Synthesis of polyamines *via* hydroaminomethylation of alkenes with urea—a new, effective and versatile route to dendrons and dendritic core molecules

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Polyamines, structurally related to putrescines and spermidines, are easily obtainable *via* hydroaminomethylation of methylallylphthalimide with primary or secondary amines. In addition, hydroaminomethylation of monoolefins with urea as a synthetic equivalent for ammonia, in contrast to other methods (*e.g.* the alkylation of ammonia or ammonium salts), allows selective synthesis of symmetric tertiary amines. By combining both methods dendrons and dendrimer cores are conveniently obtained.

Polyamines, structurally related to spermine, spermidine and putrescine, are useful dendrons and dendrimer cores for the synthesis of polyamine dendrimers (Fig. 1). They are also attracting interest as potential pharmaceuticals. Putrescine derivatives are used as antimalaria pharmaceuticals,[1] in the medical treatment of malaria[2] and plasmodics.[3] They are active in protein-[4] and enzyme inhibition,[5] and as ligands for iron ions in human cells.[6] Use of polyamines of this type is also of importance in other fields of current research,[7] *e.g.* metabolism[8] and biogenesis,[9] antibiotics,[10] coagulation inhibitors,[11] antidiarrhoics[12] and cytostatics.[13]

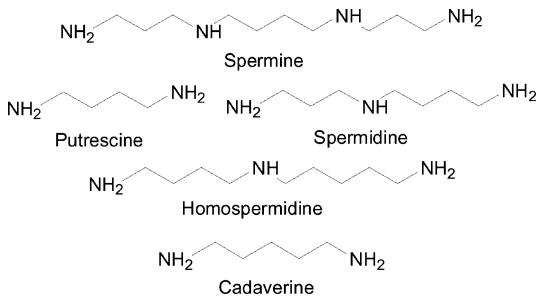


Fig. 1 Different primary polyamines.

Synthesis of polyamines[14] is achieved *via* substitution reactions of primary or secondary amides[15] and amines,[16] reductive amination of aldehydes and ketones,[17] of reduction of amides[11,13b] or nitriles[18] or azides.[16] In many cases protective groups are needed for selective amine formation.[15,19]

Polyamine dendrimers with varying properties depending on their core and their shell structures have attracted growing interest in the past 25 years[20,21] and require special synthetic methods. For these highly symmetric molecules convergent[22] and divergent[20,23] routes have been developed. The very first efforts towards dendrimer synthesis also constituted the start of synthetic polyamine chemistry.[24] In Vögtle's approach polyamine dendritic structures were obtained *via* Michael addition of amines to acrylonitrile and subsequent reduction of the nitrile groups leading to new and higher functionalized Michael donors for new conversions with acrylonitrile. Later this method became a standard procedure for polyamines,[25] but in general the aim was focused on the shell formation of polyamine dendrimers.[26] Systematic studies on dendrimer core synthesis are likewise interesting but less intensively investigated,[27] and are often even avoided because dendrimer core synthesis is problematic as exemplarily shown in one of Newkome and coworkers' publications.[27c]

We have recently[28,29] introduced hydroaminomethylation as a powerful tool in the synthesis of similarly structured polyamines[30] as well as macroheterocyles as complexing agents for metal ions.[31,32] Hydroaminomethylation combines hydroformylation and reductive amination to a synthetically versatile one-pot procedure for secondary and tertiary amines (Fig. 2).[33] Following these lines hydroaminomethylation of N-protected unsaturated amines appears as a promising tool for polyamine dendrimers, not only *via* divergent pathways, but also through convergent coupling of dendrons to suitable cores. We here present further applications of this effective pathway towards polyamine dendrons and dendrimer cores *via* hydroaminomethylation of amines with *N*-methylallylphthalimide (**1**).[34] The basic transformations are described in Scheme 1.

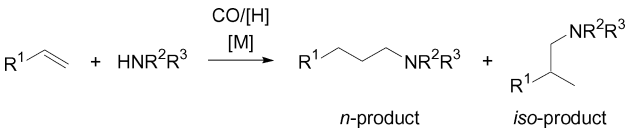
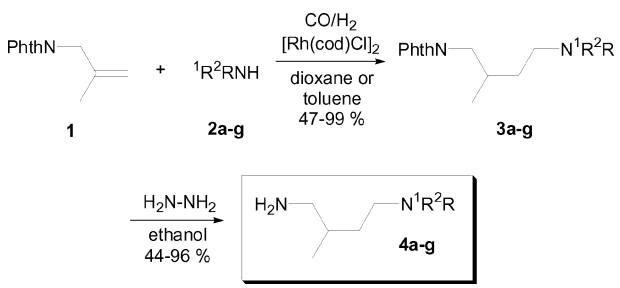


Fig. 2 Hydroaminomethylation.



Scheme 1 Synthesis of the putrescine derivatives **4a–g**.

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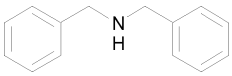
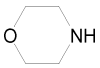
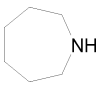
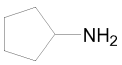
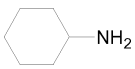
Table 1 Results of the mono-hydroaminomethylation of 1° and 2° amines with *N*-methylallylphthalimide and the subsequent hydrazinolysis to the primary polyamines

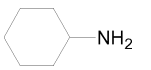
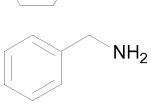
			Phthalimide		Amine	
Entry	HN^1R^2R **2a–g**	t/d	Prod.	Yield (%)	Prod.	Yield (%)
1[a]		1	**3a**	99	**4a**	70
2[b]		2	**3b**	96	**4b**	94
3[b]		2	**3c**	94	**4c**	96
4[a]		3	**3d**	68	**4d**	89
5[a]		1	**3e**	93	**4e**	84
6[a]		1	**3f**	85	**4f**	67
7[a]		1	**3g**	47	**4g**	44

[a] 40 bar CO, 40 bar H_2, 140 °C. [b] 50 bar CO, 50 bar H_2, 100 °C.

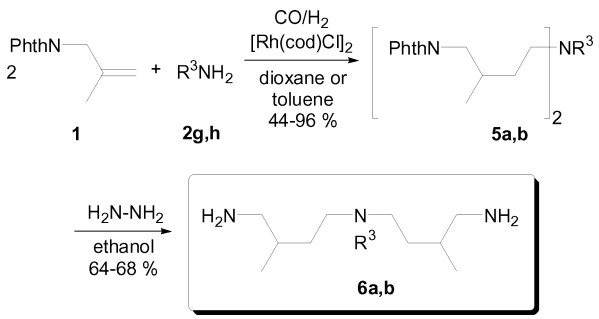
Using this protocol with *N*-methylallylphthalimide (**1**) as the olefin component and secondary amines **2a–g**, the corresponding phthalimide-protected tertiary amines **3a–g** are obtained in good to quantitative yields. Hydrazinolysis of the phthalimides **3a–g** is performed by the Ing–Manske-protocol[35] to give the free primary amines **4a–g** in high yields (Table 1).

In principle this method can also be applied to the synthesis of triamines if primary amines such as benzylamine[29] (**2g**) or cyclohexylamine (**2h**) and two moles of *N*-methylallylphthalimide (**1**) are converted to form a tertiary amine with two phthalimide-protected chains in excellent yields (Scheme 2). Hydrazinolysis of the phthalimides **5a,b** to the homospermidine type derivatives **6a,b** again proceeds in good yields (Table 2).

Table 2 Results of the bis-hydroaminomethylation of 1° amines with *N*-methylallylphthalimide and followed by hydrazinolysis to the primary polyamines[a]

			Phthalimide		Amine	
Entry	HN^1R^2R **2g,h**	t/d	Prod.	Yield (%)	Prod.	Yield (%)
1		2	**5a**	96	**6a**	68
2		3	**5b**[29]	94	**6b**	64

[a] 40 bar CO, 40 bar H_2, 140 °C.



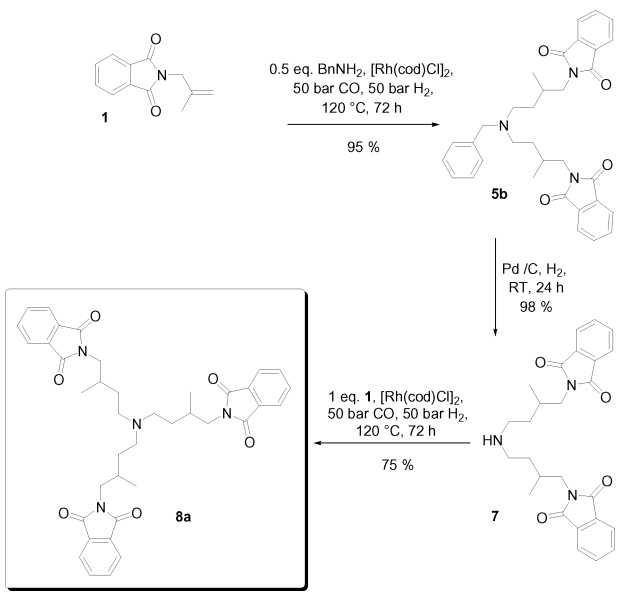
Scheme 2 Synthesis of the spermidine derivatives **6a,b**.

