 51(11).

Data of **13g** (from mixture): IR: 3330 (br.), 2920*m*, 1630*s*, 1530*s*, 1450*m*, 1390*m*, 1290*m*, 1230*m*, 730*m*, 700*s*. ^{1}H-NMR: 7.26–7.16 (*m*, 5 arom. H); 6.69 (*s*, 1 NH, exchange with D_2O); 4.33 (*d*, J = 5.4, with D_2O: *s*, $PhCH_2$); 3.22 (*t*, J = 6.1, CONMeCH_2); 2.82 (*s*, MeN); 2.63 (*t*, J = 6.0, MeNCH_2); 1.56 (*quint.*, J = 6.1, $CH_2CH_2CH_2$); 1.32 (*s*, NH, exchanged with D_2O). ^{13}C-NMR: 159.3 (*s*, CO); 140.2 (*s*, arom. C); 128.3, 127.5 (2*d*, 2 × 2 arom. C);

126.8 (*d*, arom. C); 45.0 (*t*, $CONMeCH_2$); 44.7 (*t*, $PhCH_2$); 37.2 (*t*, NH_2CH_2); 33.7 (*q*, MeN); 29.8 (*t*, $CH_2CH_2CH_2$). CI-MS: 222 ($[M + H]^+$).

3.8. *N-[3-(Methylamino)propyl]-N'-phenylurea* (**12h**) *and N-(3-Aminopropyl)-N-methyl-N'-phenylurea* (**13h**). With **9a** (*Entry 8*): Analogously to *3.6*, **9a** (365 mg, 3.20 mmol) reacted with PhNCO (381 mg, 3.20 mmol) to **12h** (570 mg, 86%), a colorless solidifying oil, as the only product. *With* **9b** (*Entry 11*): **9b** (1.00, 7.81 mmol) reacted likewise with PhNCO (929 mg, 7.81 mmol) to **12h** (1.41 g, 87%) as the only product. *With* **9c** (*Entry 14*): **9c** (454 mg, 3.20 mmol) reacted with PhNCO (381 mg, 3.20 mmol) to a solid (570 mg, 86%), consisting of **12h** (18%) and **13h** (82%), which could not be further separated. *With* **9d** (*Entry 17*): likewise, **9d** (563 mg, 3.20 mmol) reacted with PhNCO (381 mg, 3.20 mmol) to a mixture (573 mg, 87%) of **12h** (7%) and **12h** (93%).

Data of **12h**: IR (KBr): 3280*m*, 3240*m*, 3080*w*, 3040*w*, 3020*w*, 2980*w*, 2950*w*, 2920*m*, 2860*w*, 2790*w*, 1668*m*, 1645*s*, 1590*m*, 1560*s*, 1550*m*, 1525*w*, 1490*s*. ^{1}H-NMR: 8.40 (br. *s*, NH, exchanged with D_2O); 7.94–7.21 (*m*, 4 arom. H); 7.01–6.96 (*m*, 1 arom. H); 5.79 (br. *s*, NH, exchanged with D_2O); 3.29 (*td*, J = 6.2, 6.0, with D_2O: *t*, J = 6.2, $CONHCH_2$); 2.64 (*t*, J = 6.3, $MeNHCH_2$); 2.35 (*s*, MeN); 1.67 (br. *s*, NH, exchanged with D_2O); 1.64 (*quint.*, J = 6.2, $CH_2CH_2CH_2$). ^{13}C-NMR: 157.0 (*s*, CO); 139.4 (*s*, arom. C); 128.9 (*d*, 2 arom. C); 122.8 (*d*, arom. C); 120.1 (*d*, 2 arom. C); 49.1 (*t*, $CONHCH_2$); 38.7 (*t*, $MeNHCH_2$); 36.2 (*q*, MeN); 29.6 (*t*, $CH_2CH_2CH_2$). EI-MS: 208 (4, $[M + H]^+$), 207 (4, $M^{+\cdot}$), 164(5), 115(27), 94(6), 93(100), 77(8), 71(5), 70(9), 66(5), 65(7), 58(10), 57(6), 56(11).

