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Assembly of the Bis(imidazolyl)propene Core of Nagelamides C and S by Double Grignard Reaction

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Dedicated to Professor Richard Neidlein on the occasion of his 80th birthday

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As characteristic structural elements of several of the non-monomeric pyrrole-imidazole alkaloids, 1,1-bis(imidazolyl)-propenes were assembled in a facile manner by double Grignard reaction of metalated imidazoles with saturated esters, followed by dehydration. The presence of nitrile functions or acryl esters in the electrophile component leads to competing reactions, whereas propargyl esters are tolerated. Introduction of 2-amino groups was possible via the corresponding dimethylsulfamoyl-protected 2-azidoimidazoles, which had to be deprotected prior to hydrogenation. NOESY-based analysis revealed preferred orientation of the imidazole 5-positions towards the propenyl chain.

Introduction

Pyrrole-imidazole alkaloids constitute a branched family of biogenetically related natural products isolated from marine sponges.[1,2] Important biological activities include fish feeding deterrency[3] and anti-biofilm activity.[4] A particular group is formed by pyrrole-imidazole alkaloids containing two $C_{11}N_5$ subunits such as nagelamides C (**2**),[5] S (**3**)[6] and J (**5**)[7] or ageliferin (**4**, Figure 1), which continue to be challenging targets for total synthesis.[8] Bis(imidazolyl)-allyl- or -alkylamines of type **1** can be identified as core structures, which may function as strategic intermediates for total synthesis. Desymmetrization either by cyclization or Diels–Alder cycloaddition is possible in principal, aiming at unified approaches to nagelamide J (**5**) and ageliferin (**4**). Monofunctionalization of **1** could give access to nagelamide C (**2**). Moreover, oxidation of bis(imidazolyl)propenes or -propanes may lead to tricyclic moieties present in the axinellamines or massadines.[8,9] Therefore, we decided to develop a convenient route to bis(imidazolyl)propenes of type **1**.

Earlier we have reported the palladium-catalyzed coupling of masked 2-aminoimidazoles and acrylic esters and amides,[10] which had to contain a terminal double bond and consequently reacted with only one 2-aminoimidazole unit. Recently, Lovely et al. have shown that nonsymmetrical bis(imidazolyl)propenes can be assembled by Stille cross-coupling of 4-iodo-5-vinylimidazoles and vinylstannanes derived from the corresponding alkynylimidazole.[11]

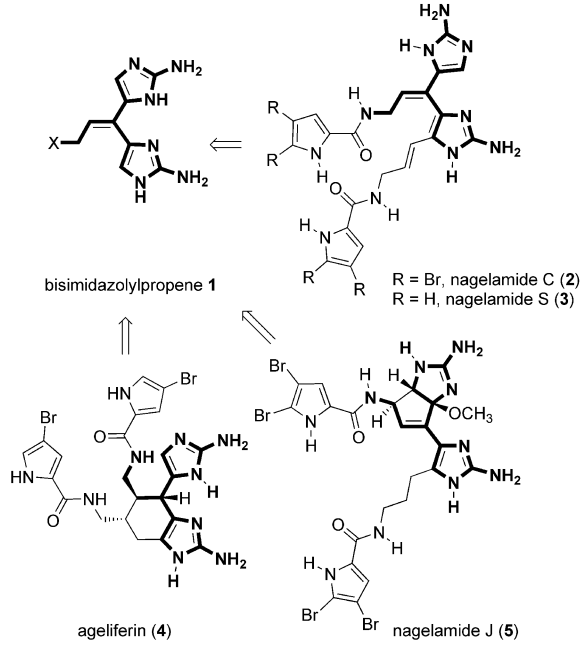

Figure 1. Bis(imidazolyl)propenes of type **1** could serve as building block in the synthesis of nagelamide (**2**, **3** and **5**) and ageliferin (**4**).

Results and Discussion

We decided to assemble symmetrical saturated and unsaturated bis(4-imidazolyl)propenes such as **1** via the corresponding carbinols by employing esters as electrophiles.