This method allows the synthesis of triamines with orthogonal protective groups. Thus product **5b** can be debenzylated to the unprotected secondary amine function for further use as a dendron (also see below) whereas hydrazinolysis leads to two free primary amine groups ready for further elongation of the dendron chains.[29] Thus all products of this type are potentially useful building blocks for the synthesis of dendrimers by convergent and the divergent pathways.

Using this protocol for selective trisalkylation of ammonia would directly lead to simple amine cores, while normal alkylation of ammonia using classical methods, like alkylation with alkyl halides, is usually accompanied by the formation of quaternary ammonium salts. With reductive amination, the formation of ammonium salts can be avoided. A common method for the synthesis of symmetric tertiary amines by reductive amination is the Leuckart-reaction[36] of ketones or aldehydes with ammonium

formate. The *in situ* generation of aldehydes is generally advantageous, since self-condensation can be avoided by trapping the aldehydes under the reaction conditions. Therefore a hydroaminomethylation sequence starting from ammonia as a core would establish a new and versatile method for the synthesis of symmetric tertiary amines. If, however, using ammonia or ammonium salts in homogeneous or heterogeneous catalyzed reductive amination reactions or in hydroaminomethylation, preferentially secondary amines are formed.[33,37] When using an excess of aldeyhde or ketone, the corresponding alcohols are observed as unwanted side products in considerable amounts. Hexamethylenetetramine as a condensation product of formaldehyde and ammonia is known as a protected form of ammonia in the Delépine-reaction[38] for the synthesis of primary amines. If hexamethylenetetramine and an olefin are converted under the conditions of hydroaminomethylation, only tertiary methyl- and dimethylamines as well as the alcohol and the corresponding secondary amines are formed in high yields, whereas the symmetric tertiary amine is not obtained.[37d]

In our first approach towards a synthesis of symmetric tertiary amines, we used benzylamine (**2h**) as an ammonia equivalent in order to circumvent the problems of direct alkylation of ammonia *via* reductive amination. Benzylamine (**2h**) is a useful equivalent of ammonia, because the resulting amine **5b** can be deprotected by debenzylation to the secondary amine **7**,[29] which can be used again in the hydroaminomethylation procedure, to form the desired tertiary amine **8a** by the three step method in a high overall yield of 70% (Scheme 3).



Scheme 3 Synthesis of polyamine **8a** by the hydroaminomethylation–debenzylation sequence.

This three step method for symmetrical tertiary amines, although the yields are high, is neither very effective nor really versatile. A direct hydroaminomethylation with ammonia would be more favorable. As already mentioned above, the rhodium catalyzed hydroaminomethylation reaction of olefins in the presence of an excess of ammonia only leads to secondary amines as the main product[33,37d] and if ammonia is not present in high concentrations in the reaction mixture, the corresponding alcohol is obtained in large amounts. Due to these problems with ammonia itself, an equivalent had to be found, allowing selective trisalkylation. For this we have envisaged urea as an ammonia source since it forms ammonia upon hydrolysis and simultaneously may act as a scavenger for aldehydes protecting these against reduction (Fig. 3).

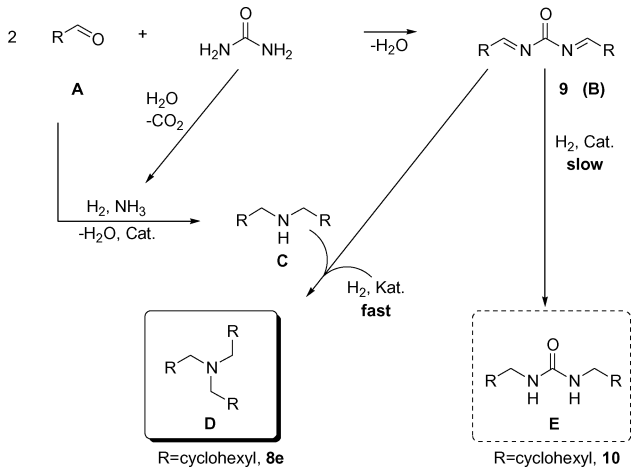


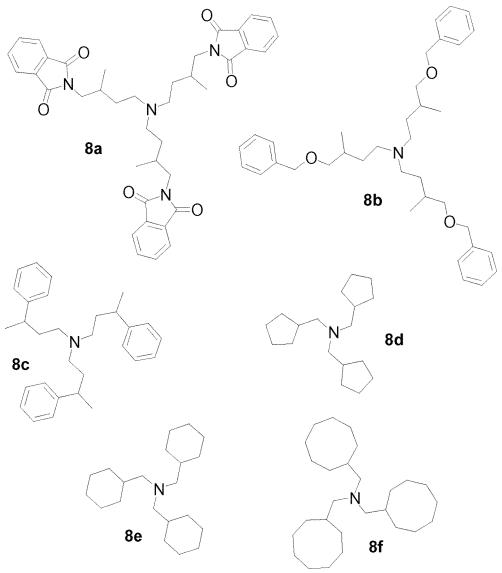
Fig. 3 Mechanism of the formation of tertiary amines—urea as an ammonia source and a protective group.

Indeed urea under the conditions of hydroaminomethylation leads to the formation of symmetric tertiary amines **8a–8f** in good to excellent yields (Table 3, Scheme 4). No reduction of the aldehydes to alcohols was observed under the conditions chosen.

Table 3 Results of the synthesis of tertiary amines by hydroaminomethylation with urea[a]

Entry	Olefin	T/°C	t/d	Product	Yield (%)
1	**1**	120	2	**8a**	78
2	**11**	120	3	**8b**	94
3	**12**	120	2	**8c**	85
4	**13**	100	2	**8d**	77
5	**14**	100	2	**8e**	74
6	**15**	100	2	**8f**	67

[a] 40 bar CO, 40 bar H_2.



Scheme 4 Products **8a–f** of the hydroaminomethylation with urea.

The mechanism of this conversion was clarified by a modification of the general procedure (Fig. 3). If carried out in water and dioxane with cyclohexene as the olefin, the alkyl urea (R = cyclohexyl) **10** (**E**) was isolated as the main product (24%), being formed by reduction of **9** (**B**). Here amine **8e** (**D**) was found only as the minor product (12%). Interestingly this is to our knowledge the first example of the synthesis of a bisalkylurea by reductive amination. Additionally, intermediate **9** was found as a colourless solid, if lower pressures or different ratios of methanol and dioxane were applied or no acetic acid was used. The structure of **9** was proven by MS and H-NMR spectroscopy.

Using this method the synthesis of **8a** as described above (Scheme 3) can be shortened to a one step procedure yielding 78% (Scheme 5 and Table 3, entry 1). Hydrazinolysis of **8a** afforded the primary amine **16** in 93% yield which then was converted under typical hydroaminomethylation conditions with 9 equivalents of *N*-methylallylphthalimide (**1**) yielding 62% of **17** (Scheme 5).

Similarly, with benzylmethylallylether under hydroaminomethylation conditions 94% of the tertiary amine **8b** is obtained, which can be deprotected by debenzylation to form a versatile starting core for polyether or polyester dendrimers as well (Table 3, entry 2). Methylstyrene as an aromatic vinylamine can be converted to the tertiary amine **8c** in 85% yield (Table 3, entry 3). The cyclic olefins **13–15** give comparable results (entry 4–6). A rather unusual structure of compound **8e** was determined by X-ray analysis (Fig. 4).[39]

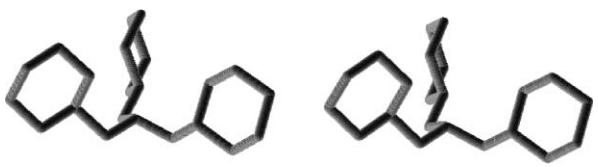
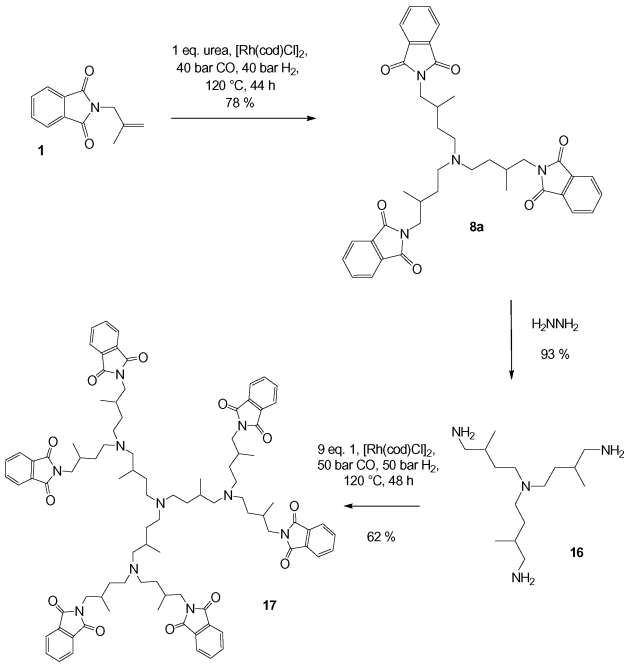


Fig. 4 Result of the X-ray structure analysis of **8e**.