Data of **13h** (from mixture): IR (KBr): 3440*s*, 3375*s*, 1645*s*, 1590*s*, 1550*s*. ^{1}H-NMR: 9.56 (br. *s*, NH, exchanged with D_2O); 7.37–7.34 (*m*, 2 arom. H); 7.26–7.13 (*m*, 2 arom. H); 6.89–6.84 (*m*, arom. H); 3.42 (*t*, J = 5.9, $MeNCH_2$); 2.86 (*s*, MeN); 2.79 (*t*, J = 5.9, NH_2CH_2); 1.65 (*quint.*, J = 5.9, $CH_2CH_2CH_2$); 1.54 (br. *s*, H_2N, exchanged with D_2O). ^{13}C-NMR: 157.4 (*s*, CO); 140.8 (*s*, arom. C); 128.6 (*d*, 2 arom. C); 121.6 (*d*, arom. C); 118.9 (*d*, 2 arom. C); 45.1 (*t*, $MeNCH_2$); 36.5 (*t*, NH_2CH_2); 33.4 (*q*, MeN); 28.7 (*t*, $CH_2CH_2CH_2$). EI-MS: 208 (28, $[M + H]^+$), 207 (30, $M^{+\cdot}$), 206(8), 191(5), 190(5), 189(5), 163(9), 149(6), 120(6), 119(9), 115(28), 106(6), 98(5), 94(9), 93(100), 92(11), 91(9), 89(15), 87(5), 84(11), 77(18), 72(16), 71(80), 70(19), 66(7), 65(19), 64(6), 59(5), 58(45), 57(34), 56(46), 51(9).

4. *Spermine Derivatives*. 4.1. *1,1'-(Butane-1,4-diyl)-2,2'-diphenylbis(hexahydropyrimidine)* (**14**). Analogously to *2.1*, **1** (10.1, 50.0 mmol) reacted with PhCHO (10.6 g, 100.0 mmol) to give **14** (18.0 g, 95%). Colorless solid. M.p. (CH_2Cl_2/hexane): 66–67°. IR: 3670*w*, 3610*s*, 3460 (br.), 3020*w*, 2970*s*, 2890*m*, 1610*m*, 1450*w*, 1390*m*, 1220*s*, 1050*s*, 880*s*. ^{1}H-NMR: 7.66–7.04 (*m*, 10 arom. H); 3.80 (*s*, 2 H–C(2)); 3.21–2.97 (*m*, 2 H_{eq}–C(4), 2 H_{eq}–C(6)); 2.76–2.53 (*m*, 2 H_{ax}–C(4), 2 H_{ax}–C(6)); 2.24–1.98 (*m*, $2NCH_2CH_2$); 1.89–1.60 (*m*, 4 H–C(5)); 1.39–1.11 (*m*, 2 NCH_2CH_2). ^{13}C-NMR: 142.5 (*s*, 2 arom. C); 128.5 (*d*, 4 arom. C); 128.2 (*d*, 2 arom. C); 127.3 (*d*, 2 arom. C); 81.9 (*d*, 2C(2)); 53.5 (*t*, 2C(6)); 52.0 (*t*, 2 NCH_2CH_2); 45.7 (*t*, 2C(4)); 27.2 (*t*, 2C(5)); 24.1 (*t*, 2 NCH_2CH_2). ESI-MS: 380(28), 379 ($[M + H]^+$), 291(11), 253(13), 215(10).

4.2. *(E)-3,3'-Diphenyl-N,N'-(4,9-diazadodecane-1,12-diyl)bis[prop-2-enamide]* (**15**). A soln. of **4a** · 2 HCl (0.071 g, 0.13 mmol) and *t*-BuOK (0.1 g, 0.89 mmol) in toluene (40 ml) was heated to reflux for 4 h. Addition of sat. aq. K_2CO_3 soln., extraction with CH_2Cl_2 and evaporation of the volatiles gave **15** (0.054 g, 88%) as a slightly yellow oil. IR: 3310*s*, 2960*s*, 2790*s*, 1655*s*, 1620*s*, 1540*s*, 1340*s*, 1230*m*, 970*s*. ^{1}H-NMR: 7.56 (*d*, J = 15.7, 2 COCH=CH); 7.51–7.10 (*m*, 10 arom. H); 6.41, 6.39 (2*d*, J = 15.7 each, 2 COCH=CH, ratio *ca.* 4:1); 3.43, 3.26 (2*m*, appearing as *q*, J = 5.9, 6.1, 2 $CONHCH_2$, ratio *ca.* 4:1); 2.92, 2.71, 2.65–2.51, 2.42 (*t*, *t*, *m*, *t*, J = 7.7, 6.3, 7.7, 2 $NHCH_2(CH_2)_2NHCO$, $CH_2(CH_2)_2CH_2$); 1.70, 1.62–1.45 (*q*, *m*, J = 6.3, 2 CH_2CH_2NHCO, $CH_2(CH_2)_2CH_2$). ^{13}C-NMR (signals of major isomer): 166.1 (*s*, 2 CO); 140.3 (*d*, 2 COCH=CH); 135.0 (*s*, 2 arom. C); 129.5, 128.8, 128.5, 128.4, 127.7 (5*d*, 5×2 arom. C); 49.5, 48.0, 38.8, 28.7, 27.8 (5*t*, 5×2 CH_2). ESI-MS: 463 (20, $[M + H]^+$), 260(15), 259(100), 205(69), 200(23), 187(39).