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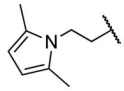
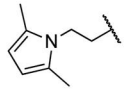
On the imidazole side, we preferred iodine/metal exchange over deprotonation, because protection of the imidazole 2-position would not be required.[12] Magnesation with EtMgBr was preferred over lithiation, because the latter may generate 2-lithioimidazoles in competition.[13] Breslow et al.,[14] Katritzky et al.,[15] Imanishi et al.[16] and Nicholas et al.[17] reacted 5-lithiated imidazoles with aldehydes, esters, and alkyl carbonates obtaining hydroxy-alkylated imidazoles, bis(imidazolyl) carbinols, and tris(imidazolyl) carbinols. 4-Iodo-1-tritylimidazole has also been treated with EtMgBr and the resulting Grignard nucleophiles were treated with DMF, *N*-formylpiperidine,[18] substituted benzaldehydes,[19] thiophenecarbaldehydes, esters,[20] and Weinreb amides.[21]

4-Iodo-1-tritylimidazole (**6**)[22] and 1-(dimethylamino)-sulfonyl-4-iodoimidazole (**7**)[23] were prepared following literature procedures. Iodine/magnesium exchange was carried out with EtMgBr.[12] When saturated methyl esters without heteroatom-H-bonds were offered as electrophiles, yields of bis(imidazolyl) carbinols **8**–**18** were consistently high both for trityl- and DMAS-protected 4-iodoimidazoles (50–95%, Scheme 1).

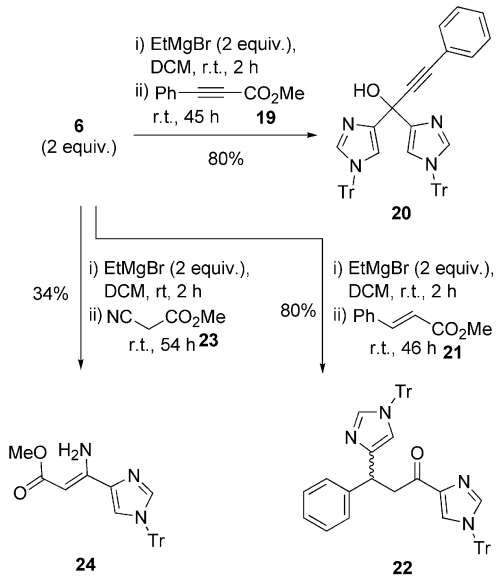
We also studied ambident unsaturated electrophiles. Phenylpropiolic methyl ester (**19**) reacted twice at the carbonyl carbon affording the alkynylated bis(imidazolyl) carbinol **20** (Scheme 2). Methyl cinnamate (**21**), however, was attacked both in the β-position and at the carbonyl carbon providing compound **22** with two imidazole units connected via a C_3 chain. Thus, α,β-unsaturated esters appear not to be suitable for direct bis(imidazolyl) carbinol formation following Scheme 2. A nitrile function is also able to compete with the methyl ester group. On reaction of α-cyanoacetate **23** with 2 equiv. of **6**/EtMgBr, enamine **24** was the major product (34%), accompanied by considerable decomposition.

Formation of dimethylamino, dibenzylamino and 2,5-dimethylpyrrole compounds **12**, **13**, **15**, **17** and **18** shows that nitrogen can be incorporated in the C3 side chain. We expected that the 2,5-dimethylpyrrole moiety of **18** could be cleaved off by treatment with hydroxylamine,[24] but we were not successful. Fortunately, doubly Boc-protected β-alanine methyl ester (**25**) reacted to bis(imidazolyl) carbinol **27** (61%, Scheme 3), accompanied by ketone **26** (12%). The main product **27** contained only one Boc group. Side product **26** was possibly formed via retro Michael elimination of the amine, followed by Michael addition of **6** to the resulting acryl imidazole.

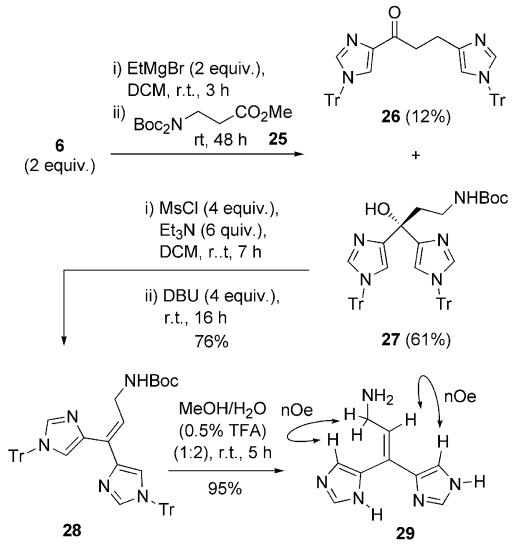
Elimination of water from tertiary carbinol **27** was achieved by employing excess MsCl/NEt_3 over 7 h, followed by treatment with DBU. The remaining Boc-group was removed quantitatively together with the two trityl groups under acidic conditions affording the novel bis(imidazolyl)-allylamine **29**.[25] NOESY spectra (CD_3OD) showed correlations between the olefinic proton (δ = 6.56 ppm) and one of the imidazole protons (δ = 7.59 ppm), whereas the other imidazole proton (δ = 7.74 ppm) is in proximity of the methylene protons (δ = 3.88 ppm). Thus, the allylamine double bond is in *cisoid* arrangement to both C=C bonds