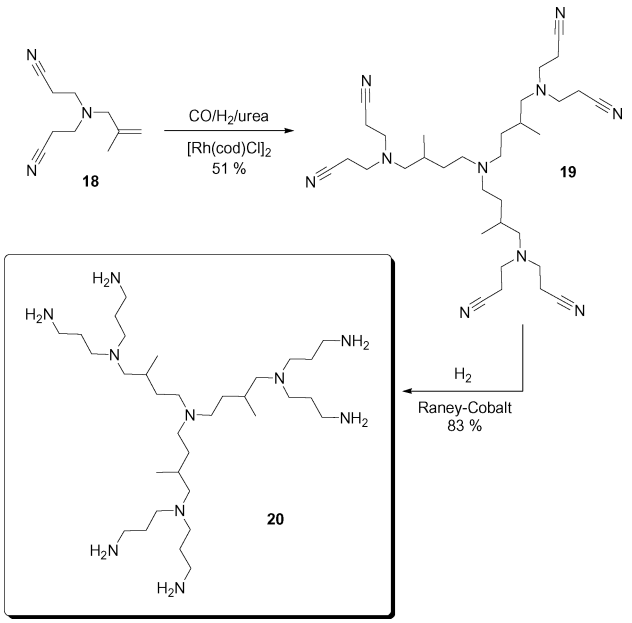
Scheme 5 Direct synthesis of polyamine **8a** from **1** and urea and further conversion to polyamine **17**.

According to this crystal structure the free electron pair of the nitrogen atom is completely shielded by the cyclohexyl rings. Thus it resists the quaternisation with methyl iodide and even with trimethyl oxonium tetrafluoroborate quaternisation to form an ammonium salt is incomplete. Compounds of this type may be used as sterically hindered bases comparable to Hünig's base.

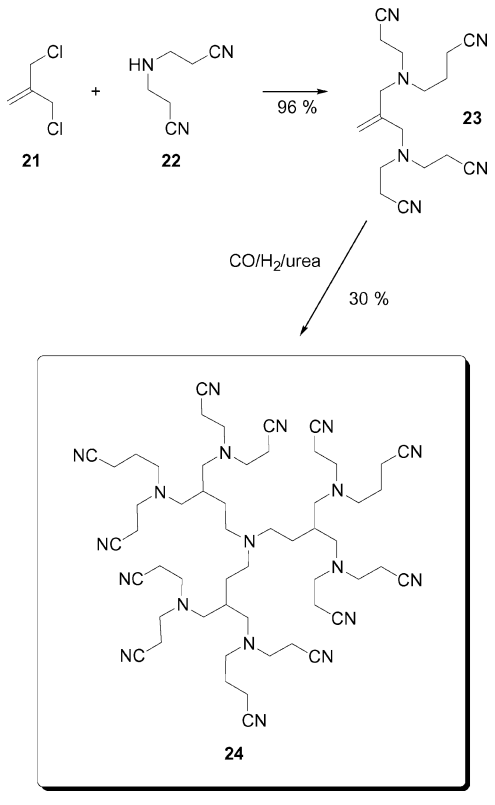
Dendrimers similarly structured as **17** can likewise be obtained by this one step procedure. To show this exemplarily the method presented here was applied to the unsaturated dinitrile **18** which is easily obtained in high yields from commercially available compounds. After hydroaminomethylation in the presence of urea, the hexanitrile **19** can be reduced by standard procedures to form the primary amine functionalities in the highly symmetric dendritic structured molecule **20** (Scheme 6). In another example the method was extended to the tetranitrile **23**, which was quantitatively synthesized from the commercially available chloromethylallylchloride **21** and the dinitrile **22**. Hydroaminomethylation of **23** affords the polynitrile **24** (Scheme 7) in 30% yield after column chromatography, which can now likewise be reduced to the polyamine as shown above and again serve as an initial core molecule for the synthesis of different macromolecules *e.g.* dendrimers and hyperbranched polymers.

Conclusions

The synthesis of polyamines *via* hydroaminomethylation of methylallylphthalimide (**1**) with primary or secondary amines is performed in high yields. The deprotection of the phthalimides leads to polyamines with primary amino groups. Hydroaminomethylation of olefins with urea is presented as a useful method for the selective and efficient synthesis of symmetrical tertiary amines. Obviously the steric hindrance does not affect the formation of the products. The method tolerates various protective groups for alcohols and amines. Even the use of dendrons following the



Scheme 6 Synthesis of the primary decaamine **20** by hydroaminomethylation of **18** with urea and reduction of the resulting hexanitrile **19**.



Scheme 7 Synthesis of the polynitrile **24** by hydroaminomethylation of **23** with urea.

convergent route of dendrimer synthesis can be applied to this method for the synthesis of these dendritic molecules with defined structure. Thus this protocol is a powerful tool for the coupling of dendrons and the synthesis of dendrimer cores in a one-pot procedure with high yields and selectivity.

Experimental

General procedure A: hydroaminomethylation of methylallylphthalimide

15 mmol of the amine (in case of the primary amines 7.5 mmol) and 15 mmol of methylallylphthalimide (**1**) were dissolved in 10 ml of dioxane or toluene, 15 mg $[Rh(cod)Cl]_2$ were added and the mixture was placed in a pressure vessel, treated under typical hydroaminomethylation conditions (80–100 bar syngas, 100–120 °C, 2–3 d) and was filtered through a column of Alumina N (Act. III) with diethyl ether. After evaporation of the solvent, the crude mixture was purified by column chromatography if necessary.

General procedure B: hydrazinolysis of the phthalimides

The phthalimide was treated with 3 equiv. of hydrazine hydrate in 50 ml ethanol for 20 h under reflux. To the cooled mixture 30 equiv. of conc. hydrochloric acid were added and the solid was filtered off and washed with water. The filtrate was evaporated under reduced pressure and the residue was treated with 30 equiv. of half conc. sodium hydroxide solution and extracted with diethyl ether or ethyl acetate. The organic layer was dried with magnesium sulfate and the solvent was removed under reduced pressure. If necessary, the crude product was purified by column chromatography.

2-(4-Dibenzylamino-2-methylbutyl)-isoindol-1,3-dione (3a)

According to the general procedure A **3a** was synthesized by hydroaminomethylation (40 bar CO, 40 bar H_2, 140 °C, 1 d) in toluene yielding 6.10 g (15.0 mmol, 99%) as a yellow oil. ^{1}H-NMR ($CDCl_3$, δ): 0.75 (3H, t, ^3J = 6.7 Hz), 0.81 (1H, m), 1.34 (1H, m), 2.35 (1H, m), 2.48 (2H, t, ^3J = 7.2 Hz), 3.57 (6H, m), 7.19–7.20 (2H), 7.25–7.28 (4H), 7.68–7.71 (4H), 7.81–7.82 (2H), 7.83–7.85 (2H). ^{13}C-NMR ($CDCl_3$, δ): 17.3, 30.6, 31.7, 44.1, 50.9, 58.4, 123.1, 126.7, 128.1, 128.8, 132.0, 133.8, 139.7, 168.6. FTIR (neat): 3084, 3061, 3027, 3003, 2859, 2929, 2873, 2855, 2797, 1772, 1713, 1494, 1467, 1453, 1434, 1397, 1380, 1361, 1334, 1067, 1052, 910, 723, 713, 699. ESI-MS: m/z = 413.3 (M + H$^+$, Pos.-Mod.). $C_{27}H_{28}N_2O_2$ calc. (%): C: 78.6; H: 6.8; N: 6.8. Found (%): C: 78.9; H: 6.8; N: 6.6.