4.3. *N-(12-Phthalimido-4,9-diazadodecyl)phthalimide* (**16**). To a soln. of **1** (1.01 g, 5.0 mmol) in THF (25 ml) was added a soln. of *N*-(ethoxycarbonyl)phthalimide (*Nefkens* reagent, 2.41 g, 11.0 mmol) in THF (25 ml) at 23° within 30 min. After stirring for 2 h, the volatiles were evaporated, and the residue was transferred into its dihydrochloride by addition of 1N HCl soln. to give 2.34 g (87%) **16** · 2 HCl as a crude product. By recrystallization from EtOH/H_2O colorless crystals were obtained. M.p. 271–272°. IR(KBr): 3450*m*, 2940*m*, 2780*m*, 1770*m*, 1710*s*, 1610*w*, 1470*m*, 1430*m*, 1400*s*, 1370*m*, 1340*m*, 1190*w*, 1050*m*, 890*w*, 730*s*. ^{1}H-NMR (MeOD/D_2O, 1:1, MeOD as internal standard): 7.94–7.85 (*m*, 8 arom. H); 3.84 (*t*, J = 6.8, 2 $PhtN=CH_2$); 3.16–3.10 (*t*, J = 7.6, 2 CH_2NHCH_2); 2.12 (*tt*, J = 6.8, 7.6, 2 $PhtN=CH_2CH_2$); 1.87–1.82 (*m*, $CH_2(CH_2)_2CH_2$). ^{13}C-NMR (MeOD/D_2O, 1:1, MeOD as internal standard): 171.9 (*s*, 4 CO); 137.1 (*d*, 4 arom. C); 133.9 (*s*, 4 arom. C); 125.6 (*d*, 4 arom. C); 49.3, 47.7, 37.0, 27.6, 25.3 (5*t*, 2 CH_2 each). CI-MS: 464(30), 463 (100, $[M + H]^+$), 445(53). Data in accordance to [8].

4.4. *N,N'-(Butane-1,4-diyl)-3,3'-diphenyl-N,N'-bis(3-phthalimidopropyl)bis[prop-2-enamide]* (**17**). To a suspension of **16** (0.535 g, 1.0 mmol) in CH_2Cl_2 (20 ml) was added Et_3N (2.0 ml) and 4-(dimethylamino)pyridine