product	R	PG	yield
8	H	Tr	99%
9	Me	Tr	84%
10	Et	Tr	93%
11	*n*Pr	Tr	90%
12	Bn_2N	Tr	70%
13		Tr	81%
14	Et	DMAS	64%
15	Bn_2N	DMAS	72%
16	MeO	DMAS	71%
17	Me_2N	DMAS	51%
18		DMAS	76%

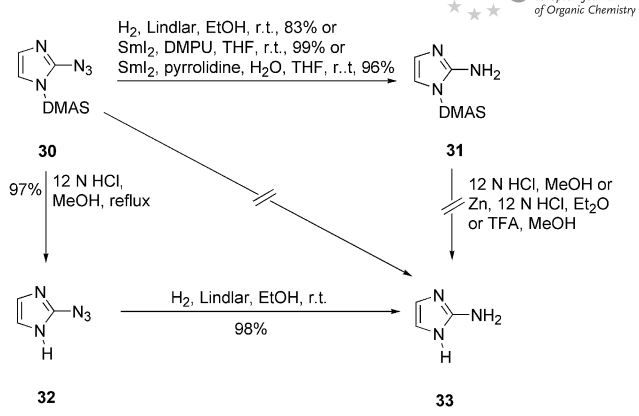
Scheme 1. Synthesis of bis(imidazolyl) carbinols by double Grignard reaction (Tr = triphenylmethyl; DMAS = (dimethylamino)-sulfonyl).



Scheme 2. Reaction of imidazolylmagnesium bromide with ambident electrophiles.



Scheme 3. Synthesis and conformation of the bis(imidazolyl)allylamine **29**.



Scheme 4. Conversion of DMAS-protected 2-azidoimidazole (**30**) to 2-aminoimidazole (**33**).

of the imidazole units, making a hydrogen bond between the two imidazoles possible. According to MM2 analysis, compound **29** is not planar with at least one of the imidazole rings twisted out of the plane.

The chemistry of pyrrole-imidazole alkaloids is strongly influenced by the amino groups located in the imidazole 2-positions. Amination of the imidazole 2-position is possible by azidation and reduction[26] and has also been applied simultaneously for two *N*-methylated[27] and for two DMAS-protected imidazole units.[11] We switched from trityl- to DMAS-protection[11,12] of the imidazole, because we expected greater stability of the rather sensitive azides, and more simple ^{1}H NMR spectra.