N^1,N^1-Dibenzyl-3-methylbutan-1,4-diamine (4a)

According to the general procedure B hydrazinolysis of 3.09 g (10.3 mmol) **3a** yielded 2.04 g (7.2 mmol, 70%) **4a** as a colourless oil. ^{1}H-NMR ($CDCl_3$, δ): 0.67 (3H, d, ^3J = 6.5 Hz), 1.23–1.62 (3H), 1.91 (2H, bs), 2.33 (2H, m), 2.35 (2H, t, ^3J = 7.3 Hz), 3.54 (4H, m), 7.11–7.30 (10H). ^{13}C-NMR ($CDCl_3$, δ): 17.4, 31.5, 34.2, 48.3, 51.1, 58.3, 126.7, 128.0, 128.8, 139.8. FTIR (neat): 3085, 3062, 3027, 3003, 2952, 2924, 2797, 1602, 1585, 1494, 1453, 1366, 1124, 1074, 1069, 1028, 910, 732, 698. ESI-MS: m/z = 283.3 (M + H$^+$, Pos.-Mod.). GC-MS (EI, 70 eV): m/z (%) = 282 (M$^+$, 1), 210 (100), 181 (100), 176 (56), 118 (12), 91 (100), 65 (12). $C_{19}H_{26}N_2$ calc. (%): C: 80.8; H: 9.8; N: 9.9. Found (%): C: 80.6; H: 9.6; N: 9.5.

2-(2-Methyl-4-morpholin-4-yl-butyl)-isoindol-1,3-dione (3b)

According to the general procedure A **3b** was synthesized by hydroaminomethylation (50 bar CO, 50 bar H_2, 100 °C, 3 d) in

toluene yielding 4.36 g (14.0 mmol, 96%) as a yellow oil. ^{1}H-NMR ($CDCl_3$, δ): 0.91 (3H, d, ^3J = 6.8 Hz), 1.33 (1H, m), 1.56 (1H, m), 1.98 (1H, m), 2.30–2.43 (6H), 3.53 (2H, m), 3.64 (4H, t, ^3J = 4.8 Hz), 7.67–7.70 (2H), 7.80–7.82 (2H). ^{13}C-NMR ($CDCl_3$, δ): 17.6, 31.1, 31.3, 44.1, 53.7, 56.7, 66.9, 123.1, 131.9, 133.9, 168.7. FTIR (neat): 2957, 2929, 2893, 2854, 2659, 1772, 1711, 1466, 1456, 1434, 1397, 1356, 1334, 1316, 1288, 1275, 1188, 1117, 1070, 1054, 1004, 869. ESI-MS: m/z = 302.9 (M + H$^+$, Pos.-Mod.). GC-MS (EI, 70 eV): m/z (%) = 302 (M$^+$, 4), 271 (4), 160 (21), 133 (7), 100 (100), 70 (9). $C_{17}H_{22}N_2O_3$ calc. (%): C: 67.5; H: 7.3; N: 9.3. Found (%): C: 67.7; H: 7.2; N: 8.9.

2-Methyl-4-morpholin-4-ylbutylamine (4b)

According to the general procedure B hydrazinolysis of 3.72 g (13.0 mol) **3b** yielded 1.94 g (12.2 mmol, 94%) **4b** as a yellow oil. ^{1}H-NMR ($CDCl_3$, δ): 0.85 (3H, d, ^3J = 6.7 Hz), 1.22 (1H, m), 1.36–1.65 (2H), 1.58 (2H, bs), 2.29 (2H, m), 1.58 (4H, m), 2.44 (1H, m), 2.55 (1H, m), 3.64 (4H, t, ^3J = 4.6 Hz). ^{13}C-NMR ($CDCl_3$, δ): 17.5, 30.9, 34.7, 48.2, 53.7, 56.9, 66.8. FTIR (neat): 3444, 3379, 2961, 2924, 2856, 2809, 1459, 1306, 1261, 1117, 1071, 1020, 867, 800. ESI-MS: m/z = 172.9 (M + H$^+$, Pos.-Mod.). HR-MS (EI, 60 eV): m/z (%) = 173.1667 (M + H$^+$, 100) (+1.4 mmu).

2-(4-Azepan-1-yl-2-methylbutyl)-isoindol-1,3-dione (3c)

According to the general procedure A **3c** was synthesized by hydroaminomethylation (50 bar CO, 50 bar H_2, 100 °C, 2 d) in dioxane yielding 4.44 g (14.1 mmol, 94%) as a yellow oil. ^{1}H-NMR ($CDCl_3$, δ): 0.92 (3H, d, ^3J = 6.7 Hz), 1.33 (1H, m), 1.50–1.58 (9H), 2.03 (1H, m), 2.48 (1H, m), 2.54–2.62 (5H), 3.52 (1H, m), 3.60 (1H, m), 7.70–7.74 (2H), 7.83–7.88 (2H). ^{13}C-NMR ($CDCl_3$, δ): 17.6, 26.9, 27.9, 31.3, 32.1, 44.2, 55.5, 55.9, 123.1, 132.0, 133.8, 168.6. FTIR (neat): 2927, 2854, 2812, 2776, 1773, 1716, 1663, 1615, 1467, 1455, 1433, 1397, 1380, 1357, 1056, 724. ESI-MS: m/z = 314.9 (M + H$^+$, Pos.-Mod.). $C_{19}H_{26}N_2O_2$ calc. (%): C: 72.6; H: 8.3; N: 8.7. Found (%): C: 72.6; H: 8.2; N: 8.7.

Azepan-1-yl-3-methylbutylamine (4c)

According to the general procedure B hydrazinolysis of 4.09 g (13.0 mmol) **3c** yielded 2.30 g (12.4 mmol, 96%) **4c** as a yellow oil. ^{1}H-NMR ($CDCl_3$, δ): 0.85 (3H, d, ^3J = 6.5 Hz), 1.23 (1H, m), 1.38–1.58 (10H), 2.36–2.49 (4H), 2.53–2.56 (4H). ^{13}C-NMR ($CDCl_3$, δ): 17.6, 26.8, 27.9, 32.0, 34.9, 48.4, 55.5, 56.2. FTIR (neat): 2925, 2854, 2812, 2773, 1467, 1456, 1261, 1121, 1021, 800. ESI-MS: m/z = 184.9 (M + H$^+$, Pos.-Mod.). GC-MS (EI, 70 eV): m/z (%) = 185 (M + H$^+$, 67), 173 (60), 141 (4), 100 (100), 86 (16), 70 (20), 56 (34). HR-MS (EI, 60 eV): m/z (%) = 185.2008 (M + H$^+$, 88) (−0.9 mmu).

2-(2-Methyl-4-piperidin-1-ylbutyl)-isoindol-1,3-dione (3d)

According to the general procedure A **3d** was synthesized by hydroaminomethylation (40 bar CO, 40 bar H_2, 140 °C, 3 d) in toluene after absorptive filtration (Alumina N (Act. III)/methanol) yielding 3.08 g (10.2 mmol, 68%) as a yellow oil. ^{1}H-NMR ($CDCl_3$, δ): 0.90 (3H, d, ^3J = 6.7 Hz), 1.32–1.44 (2H), 1.50–1.58 (6H), 1.94–2.20 (1H), 2.27–2.46 (6H), 3.53 (2H, m), 7.67–7.70 (2H), 7.80–7.82 (2H). ^{13}C-NMR ($CDCl_3$, δ): 17.6, 24.4, 25.8, 31.4, 31.5, 44.1, 54.5, 57.1, 123.1, 132.0, 133.8, 168.6. FTIR (neat): 2932, 2878, 2854, 2802, 2768, 1772, 1715, 1467, 1455, 1440, 1435, 1397, 1356, 1051, 912. ESI-MS: m/z = 300.7 (M, Pos.-Mod.). MS (EI (Pos.-Mod.), 60 eV): m/z (%) = 300 (M, 2), 203 (8), 160 (100), 149 (35), 133 (13), 130 (14), 104 (23), 98 (64), 85 (16), 77 (24), 55 (11), 50 (13), 41 (18), 31 (10), 27 (8). HR-MS (EI, 60 eV): m/z (%) = 300.1866 (M, 3) (+2.8 mmu).

2-Methyl-4-piperidin-1-ylbutylamine (4d)

According to the general procedure B hydrazinolysis of 1.95 g (6.5 mmol) **3d** after absorptive filtration (Alumina (Act. III)/cyclohexane–methyl-*tert*-butyl ether = 10 : 1) yielded 0.99 g (5.8 mmol, 89%) **4d** as a yellow oil. ^{1}H-NMR ($CDCl_3$, δ): 0.90 (3H, m), 1.24–1.71 (8H), 1.91 (1H, m), 2.18–2.66 (8H). ^{13}C-NMR ($CDCl_3$, δ): 24.4, 24.4, 24.9, 31.4, 31.4, 48.4, 54.6, 57.4. FTIR (neat): 3305, 2931, 2854, 2802, 2767, 1689, 1469, 1446, 1442, 1376, 1300, 1099, 1041, 737. MS (EI (Pos.-Mod.), 60 eV): m/z (%) = 171 (M + H$^+$, 82), 154 (39), 138 (21), 98 (100), 84 (36), 73 (11), 56 (19), 44 (17). HR-MS (EI, 60 eV): m/z (%) = 171.1882 (M + H$^+$, 100) (+2.1 mmu), 169.1719 (M − H$^+$, 31) (+1.4 mmu).