(0.02 g) and the resulting mixture stirred at 23° for 30 min, 3-phenylprop-2-enoyl chloride (0.34 g, 2.04 mmol) was added and stirring continued for 4 h. Washing of the org. soln. with sat. aq. NH_4Cl soln. and sat. aq. K_2CO_3 soln., and evaporation of the volatiles gave **17** (0.714 g, quant.). Colorless, crystalline residue. M.p. (from oil) 161–163°. IR: 3460*m*, 2930*m*, 1770*m*, 1710*s*, 1650*s*, 1600*m*, 1400*m*, 1330*w*, 1190*w*, 1070*w*, 1030*w*, 980*w*, 880*w*, 760*m*. ^{1}H-NMR: 7.71–7.21 (*m*, 18 arom. H); 6.80, 6.67 (2*d*, J = 15.6, 15.4, 2 COC*H*=CH); 3.72–3.57 (*m*, 2 Pht=NCH_2); 3.54–3.27 (*m*, 2 CH_2NCORCH_2); 2.05–1.84 (*m*, 2 Pht=NCH$_2$CH_2); 1.71–1.48 (*m*, CH$_2$(CH_2)$_2$CH$_2$). ^{13}C-NMR: 168.0 (*s*, 2 *C*OCH=CH); 166.1 (*s*, 2 *C*ONR*C*O); 142.8, 142.5 (2*d*, 2 COCH=*C*H); 134.9 (*s*, 2 arom. C); 133.9, 133.7 (2*d*, 2 arom. C); 131.8, 131.6 (2*s*, 4 arom. C); 129.3 (*d*, 2 arom. C); 128.5 (*d*, 4 arom. C); 127.6 (*d*, 4 arom. C); 123.1, 123.0 (2*d*, 2 arom. C); 117.1, 116.8 (2*d*, 2 CO*C*H=CH); 47.7, 45.7 (2*t*, 2 Pht=N(CH$_2$)$_2$*C*H$_2$); 45.6, 44.3 (2*t*, *C*H$_2$(CH$_2$)$_2$CH$_2$); 35.8, 35.3 (2*t*, 2 Pht=N*C*H$_2$); 28.6, 27.0 (2*t*, 2 NCH$_2$*C*H$_2$CH$_2$N); 26.8, 25.1 (2*t*, CH$_2$(*C*H$_2$)$_2$CH$_2$). ESI-MS: 745 (100, [*M* + Na]$^+$), 593(14).

4.5. *(*E*)-*N,N'*-Bis(3-aminopropyl)*-N,N'*-(butane-1,4-diyl)-3,3'-diphenylbis[prop-2-enamide]* (**4a**). To a soln. of **17** (0.58 g, 0.85 mmol) in dry EtOH (99.5%, 20 ml) was added aq. N_2H_4 (0.5 ml), the mixture was heated to reflux for 1 h. After evaporation of the solvent, addition of aq. 2N HCl soln. (5.0 ml), and filtration, the filtrate was basified with sat. aq. K_2CO_3 soln. and extracted with CH_2Cl_2 to give, after removal of the solvent, **4a** (0.376 g, 95%). Slightly yellow oil.

Alternatively, **4a** was prepared by adding Et_3N (10.0 ml) and 3-phenylprop-2-enoyl chloride (1.0 g, 6.0 mmol) within 2 h to a soln. of **14** (1.0 g, 2.6 mmol) in toluene (25 ml) at 4°. Stirring was continued. After 4 h aq. 1N HCl soln. (10.0 ml) was added and the mixture heated to reflux under vigorous stirring for 4 h. The soln. was allowed to cool to 23°, and the generated PhCHO was removed by extraction of the acidic soln. with toluene. The aq. layer was basified with sat. aq. K_2CO_3 soln. and extracted with CH_2Cl_2 to give after evaporation, **4a** (1.04 g, 86%). IR: 3410 (br.), 2930 (br.), 1645*s*, 1590*s*, 1485*s*, 1460*s*, 1430*s*, 1180*m*, 980*m*, 765*s*, 710*w*, 685*w*. ^{1}H-NMR: 7.64, 7.62 (2*d*, J = 15.4 each, 2 COCH=C*H*, ratio 1:1); 7.54–7.17 (*m*, 10 arom. H); 6.92, 6.83, 6.74 (3*d*, J = 15.4 each, 2 COC*H*=CH, ratio *ca.* 6:3:1); 3.52–3.30 (*m*, 8 H); 2.72–2.64 (*m*, 4 H); 1.70–1.61 (*m*, 8 H). ^{13}C-NMR (131.2 MHz): 166.2, 166.0 (2*d*, 2 CO); 142.8, 142.5, 142.4, 142.1 (4*d*, 2 COCH=*C*H); 135.1, 135.0 (2*s*, 2 arom. C); 129.4, 129.3, 129.2, 128.5, 127.6, 127.5 (6*d*, 10 arom. C); 117.6, 117.3, 117.1 (3*d*, 2 CO*C*H=CH); 47.3, 46.0, 45.7, 45.3, 43.4, 38.8, 38.7, 32.8, 32.7, 30.8, 26.9, 26.7, 25.0 (13*t*, 10 CH_2).

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