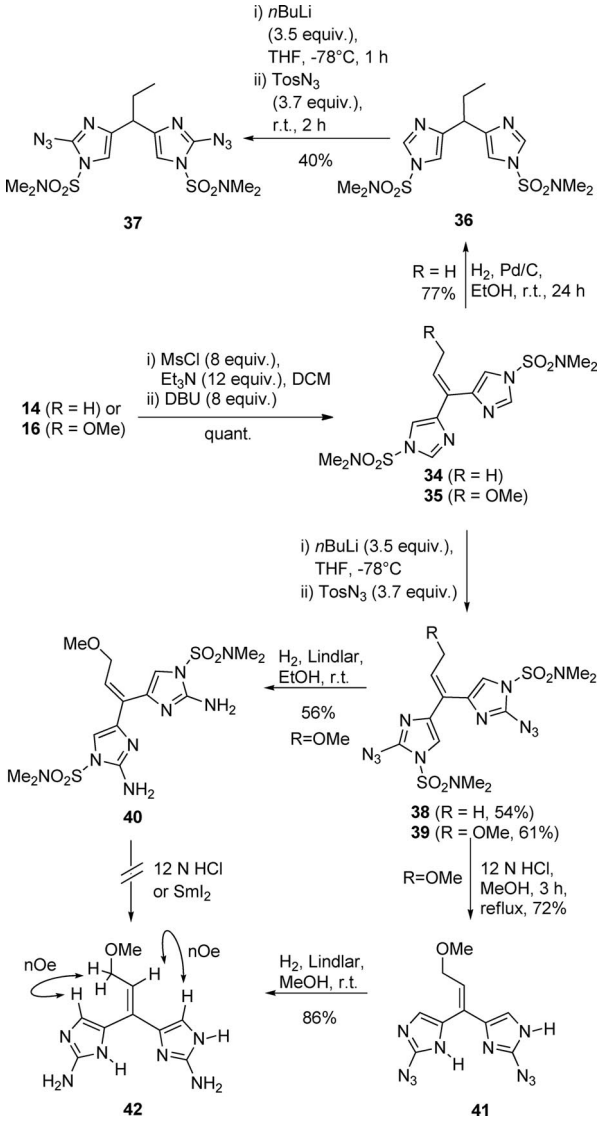
Scheme 4 summarizes a model study on the deprotection strategy towards 2-aminoimidazoles. DMAS-protected 2-azidoimidazole (**30**) can smoothly be reduced to DMAS-protected 2-aminoimidazole **31**. However, it turned out to be impossible to cleave off the DMAS group in the presence of the 2-amino group. Compound **31** persisted even under drastic acidic conditions, whereas 2-azidoimidazole **30** smoothly underwent deprotection when treated with 12 N HCl, in accordance with results obtained by Lovely's group.[11,28] DMAS-protected 2-azidoimidazole **30** also resisted reductive cleavage of the N–S bond with samarium diiodide. In the case of other N-heterocycles, however, DMAS groups have been removed under reductive conditions.[29] The reason for the great stability of DMAS-protected 2-aminoimidazole under acidic conditions remains unclear. Apparently, even a protonated 2-amino substituent does not generate sufficient electron deficiency for cleaving off DMAS. In the case of 2-free and 2-azidoimidazoles, however, DMAS is removed. Differing from 1-DMAS-protected 2-aminoimidazoles, hydrolysis of the N-trityl analogs is facile.[25,30] It can be concluded that DMAS-protected 2-azidoimidazoles first have to be deprotected, followed by reduction of the azide.

For the synthesis of the desired bis(2-aminoimidazolyl)-propenes, we first investigated the double azidation of DMAS-protected bisimidazoles in the absence and presence of the vinyl double bond. Bis(imidazolyl)propane **36** was obtained from carbinol **14** in two steps by dehydration to compound **34** and hydrogenation with Pd/C (Scheme 5). Double azidation of the hydrogenated precursor **36** was possible in satisfactory yield (40%) and gave access to the 1,1-disubstituted propane **37**. Fortunately, azidation of **34** was also possible without prior hydrogenation and proceeded smoothly affording bisazide **38** in 54% yield. This sequence could be applied to the methoxylated precursor **16** which afforded product **39** in about 60% yield over two steps.

A second issue concerned DMAS removal and chemoselective azide hydrogenation in the presence of the vinyl double bond. Lindlar hydrogenation of **39** to compound **40** only affected the azide groups retaining the vinyl double bonds. As expected from our model study (Scheme 4), it turned out to be impossible to cleave off the DMAS groups from **40**.

However, we were pleased to observe that by following the reversed order via deprotected bisazide **41**, we were able to synthesize the target compound **42**. As compound **29** (Scheme 3), the diaminated compound **42** exhibits NOESY correlations between the olefinic proton (δ = 6.31 ppm) and one of imidazole protons (δ = 6.78 ppm) and between the methylene protons (δ = 4.11 ppm) and the other imidazole proton (δ = 6.94 ppm). The overall yield of bis(imidazolyl)-propene **42** was 27% over 5 steps.

In summary, we have shown that sp^2-bridged 2-aminoimidazoles can be assembled in a very facile and high yielding manner by double Grignard reaction of metalated imidazoles with saturated esters, followed by dehydration. The presence of nitrile functions or acryl esters leads to competing Grignard reactions, whereas propargyl esters are tolerated. Introduction of the 2-amino groups proceeds via the corresponding azides. We are currently studying further desymmetrization of our building blocks towards the synthesis of dimeric pyrrole-imidazole alkaloids.



Scheme 5. Synthesis of DMAS-protected bis-2-aminoimidazoles via double azidation.