2-(2-Methyl-4-pyrrolidin-1-ylbutyl)-isoindol-1,3-dione (3e)

According to the general procedure A **3e** was synthesized by hydroaminomethylation (40 bar CO, 40 bar H_2, 140 °C, 1 d) in toluene yielding 3.99 g (14.0 mmol, 93%) as a yellow oil. ^{1}H-NMR ($CDCl_3$, δ): 0.90 (3H, d, ^3J = 6.8 Hz), 1.39 (1H, m), 1.58 (1H, m), 1.74 (4H, m), 1.97–2.06 (1H), 2.46–2.53 (6H), 3.52 (2H, m), 7.67–7.70 (2H), 7.80–7.82 (2H). ^{13}C-NMR ($CDCl_3$, δ): 17.6, 25.3, 31.4, 33.4, 44.0, 54.0, 54.1, 128.1, 131.9, 133.9, 168.6. FTIR (neat): 2962, 2931, 2875, 2789, 1714, 1467, 1398, 1054, 724. ESI-MS: m/z = 286.7 (M, Pos.-Mod.). MS (EI (Pos.-Mod.), 60 eV): m/z (%) = 287 (M + H$^+$, 4), 286 (M, 10), 160 (21), 84 (100), 55 (10), 42 (25), 29 (5). HR-MS (EI, 60 eV): m/z (%) = 286.1661 (M + H$^+$, 18) (−2.1 mmu).

2-Methyl-4-pyrrolidin-1-ylbutylamine (4e)

According to the general procedure B hydrazinolysis of 2.00 g (7.0 mmol) **3e** yielded 0.92 g (5.9 mmol, 84%) **4e** as a colourless oil. ^{1}H-NMR ($CDCl_3$, δ): 0.86 (3H, d, ^3J = 6.7 Hz), 1.25 (1H, m), 1.43 (1H, m), 1.54 (1H, m), 1.64–1.75 (4H), 2.33–2.41 (7H), 2.56 (1H, m). ^{13}C-NMR ($CDCl_3$, δ): 17.5, 23.3, 33.4, 35.0, 48.4, 54.1, 54.4. FTIR (neat): 3409, 2927, 2874, 2787, 2360, 2343, 1698, 1646, 1142, 1108, 1092, 879. GC-MS (EI, 70 eV): m/z (%) = 157 (M$^+$, 40), 84 (100), 79 (20), 55 (17). MS (EI (Pos.-Mod.), 60 eV): m/z (%) = 156 (M, 5), 84 (100), 70 (12), 42 (13), 30 (18), 18 (12). HR-MS (EI, 60 eV): m/z (%) = 156.1664 (M, 10) (+1.7 mmu).

2-(4-Cyclopentylamino-2-methylbutyl)-isoindol-1,3-dione (3f)

According to the general procedure A **3f** was synthesized by hydroaminomethylation (40 bar CO, 40 bar H_2, 140 °C, 1 d) in toluene after absorptive filtration (Alumina N (Act. III)/dichloromethane–ethanol = 10 : 1) yielding 3.82 g (12.7 mmol, 85%) as a yellow oil. ^{1}H-NMR ($CDCl_3$, δ): 0.94 (3H, d, ^3J = 6.7 Hz), 1.25–2.18 (11H), 2.59 (1H, m), 2.69 (1H, m), 3.04 (1H, m), 3.56 (2H, m), 7.68–7.72 (2H), 7.80–7.84 (2H). ^{13}C-NMR ($CDCl_3$, δ): 17.6, 24.0, 30.9, 33.2, 34.9, 44.0, 46.3, 60.0, 123.1,

132.0, 133.8, 168.6. FTIR (neat): 3467, 2959, 2872, 2254, 2182, 1772, 1719, 1469, 1455, 1436, 1399 (vs), 1380, 1358, 1336, 1189, 1056, 908. ESI-MS: m/z = 300.7 (M + H$^+$, Pos.-Mod.). MS (EI (Pos.-Mod.), 60 eV): m/z (%) = 300 (M, 1), 160 (18), 148 (15), 104 (13), 98 (100), 85 (38), 76 (16), 70 (20), 56 (22), 41 (41), 30 (31). HR-MS-fragment $C_9H_6NO_2$ (EI, 60 eV): m/z (%) = 160.0413 (M, 100) (+1.4 mmu).

N^1-Cyclopentyl-3-methylbutan-1,4-diamine (4f)

According to the general procedure B hydrazinolysis of 1.20 g (4.0 mmol) **3f** yielded 0.46 g (2.7 mmol, 67%) **4f** as a colourless oil. ^{1}H-NMR ($CDCl_3$, δ): 0.90 (3H, d, ^3J = 6.7 Hz), 1.25–1.34 (3H), 1.54 (4H, m), 1.62–1.78 (2H), 1.78–1.88 (2H), 2.49 (1H, m), 2.55–2.67 (3H), 3.05 (1H, m). ^{13}C-NMR ($CDCl_3$, δ): 17.5, 24.0, 33.1, 33.2, 34.6, 35.0, 46.5, 48.3, 59.9. FTIR (neat): 3368, 3293, 2953, 2868, 1690, 1590, 1455, 1130, 812, 737. ESI-MS: m/z = 170.6 (M, Pos.-Mod.). GC-MS (EI, 70 eV): m/z (%) = 171 (M + H$^+$, 100), 98 (34), 84 (69), 68 (11), 56 (31). MS (EI (Pos.-Mod.), 60 eV): m/z (%) = 170 (M, 2), 98 (18), 84 (26), 56 (13), 41 (23), 30 (100), 28 (16). HR-MS (EI, 60 eV): m/z (%) = 170.1797 (M, 8) (+1.4 mmu).

2-(4-Cyclohexylamino-2-methylbutyl)-isoindol-1,3-dione (3g)

According to the general procedure A **3g** was synthesized by hydroaminomethylation (40 bar CO, 40 bar H_2, 140 °C, 1 d) in toluene after absorptive filtration (Alumina N (Act. III)/dichloromethane–methanol = 3 : 4) yielding 1.12 g (3.56 mmol, 47%) as a yellow oil. ^{1}H-NMR ($CDCl_3$, δ): 0.90 (3H, d, ^3J = 6.8 Hz), 0.93–1.85 (12H), 2.01 (1H), 2.41 (1H, m), 2.60 (1H, m), 2.71 (1H, m), 3.51 (2H, m), 7.64–7.70 (2H), 7.76–7.81 (2H). ^{13}C-NMR ($CDCl_3$, δ): 17.6, 25.0, 29.8, 30.9, 33.4, 33.5, 34.7, 43.9, 44.4, 56.9, 123.1, 132.0, 133.8, 168.5. FTIR (neat): 3409, 2930, 2855, 1773, 1713, 1687, 1647, 1399, 1381, 1090, 1053, 911, 733. ESI-MS: m/z = 314.8 (M + H$^+$, Pos.-Mod.). MS (EI, 60 eV): m/z (%) = 314 (M$^+$, 3), 217 (11), 229 (24), 186 (26), 160 (27), 148 (67), 138 (43), 130 (23), 112 (100), 98 (21), 84 (20), 77 (27), 70 (34), 56 (37), 41 (7), 30 (4). HR-MS (EI, 60 eV): m/z (%) = 314.1982 (M$^+$, 29) (−1.2 mmu).

N^1-Cyclohexyl-3-methylbutan-1,4-diamine (4g)

According to the general procedure B hydrazinolysis of 1.63 g (5.2 mmol) **3g** yielded 0.42 g (2.3 mmol, 44%) **4g** as a colourless oil. ^{1}H-NMR ($CDCl_3$, δ): 0.87 (3H, d, ^3J = 6.5 Hz), 0.93–1.40 (6H), 1.40–1.54 (2H), 1.54–1.64 (2H), 1.64–1.77 (3H), 1.77–1.96 (3H), 2.36 (1H, m), 2.43 (1H, m), 2.54–2.68 (3H). ^{13}C-NMR ($CDCl_3$, δ): 17.5, 25.0, 26.1, 33.6, 34.7, 35.0, 44.7, 48.4, 56.9. FTIR (neat): 3442, 3278, 3040, 2927, 2853, 1667, 1573, 1450, 1383, 1372, 1260, 1092, 1021, 800. ESI-MS: m/z = 184.6 (M + H$^+$, Pos.-Mod.). GC-MS (EI, 70 eV): m/z (%) = 185 (M$^+$, 100), 168 (8), 152 (5), 141 (8), 124 (41), 112 (62), 98 (89), 84 (78), 70 (24), 56 (85). HR-MS-fragment $C_7H_{14}N$ (EI, 60 eV): m/z (%) = 112.1097 (M, 90) (−3.0 mmu).