Experimental Section

General: NMR spectra were taken with a Bruker DRX-400 (400.1 MHz for ^{1}H, 100.6 MHz for ^{13}C), a Bruker AV III-400 (400.1 MHz for ^{1}H, 100.6 MHz for ^{13}C) and a Bruker AV II-600 (600.1 MHz for ^{1}H; 150.9 MHz for ^{13}C), referenced to the solvent signal or TMS. All measurements were carried out at 300 K. Mass spectra were obtained with a LTQ Orbitrap Velos, a Thermo Finnigan LTQ FT, a Thermo Finnigan MAT95 and a Finnigan MAT 95 XLT spectrometer. IR spectra were recorded with a Bruker Tensor 27 spectrometer. UV/Vis spectra were measured with a Varian Cary 100 Bio UV/Vis-spectrometer. Melting points were measured with a Büchi 530 melting point apparatus. Chemicals were purchased from commercial suppliers and used without further purification. Silica gel 60 (40–63 μm, Merck) was used for column chromatography.

General Procedure for the Synthesis of Compounds 8–18: To a solution of **6** or **7** (1.00 equiv.) in dry CH_2Cl_2 (40 mL) under Ar atmosphere was added EtMgBr (1.00 equiv.) and the solution was stirred 2 h at room temp. The electrophile (0.45 or 1.00 equiv.) was added and the reaction mixture was stirred at room temp. for 37.5 to 51 h. The reaction was quenched by addition of saturated aqueous NH_4Cl (50 mL). The layers were separated and the water phase was extracted with CH_2Cl_2 (3 to 6 times with 25–70 mL). The combined organic layers were dried with $MgSO_4$ and the solvent was removed under reduced pressure, followed by flash column chromatography.

Bis(1-trityl-1*H*-imidazol-4-yl)methanol (8): From **6** (4.36 g, 10.0 mmol), EtMgBr (3.57 mL, 10.0 mmol, 2.8 M in Et_2O) and methyl formate (0.28 mL, 4.50 mmol) applying the general procedure. Column chromatography [silica, $CHCl_3$, then $CHCl_3$/MeOH (50:1 to 20:1)] afforded **8** (2.89 g, 99%) as colorless solid. Mp 109 °C. R_f ($CHCl_3$/EtOAc, 20:1) = 0.04. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 (d, ^4J = 1.4 Hz, 2 H, NC*H*N), 7.29–7.23 (m, 18 H, phenyl-C*H*), 7.10–7.07 (m, 12 H, phenyl-C*H*), 6.73–6.72 (m, 2 H, NC*H*CN), 5.80 (s, 1 H, C*H*OH), 3.59 (br. s, 1 H, O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.1 (2 C, NCH*C*N), 142.4 (6 C, phenyl-$C_{quart.}$), 138.5 (2 C, N*C*HN), 129.7 (12 C, phenyl-*C*H), 128.0 (12 C, phenyl-*C*H), 127.9 (6 C, phenyl-*C*H), 118.6 (2 C, N*C*HCN), 75.3 (2 C, *C*Ph$_3$), 65.9 (*C*OH) ppm. MS (ESI$^+$): *m*/*z* (%) = 1299 (42) [2M + 2H]$^+$, 649 (100) [M + H]$^+$, 407 (28) [M – CPh$_3$ + 2H]$^+$, 243 (13). HRMS (ESI): calcd. 649.2962 ($C_{45}H_{37}N_4O$); found 649.2963. IR (ATR): $\tilde{\nu}$ = 3346 (w), 1488 (m), 1444 (m), 1188 (m), 1156 (m), 1128 (m), 1086 (m), 1035 (m), 1002 (m), 963 (m), 907 (w), 872 (m), 835 (m), 813 (m), 748 (s), 699 (s), 659 (s), 637 (m) cm^{-1}. UV (CH_3Cl): λ_{max} (lgε) = 290 (2.41), 260 (3.27), 204 nm (3.74).