Cyclohexyl-bis-[4-(isoindol-1,3-dione)-3-methylbutyl]-amine (5a)

According to the general procedure A **5a** was synthesized by hydroaminomethylation (40 bar CO, 40 bar H_2, 140 °C, 2 d) in toluene after absorptive filtration (Alumina N (Act. III)/methyl-*tert*-butyl ether) yielding 3.82 g (7.2 mmol, 96%) as a yellow oil. ^{1}H-NMR ($CDCl_3$, δ): 0.85, 0.86 (6H, d, ^3J = 6.7 Hz), 1.01–1.20 (4H), 1.21–1.29 (2H), 1.42–1.69 (8H), 1.93–2.10 (2H), 2.33–2.51 (5H), 3.47 (2H, m), 3.56 (2H, m), 7.69–7.73 (4H), 7.82–7.85 (4H). ^{13}C-NMR ($CDCl_3$, δ): 17.6, 26.2, 26.4, 28.9, 29.9, 30.9, 33.7, 44.1, 48.0, 59.7, 123.1, 132.0, 133.8, 168.6. FTIR (neat): 2929, 2854, 2811, 2371, 1773, 1724, 1398, 1053, 911, 726. ESI-MS: m/z = 530.1 (M + H$^+$, Pos.-Mod.). MS (FAB (mNBA), 60 eV): m/z (%) = 530 (M + H$^+$, 26), 307 (29), 289 (16), 240 (6), 198 (39), 154 (100), 136 (60), 107 (17), 90 (14), 56 (6). HR-MS (FAB (mNBA), 60 eV): m/z (%) = 530.3004 (M + H$^+$, 100) (−1.5 mmu). $C_{29}H_{39}N_3O_4$ calc. (%): C: 72.6; H: 7.4; N: 7.9. Found (%): C: 72.6; H: 7.7; N: 7.4.

N^1-(4-Amino-3-methylbutyl)-N^1-cyclohexyl-3-methylbutane-1,4-diamine (6a)

According to the general procedure B hydrazinolysis of 2.20 g (4.2 mmol) **5a** after absorptive filtration (Alumina N (Act. III)/cyclohexane–methyl-*tert*-butyl ether = 10 : 1) yielded 0.76 g (2.8 mmol, 68%) **6a** as a colourless oil. ^{1}H-NMR ($CDCl_3$, δ): 0.82 (6H, d, ^3J = 6.5 Hz), 1.08–1.14 (6H), 1.40 (4H), 1.52 (2H, m), 1.64–1.77 (4H), 2.30–2.42 (8H), 2.51–2.54 (1H). ^{13}C-NMR ($CDCl_3$, δ): 17.5, 26.1, 26.3, 28.8, 33.5, 34.6, 48.2, 48.3. FTIR (neat): 3381, 2856, 2252, 1644, 1581, 1464, 1378, 1347, 909, 649. ESI-MS: m/z = 269.8 (M, Pos.-Mod.). MS (EI (Pos.-Mod.), 60 eV): m/z (%) = 269 (M, 15), 197 (79), 183 (62), 166 (36), 154 (38), 138 (35), 124 (31), 112 (58), 98 (81), 86 (100), 55 (34), 41 (35), 30 (100). HR-MS (EI, 60 eV): m/z (%) = 269.2832 (M, 12) (+0.1 mmu).

Benzyl-bis-[4-(isoindol-1,3-dione)-3-methylbutyl]-amine (5b)[29]

According to the general procedure A **5b** was synthesized by hydroaminomethylation (40 bar CO, 40 bar H_2, 140 °C, 3 d) in toluene after absorptive filtration (Alumina N (Act. III)/ethyl acetate) yielding 3.77 g (7.0 mmol, 94%) as a yellow oil.

N^1-(4-Amino-3-methylbutyl)-N^1-benzyl-3-methylbutane-1,4-diamine (6b)

According to the general procedure B hydrazinolysis of 2.87 g (5.3 mmol) **5b** yielded 0.95 g (3.4 mmol, 64%) **6b** as a colourless oil. ^{1}H-NMR ($CDCl_3$, δ): 0.84, 0.85 (6H, d, ^3J = 6.5 Hz), 1.25 (2H, m), 1.36–1.60 (8H), 2.38–2.50 (6H), 2.56 (2H, m), 3.54 (2H, m), 7.21–7.34 (5H). ^{13}C-NMR ($CDCl_3$, δ): 17.5, 31.4, 34.5, 48.3, 48.4, 51.5, 58.5, 126.6, 128.0, 128.8, 139.9. FTIR (neat): 3380, 3295, 2951, 2922, 2867, 2800, 1697, 1665, 1494, 1453, 1370, 1071, 845. ESI-MS: m/z = 277.8 (M + H$^+$, Pos.-Mod.). GC-MS (EI, 70 eV): m/z (%) = 278 (M + H$^+$, 50), 205 (34), 191 (48), 174 (40), 122 (12), 103 (82), 98 (43), 91 (60), 86 (100), 30 (33). HR-MS (EI, 60 eV): m/z (%) = 277.2522 (M + H$^+$, 6) (+0.4 mmu).

General procedure C: hydroaminomethylation with urea

A solution of 10 mmol of the olefin, 10 mmol urea and 0.29 mol% [Rh(cod)Cl]$_2$-catalyst in 90 ml absolute. dioxane, 9 ml methanol and 1 ml glacial acetic acid was treated under hydroaminomethylation conditions (40 bar CO, 40 bar H_2) at 100–120 °C for 2–3 days. After cooling the pressure was removed and the solvent was evaporated to dryness. The resulting mixture was

treated with 10 ml conc. sodium hydroxide solution and 10 ml of water. The mixture was extracted with 200 ml ethyl acetate, the organic layer was dried with sodium sulfate and the solvent was evaporated in vacuum. The crude product was cleaned by column chromatography on Alumina N (Act. III) with different solvent mixtures.

2-(4-{Bis-[4-(2-isoindol-1,3-dione)-3-methylbutyl]-amino}-2-methylbutyl)-isoindol-1,3-dione (8a)

According to the general procedure C (40 bar CO, 40 bar H_2, 120 °C, 2 d) compound **8a** was isolated by absorptive filtration on Alumina N (Act. III)/dichloromethane–methanol = 10 : 1 yielding 1.72 g (2.6 mmol, 78%) as a colourless oil. Alternatively **8a** can be obtained by hydroaminomethylation of 0.15 g (0.34 mmol) **7**[29] and 0.07 g (0.35 mmol) **1**, with 1 mg $[Rh(cod)Cl]_2$ in 10 ml dry toluene at 120 °C, 50 bar CO and 50 bar H_2. After removing of the solvent and purification by column chromatography on silica with dichloromethane–methanol (10 : 1) 0.17 g (0.25 mmol, 75%) of **1** were isolated. ^{1}H-NMR ($CDCl_3$, δ): 0.84, 0.85 (9H, d, ^3J = 6.5 Hz), 1.22–1.40 (3H), 1.42–1.57 (3H), 1.96 (3H, m), 2.43 (6H, m), 3.56 (6H, m), 7.65–7.72 (6H), 7.79–7.84 (6H). ^{13}C-NMR ($CDCl_3$, δ): 17.5, 31.1, 36.4, 44.1, 51.4, 123.1, 132.0, 133.8, 168.6. FTIR (neat): 2960, 2931, 2873, 2808, 1772, 1712, 1468, 1435, 1398, 1188, 1053, 912, 723. MS (FAB (mNBA), 60 eV): m/z (%) = 663 ($M + H^+$, 100), 397 (51). HR-MS (FAB (mNBA), 60 eV): m/z (%) = 663.3211 ($M + H^+$, 100) (+2.8 mmu).

Tris-(4-benzyloxy-3-methylbutyl)-amine (8b)

According to the general procedure C (40 bar CO, 40 bar H_2, 120 °C, 3 d) compound **8b** was isolated by absorptive filtration on Alumina N (Act. III)/dichloromethane–methanol = 10 : 1 yielding 1.70 g (3.1 mmol, 94%) as a yellow oil. ^{1}H-NMR ($CDCl_3$, δ): 0.94 (9H, d, ^3J = 6.7 Hz), 1.24 (3H, m), 1.58 (3H, m), 1.78 (3H, m), 2.44 (6H, m), 3.17–3.49 (6H), 4.49 (6H, m), 7.25–7.36 (15H). ^{13}C-NMR ($CDCl_3$, δ): 17.3, 30.6, 31.9, 51.6, 72.9, 75.8, 127.4, 128.3, 138.7. FTIR (neat): 3087, 3062, 3030, 2927, 2856, 1662, 1601, 1454, 1363, 1097, 735, 698. MS (FAB (mNBA), 60 eV): m/z (%) = 546 ($M + H^+$, 46), 454 (25), 382 (17), 135 (17), 92 (100). HR-MS (FAB (mNBA), 60 eV): m/z (%) = 546.3974 ($M + H^+$, 100) (+2.7 mmu).

Tris-(3-phenylbutyl)-amine (8c)

According to the general procedure C (40 bar CO, 40 bar H_2, 120 °C, 2 d) compound **8c** was isolated by absorptive filtration on Alumina N (Act. III)/cyclohexane–methyl-*tert*-butyl ether = 10 : 1 yielding 1.17 g (2.8 mmol, 85%) as a colourless oil. ^{1}H-NMR ($CDCl_3$, δ): 1.10, 1.11 (9H, d, ^3J = 7.0 Hz), 1.51 (6H, m), 2.03–2.35 (6H), 2.57 (3H, m), 7.03–7.11 (10H), 7.14–7.20 (5H). ^{13}C-NMR ($CDCl_3$, δ): 22.6, 22.8, 35.2, 35.7, 37.9, 38.0, 52.0, 52.2, 125.8, 126.9, 128.3, 147.5. FTIR (neat): 3082, 3060, 3026, 2956, 2802, 1603, 1493, 1452, 1373, 1149, 1088, 1027, 906, 762, 700 (s); MS (FAB (mNBA), 60 eV): m/z (%) = 414 ($M + H^+$, 100), 412 (53), 352 (10), 294 (93), 232 (8), 176 (11), 174 (10), 106 (68), 92 (50), 59 (36), 45 (13); HR-MS (FAB (mNBA), 60 eV): m/z (%) = 414.3169 ($M + H^+$, 100) (+0.8 mmu), 412.3020 ($M - H^+$, 64) (+1.5 mmu). $C_{30}H_{39}N$ calc. (%): C: 87.1; H: 9.5; N: 3.4. Found (%): C: 86.6; H: 9.6; N: 3.4.

Tris-(cyclopentylmethyl)-amine (8d)

According to the general procedure C (40 bar CO, 40 bar H_2, 100 °C, 2 d) compound **8d** was isolated by absorptive filtration on Alumina N (Act. III)/cyclohexane–methyl-*tert*-butyl ether = 10 : 1 yielding 0.68 g (2.6 mmol, 77%) as a colourless oil. ^{1}H-NMR ($CDCl_3$, δ): 1.13–1.21 (6H), 1.47–1.60 (12H), 1.65–1.73 (6H), 2.01 (3H, m), 2.18 (6H, d, ^3J = 7.5 Hz). ^{13}C-NMR ($CDCl_3$, δ): 25.2, 31.1, 38.1, 61.0. FTIR (neat): 2951, 2864, 2789, 1452, 1379, 1336, 1261, 1101, 899, 852. MS (FAB (mNBA), 60 eV): m/z (%) = 264 ($M + H^+$, 49), 262 (80), 207 (11), 194 (100), 147 (22), 124 (18), 74 (39), 56 (32), 42 (16). HR-MS (FAB (mNBA), 60 eV): m/z (%) = 263.2607, 262.2527 ($M - H^+$) (263.26130, calcd. for $C_{18}H_{33}N$). Calc. (%): C: 82.1; H: 12.9; N: 4.6. Found (%): C: 81.9; H: 13.0; N: 5.3.

Tris-(cyclohexylmethyl)-amine (8e)[39]

According to the general procedure C (40 bar CO, 40 bar H_2, 100 °C, 2 d) compound **8e** was isolated by absorptive filtration on Alumina N (Act. III)/cyclohexane–methyl-*tert*-butyl ether = 10 : 1 yielding 0.75 g (2.5 mmol, 74%) as colourless crystals.

Tris-(cyclooctylmethyl)-amine (8f)

According to the general procedure C (40 bar CO, 40 bar H_2, 100 °C, 2 d) compound **27** was isolated by absorptive filtration on Alumina N (Act. III)/cyclohexane–methyl-*tert*-butyl ether = 10 : 1 yielding 0.79 g (2.0 mmol, 67%) as a colourless oil. ^{1}H-NMR ($CDCl_3$, δ): 1.15–1.29 (6H), 1.36–1.69 (39H), 1.97 (6H, d, ^3J = 7.0 Hz). ^{13}C-NMR ($CDCl_3$, δ): 25.6, 26.6, 27.2, 30.9, 35.6, 63.9. FTIR (neat): 2920, 2848, 2794, 2725, 2694, 1743, 1681, 1666, 1417, 1446, 1360, 1228, 1151, 1086, 1057. MS (FAB (mNBA), 60 eV): m/z (%) = 390 ($M + H^+$, 12), 289 (31), 388 (100), 278 (88), 166 (38), 152 (16), 84 (18), 82 (36), 70 (33), 59 (16), 56 (40), 42 (18). HR-MS (FAB (mNBA), 60 eV): m/z (%) = 388.3962 ($M + H^+$, 100) (+1.9 mmu), 389.4005 (M, 39) (−1.6 mmu). $C_{27}H_{51}N$ calc. (%): C: 83.2; H: 13.2; N: 3.6. Found (%): C: 83.0; H: 13.4; N: 3.2.

1,3-Bis-cyclohexylmethylurea (10)

Performing the reaction according to the general procedure C not in methanol–dioxane–acetic acid (40 bar CO, 40 bar H_2, 100 °C, 2 d), but in 10 ml methanol and 10 ml of water, compound **10** was isolated by absorptive filtration on Alumina N (Act. III)/cyclohexane–methyl-*tert*-butyl ether = 10 : 1. The first fraction affords 0.14 g (0.4 mmol, 12%) **8e** as colourless crystals. Washing of the column with methanol afforded 0.30 g (1.2 mmol, 24%) of **10** as colourless crystals. ^{1}H-NMR ($CDCl_3$, δ): 0.89–0.99 (4H), 1.17–1.27 (6H), 1.67–1.76 (12H), 3.07 (4H, t, ^3J = 7.0 Hz), 4.89 (2H, s). ^{13}C-NMR ($CDCl_3$, δ): 27.1, 27.6, 31.9, 38.1, 55.1, 148.0. FTIR (neat): 3427, 3226, 2923, 2844, 1697, 1634, 1600, 1497, 1449, 1425, 1370, 1103. ESI-MS: m/z = 253.2 ($M + H^+$). MS (EI, 70 eV): m/z (%) = 252 (M, 15), 169 (100), 126 (52), 87 (25), 55 (24), 44 (38), 41 (11). $C_{15}H_{28}N_2O$ calc. (%): C: 71.4; H: 11.2; N: 11.1. Found (%): C: 71.5; H: 11.0; N: 11.0.

N^1,N^1-Bis-(4-amino-3-methylbutyl)-3-methylbutane-1,4-diamine (16)

2.10 g (3.17 mmol) of **8a** were solubilized in 50 ml ethanol and treated with 1.78 g (35.6 mmol) hydrazine hydrate under reflux for 20 h. To the cooled mixture 20 ml of 5 N sodium hydroxide solution were added and the mixture was extracted with dichloromethane, the organic layer was dried with sodium sulfate and after evaporation of the solvent, 0.80 g (2.94 mmol, 93%) of **7** were isolated. ^{1}H-NMR ($CDCl_3$, δ): 0.77 (9H, d, J = 5.1 Hz), 1.01–1.12 (3H, m), 1.25–1.44 (6H, m), 1.69 (6H, bs), 2.15–2.55 (m, 12H). ^{13}C-NMR ($CDCl_3$, δ): 17.5 (CH_3), 31.1 (CH_2), 34.5 (CH), 48.1 (CH_2), 51.5 (CH_2). FTIR (neat): 1084 (s), 1123 (w), 1262 (w), 1299 (w), 1377 (m), 1463 (s), 1600 (w), 1663 (w), 1720 (m), 2195 (w), 2459 (w), 2867 (vs), 2923 (vs), 2952 (vs), 3291 (m). HR-MS (FAB (mNBA), 60 eV): m/z (%) = 273.3033 (M + H^+, 100) (+ 1.5 mmu).

N^4,N^4-Bis-(4-{bis-[4-(*N*-phthalimidyl)-3-methylbutyl]-amino}-3-methylbutyl)-N^1,N^1-bis-[4-(*N*-phthalimidyl)-3-methylbutyl]-2-methylbutane-1,4-diamine (17)

1.66 g (8.25 mmol) methylallylphthalimide (**1**), 0.25 g (0.92 mmol) of **16** and 5 mg (0.25 mol%) $[Rh(cod)Cl]_2$ are dissolved in toluene and placed in a pressure vessel. The vessel is flushed with 50 bar argon and the pressure is removed. Then the vessel is filled with 50 bar of carbon monoxide and 50 bar of hydrogen and is heated at 120 °C for 3 days. After cooling, the gas is removed and the solvent is distilled off at low pressure. The crude mixture is cleaned by column chromatography (Alumina N (Act. III)/diethyl ether–*n*-hexane 1 : 1) and the column is washed with ethyl acetate, after which the solvent is removed, yielding 0.890 g (0.57 mmol, 62%) of **17**. ^{1}H-NMR ($CDCl_3$, δ): 0.80 (27H, m), 1.20 (12H, m), 1.49 (12H, m), 1.85–2.10 (13H), 2.15–2.50 (14H), 3.30–3.65 (12H), 7.30–7.80 (24H). ^{13}C-NMR ($CDCl_3$, δ): 17.4, 17.5, 17.6, 18.5, 29.8, 30.8, 30.9, 31.6, 31.7, 43.8, 44.0, 44.1, 51.8, 52.0, 60.3, 123.0, 131.9, 133.7, 168.5. FTIR (neat): 3398, 2960, 1772, 1712, 1435, 1399, 1381, 1054. $C_{93}H_{114}N_{10}O_{12}$ ESI-MS : m/z = 1565.19 (M + H^+), 783.30 (M + $2H^+$), 522.23 (M + $3H^+$).