1,1-Bis(1-trityl-1*H*-imidazol-4-yl)ethanol (9): From **6** (4.36 g, 10.0 mmol), EtMgBr (3.57 mL, 10.0 mmol, 2.8 M in Et_2O) and methyl acetate (0.36 mL, 4.50 mmol) applying the general procedure. Column chromatography [silica, petroleum ether/ethyl acetate (3:1 to 1:1), then $CHCl_3$, then $CHCl_3$/MeOH (50:1 to 20:1)] afforded **9** (2.51 g, 84%) as colorless solid. Mp 137–145 °C. R_f ($CHCl_3$/MeOH, 20:1) = 0.27. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.20 (m, 20 H, phenyl-C*H*, NC*H*N), 7.11–7.04 (m, 12 H, phenyl-C*H*), 6.71 (d, ^4J = 1.3 Hz, 2 H, NC*H*CN), 3.60 (br. s, 1 H, O*H*), 1.85 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.3 (2 C, NCH*C*N), 142.5 (6 C, phenyl-$C_{quart.}$), 138.2 (2 C, N*C*HN), 129.8 (12 C, phenyl-*C*H), 127.9 (18 C, phenyl-*C*H), 117.3 (2 C, N*C*HCN), 75.2 (2 C, *C*Ph$_3$), 70.1 (*C*OH), 28.8 (*C*H$_3$) ppm. MS (ESI$^+$): *m*/*z* (%) = 1328 (28) [2M + 2H]$^+$, 1327 (55) [2M + H]$^+$, 663 (100) [M + H]$^+$, 421 (32) [M – CPh$_3$ + H]$^+$, 243 (18). HRMS (ESI): calcd. 663.3124 ($C_{46}H_{38}N_4O$); found 663.3134. IR (ATR): $\tilde{\nu}$ = 3164 (w), 1490 (m), 1445 (m), 1160 (m), 1140 (m), 1083 (m), 1035 (m), 974 (m), 905 (m), 870 (m), 828 (m), 744 (s), 698 (s), 658 (s), 638 (m) cm^{-1}. UV ($CHCl_3$): λ_{max} (logε) = 254 (4.98), 203 nm (3.42).

1,1-Bis(1-trityl-1*H*-imidazol-4-yl)propan-1-ol (10): From **6** (4.36 g, 10.0 mmol), EtMgBr (3.57 mL, 10.0 mmol, 2.8 M in Et_2O) and methyl propionate (0.43 mL, 4.50 mmol) applying the general procedure. Column chromatography [silica, petroleum ether/ethyl acetate (3:1 to 1:1), then $CHCl_3$, then $CHCl_3$/MeOH (50:1 to 20:1)] afforded **10** (2.83 g, 93%) as colorless solid. Mp 151 °C. R_f ($CHCl_3$/EtOAc, 20:1) = 0.14. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.31 (d, ^4J = 1.5 Hz, 2 H, NC*H*N), 7.30–7.25 (m, 18 H, phenyl-C*H*), 7.12–7.08 (m, 12 H, phenyl-C*H*), 6.80 (d, ^4J = 1.5 Hz, 2 H, NC*H*CN), 3.73 (br. s, 1 H, O*H*), 2.14, (q, ^3J = 7.3 Hz, 2 H, CH_2CH$_3$), 0.82 (t, ^3J = 7.4 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.3 (2 C, NCH*C*N), 142.5 (6 C, phenyl-$C_{quart.}$), 137.9 (2 C, N*C*HN), 129.7 (12 C, phenyl-*C*H), 127.9 (6 C, phenyl-*C*H), 127.9 (12 C, phenyl-*C*H), 117.9 (2 C, N*C*HCN), 75.2 (2 C, *C*Ph$_3$), 73.1 (*C*OH), 34.5 (*C*H$_2$CH$_3$), 8.1 (*C*H$_3$) ppm. MS (ESI$^+$): *m*/*z* (%) = 677 (100) [M + H]$^+$, 435 (27) [M – CPh$_3$ + 2H]$^+$, 243 (31). HRMS

(ESI): calcd. 677.3275 ($C_{47}H_{41}N_4O_1$); found 677.3278. IR (ATR): $\tilde{\nu}$ = 3029 (w), 1491 (m), 1445 (m), 1158 (m), 1135 (m), 1086 (m), 1035 (m), 994 (m), 967 (m), 871 (m), 852 (m), 826 (m), 745 (s), 698 (s), 658 (m), 639 (m) cm^{-1}. UV (MeOH): λ_{max} ($lg\varepsilon$) = 203 nm (5.03).

1,1-Bis(1-trityl-1*H*-imidazol-4-yl)butan-1-ol (11): From **6** (4.36 g, 10.0 mmol), EtMgBr (3.57 mL, 10.0 mmol, 2.8 M in Et_2O) and methyl butyrate (0.36 mL, 4.50 mmol) applying the general procedure. Column chromatography [silica, petroleum ether/ethyl acetate (3:1 to 1:1), then $CHCl_3$, then $CHCl_3$/MeOH (50:1 to 20:1)] afforded **11** (2.80 g, 90%) as colorless solid. Mp 137–138 °C. R_f ($CHCl_3$/MeOH, 20:1) = 0.09. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.24 (m, 20 H, phenyl-C*H*, NC*H*N), 7.13–7.07 (m, 12 H, phenyl-C*H*), 6.79 (d, ^4J = 1.5 Hz, 2 H, NC*H*CN), 3.71 (br. s, 1 H, O*H*), 2.12–2.08 (m, 2 H, COHCH_2), 1.34–1.24 (m, 2 H, C$H_2$$CH_3$), 0.86 (t, ^3J = 7.4 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.6 (2 C, NCH*C*N), 142.5 (6 C, phenyl-$C_{quart.}$), 137.9 (2 C, N*C*HN), 129.8 (12 C, phenyl-*C*H), 127.9 (6 C, phenyl-*C*H), 127.9 (12 C, phenyl-*C*H), 117.7 (2 C, N*C*HCN), 75.2 (2 C, *C*Ph_3), 72.8 (*C*OH), 44.1 (COH*C*H_2), 17.1 (*C*$H_2$$CH_3$), 14.3 (*C*$H_3$) ppm. MS ($ESI^+$): *m*/*z* (%) = 1383 (100) $[2M + 2H]^+$, 691 (38) $[M + H]^+$. HRMS (ESI): calcd. 691.3437 ($C_{48}H_{43}N_4O$); found 691.3453. IR (ATR): $\tilde{\nu}$ = 3346 (w), 2933 (m), 2862 (m), 1445 (m), 1135 (m), 1083 (m), 1036 (m), 1000 (m), 813 (m), 753 (s), 697 (s), 658 (m), 637 (m), 534 (m) cm^{-1}. UV (MeOH): λ_{max} ($\log\varepsilon$) = 203 nm (4.96).

3-(Dibenzylamino)-1,1-bis(1-trityl-1*H*-imidazol-4-yl)propan-1-ol (12): From **6** (4.36 g, 10.0 mmol), EtMgBr (3.33 mL, 10.0 mmol, 3.0 M in Et_2O) and methyl 3-(dibenzylamino)propanoate (1.27 g, 4.50 mmol) applying the general procedure. Column chromatography [silica, petroleum ether/ethyl acetate (3:1 to 1:1), then $CHCl_3$, then $CHCl_3$/MeOH (50:1)] afforded the alcohol **12** (2.75 g, 70%) as colorless solid. Mp 222–223 °C (decomp.). R_f ($CHCl_3$/MeOH, 20:1) = 0.06. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.31 (d, ^4J = 1.5 Hz, 2 H, NC*H*N), 7.27–7.17 (m, 28 H, phenyl-C*H*), 7.09–7.04 (m, 12 H, phenyl-C*H*), 6.77 (d, ^4J = 1.5 Hz, 2 H, NC*H*CN), 3.52 (s, 4 H, NCH_2C), 2.69 (t, ^3J = 5.6 Hz, 2 H, COHCH_2), 2.58 (t, ^3J = 5.4 Hz, 2 H, COHCH_2CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.1 (2 C, NCH*C*N), 142.6 (6 C, phenyl-$C_{quart.}$), 138.3 (2 C, N*C*HN), 137.3 (2 C, phenyl-$C_{quart.}$), 129.8 (12 C, phenyl-*C*H), 129.4 (4 C, phenyl-*C*H), 128.1 (4 C, phenyl-*C*H), 127.9 (12 C, phenyl-*C*H), 127.8 (6 C, phenyl-*C*H), 127.0 (2 C, phenyl-*C*H), 118.4 (2 C, N*C*HCN), 75.1 (2 C, *C*Ph_3), 74.4 (*C*OH), 56.7 (2 C, NCH_2C), 51.0 (COH*C*H_2), 35.0 (COHCH_2*C*H_2) ppm. MS (ESI^+): *m*/*z* (%) = 1745 (26) $[2M + 2H]^+$, 872 (100) $[M + H]^+$. HRMS (ESI): calcd. 872.4323 ($C_{61}H_{54}N_5O$); found 872.4300. IR (ATR): $\tilde{\nu}$ = 3059 (w), 1491 (m), 1445 (m), 1157 (m), 1132 (m), 745 (s), 698 (s), 659 (m), 637 (m) cm^{-1}. UV (MeOH): λ_{max} ($lg\varepsilon$) = 253 (3.73), 203 nm (5.05).