3-[(2-Cyanoethyl)-(2-methylallyl)-amino]-propionitrile (18)

In a 100 ml round bottomed flask equipped with a magnetic stirrer 27.06 g (220 mmol) 3-(2-cyanoethylamino)-propionitrile and 10.0 g (110 mmol) methylallylchloride were heated to reflux for 16 h. The mixture was cooled to room temperature, and the resulting solid was filtered off and washed with toluene. The solvent of the filtrate was removed yielding 12.94 g (73 mmol, 66%) of **18**. ^{1}H-NMR ($CDCl_3$, δ): 1.75 (3H, s), 2.46 (4H, t, ^3J = 6.7 Hz), 2.84 (4H, t, ^3J = 6.73 Hz), 3.04 (2H, s), 4.90 (4H, d, ^2J = 16.0 Hz). ^{13}C-NMR ($CDCl_3$, δ): 16.7, 20.3, 49.5, 60.8, 114.1, 118.5, 142.3. FTIR (neat): 3075, 2971, 2942, 2836, 2248, 1650, 1448, 1423, 1374, 1135, 1027, 904. MS (FAB (mNBA), 60 eV): m/z (%) = 200.2 (M + Na^+, 45), 178.2 (M + H^+, 75). HR-MS (FAB (mNBA), 60 eV): m/z (%) = 178.1318 (M + H^+, 60) (−2.7 mmu).

3-{[4-(Bis-{4-[bis-(2-cyanoethyl)-amino]-3-methylbutyl}-amino)-2-methylbutyl]-(2-cyanoethyl)-amino}-propionitrile (19)

According to the general procedure C (40 bar CO, 40 bar H_2, 120 °C, 3 d) compound **19** was isolated by column chromatography on Alumina N (Act. III)/dichloromethane–diethyl ether–triethylamine 8 : 4 : 1 yielding 1.00 g (1.7 mmol, 51%) as a yellow oil. ^{1}H-NMR ($CDCl_3$, δ): 0.90 (9H, d, ^3J = 6.53 Hz), 1.05–1.18 (3H, m), 1.50–1.70 (6H, m), 2.19–2.24 (3H), 2.32–2.37 (3H), 2.40–2.55 (6H, m), 2.44 (12H, t, ^3J = 6.78 Hz), 2.81 (12 H, t, ^3J = 6.78 Hz). ^{13}C-NMR ($CDCl_3$, δ): 16.7, 18.1, 30.0, 31.6, 50.1, 51.5, 118.7. FTIR (neat): 3478, 2954, 2827, 2247, 1724, 1604, 1464, 1348, 1135, 1078. MS (FAB (mNBA), 60 eV): m/z (%) = 590 (M, 30). HR-MS (FAB (mNBA), 60 eV): m/z (%) = 590.4557 (M^+, 21) (+2.5 mmu). HR-MS (FAB (mNBA), 60 eV): m/z (%) = 591.4664 (M + H^+, 100) (+3.2 mmu).

N^1,N^1-Bis-(3-aminopropyl)-N^4,N^4-bis-{4-[bis-(3-aminopropyl)-amino]-3-methylbutyl}-2-methylbutane-1,4-diamine (20)

0.80 g (1.4 mmol) of **19** were dissolved in 10 ml methanol and 90 ml of water and placed in a pressure vessel, as well as 2.0 g of wet Raney cobalt catalyst, which was washed before with 25 ml of water. The vessel was purged with Ar and then filled with 20 bar H_2 and was heated to 70 °C for 2 hours. After cooling the vessel to room temperature the H_2 was drained, the vessel was purged with Ar gas, opened and the contents were immediately filtered off. The water and methanol were evaporated under reduced pressure and 0.69 g (1.1 mmol, 83%) **20** were obtained as a colourless oil. ^{1}H-NMR ($CDCl_3$, δ): 0.75–1.05 (9H, m), 1.09–1.31 (3H, m), 1.50–1.85 (18H, m), 2.05–2.33 (6H, m), 2.36–2.59 (18H, m), 2.60–2.84 (12H, m). ^{13}C-NMR ($CDCl_3$, δ): 19.1, 30.5, 31.4, 32.7, 41.0, 52.9, 53.5, 63.2. FTIR (neat): 3282, 2945, 2857, 2791, 1720, 1597, 1463, 1374, 1083, 861. MS (FAB (mNBA), 60 eV): m/z (%) = 615.3 (M + H^+, 30). HR-MS (FAB (mNBA), 60 eV): m/z (%) = 615.6527 (M + H^+, 100) (+3.8 mmu).

4-[(2-{[Bis-(2-cyanoethyl)-amino]-methyl}-allyl)-(2-cyanoethyl)-amino]-butyronitrile (23)

12.25 g (0.1 mol) 3-(2-cyanoethylamino)-propionitrile (**22**) and 3.11 g (25 mmol) 3-chloro-2-chloromethylpropene (**21**) were heated to 80 °C for 20 h. After cooling, the solid was filtered off and was washed with dichloromethane. The solvent of the filtrate was removed and the residue was basified with half concentrated sodium hydroxide solution and extracted with ethyl acetate. The organic layer was washed with water, dried with magnesium sulfate and the solvent was removed at reduced pressure yielding 7.14 g (23 mmol, 96%) of **23**. ^{1}H-NMR ($CDCl_3$, δ): 2.55 (8H, t, ^3J = 6.53 Hz), 2.83 (8H, t, ^3J = 6.53 Hz), 3.23 (4H), 5.20 (2H). ^{13}C-NMR ($CDCl_3$, δ): 16.51, 48.85, 55.59, 119.00, 143.14. FTIR (neat): 3076 (w), 2956 (s), 2837 (vs), 2247 (vs), 1651 (m), 1463 (s), 1421 (s), 1381 (s), 1265 (m), 1136 (vs), 1030 (s), 926 (m). MS (FAB (mNBA), 60 eV): m/z (%) = 321.4 (M + Na^+, 33), 299.4 (M + H^+, 100), 258 (27), 218 (10), 97 (18), 89 (15). HR-MS (FAB (mNBA), 60 eV): m/z (%) = 321.1815 (M + Na^+, 26) (+1.1 mmu), 299.1996 (M + H^+, 100) (+1.1 mmu). $C_{16}H_{23}N_6$ calc. (%): C: 64.4; H: 7.4; N: 28.2. Found (%): C: 64.6; H: 7.4; N: 28.1.

4-[(4-[Bis-{3-([bis-(2-cyanoethyl)-amino]-methyl)-4-[(2-cyanoethyl)-(3-cyanopropyl)-amino]-butyl}-amino]-2-{[bis-(2-cyanoethyl)-amino]-methyl}-butyl)-(2-cyanoethyl)-amino]-butyronitrile (24)

According to the general procedure C (40 bar CO, 40 bar H_2, 120 °C, 3 d) compound **24** was isolated by column chromatography first on Alumina N (Act. III)/dichloromethane–diethyl ether–triethylamine 8 : 4 : 1 and then with dichloromethane–methanol 10 : 1 as solvent yielding 0.95 g (1.0 mmol, 30%) of **24** as a yellow oil. ^{1}H-NMR ($CDCl_3$, δ): 1.23 (3H), 1.64 (6H), 2.35–2.65 (42H), 2.81 (24 H). ^{13}C-NMR ($CDCl_3$, δ): 16.65, 29.61, 34.28, 49.91, 50.88, 56.88, 119.13. FTIR (neat): 2952 (s), 2846 (s), 2659 (s), 2484 (s), 2248 (s), 2204 (m), 1664 (m), 1469 (vs), 1423 (s), 1373 (s), 1275 (m), 1167 (m), 1136 (m), 1032 (s), 920 (s), 733 (s), 646 (m). MS (FAB (mNBA), 60 eV): m/z (%) = 954.7 (M, 5), 207 (20), 147 (87), 74 (100), 56.2 (20). HR-MS (FAB (mNBA), 60 eV): m/z (%) = 954.6519 (M + H^+, 100) (−1.2 mmu).

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