Methyl 3-(2,5-Dimethyl-1*H*-pyrrol-1-yl)propanoate (43): To a solution of methyl 3-aminopropanoate hydrochloride (1.00 g, 7.16 mmol) and KOH (0.38 g, 6.80 mmol) in CH_3CN (35 mL) were added hexane/2,5-dione (0.92 mL, 7.88 mmol) and MeOH (10 mL). The mixture was stirred at room temp. for 20 h before 2 N HCl (100 mL) and Et_2O (200 mL) were added. The layers were separated and the water phase was extracted with Et_2O (2 × 100 mL). The combined organic phases were washed with 2 N HCl (100 mL) and H_2O (100 mL) and dried with $MgSO_4$. After removal of the solvent under reduced pressure, column chromatography [silica, petroleum ether/ethyl acetate (10:1)] afforded **43** (1.10 g, 85%) as colorless oil. R_f (petroleum ether/EtOAc, 10:1) = 0.37. ^1H NMR (400 MHz, $CDCl_3$): δ = 5.71 (s, 2 H, NCC*H*), 4.04–4.00 (m, 2 H, NCH_2), 3.64 (s, 3 H, OCH_3), 2.58–2.54 (m, 2 H, NCH$_2$CH_2), 2.18 (s, 6 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9 (*C*O), 126.6 (2 C, N*C*CH), 105.3 (2 C, NC*C*H), 51.2 (OCH_3), 38.6 (NCH_2), 34.8 (COCH_2), 11.8 (2 C, CH_3) ppm. MS (EI): *m*/*z* (%) = 181 (100) $[M^+]$, 166 (20), 150 (12) $[M\ OMe]^+$, 122 (20) $[M - CO_2Me]^+$, 108 (87), 94 (82) $[C_6H_8N]^+$. HRMS (EI): calcd. 181.1103 ($C_{10}H_{15}NO_2$); found 181.1106. IR (ATR): $\tilde{\nu}$ = 3103 (w), 1734 (s), 1438 (m), 1408 (m), 1374 (m), 1320 (m), 1300 (m), 1250 (m), 1196 (m), 1170 (s), 1074 (m), 1018 (m), 984 (m), 748 (s) cm^{-1}. UV (MeOH): λ_{max} ($lg\varepsilon$) = 291 (1.96), 204 nm (3.92).

3-(2,5-Dimethyl-1*H*-pyrrol-1-yl)-1,1-bis(1-trityl-1*H*-imidazol-4-yl)-propan-1-ol (13): From **6** (2.19 g, 5.00 mmol), EtMgBr (1.70 mL, 5.00 mmol, 3.0 M in Et_2O) and a solution of **43** (922 mg, 5.00 mmol) in dry CH_2Cl_2 (10 mL) which was stirred with 4 Å molecular sieves for 4 h applying the general procedure. Column chromatography (RP18, MeOH/H_2O, 5:1) afforded **13** (1.56 g, 81%) as colorless solid. Mp 196–197 °C. R_f ($CHCl_3$/MeOH, 20:1) = 0.12. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.26 (m, 20 H, phenyl-C*H*, NC*H*N), 7.12–7.08 (m, 12 H, phenyl-C*H*), 6.85 (d, ^4J = 1.5 Hz, 2 H, NC*H*CN), 5.70 (s, 2 H, CH_2NCC*H*), 4.08 (br. s, 1 H, O*H*), 3.79–3.75 (m, 2 H, NCH_2), 2.39–2.34 (m, 2 H, COCH_2), 2.10 (s, 6 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.7 (2 C, NCH*C*N), 142.2 (6 C, phenyl-$C_{quart.}$), 138.2 (2 C, N*C*HN), 129.7 (12 C, phenyl-*C*H), 128.0 (18 C, phenyl-*C*H), 127.5 (2 C, CH_2N*C*CH), 117.5 (2 C, N*C*HCN), 104.6 (2 C, CH_2NC*C*H), 75.3 (2 C, *C*Ph_3), 71.7 (*C*OH), 42.1 (COH*C*H_2), 39.3 (NCH_2), 12.3 (2 C, CH_3) ppm. MS (ESI^+): *m*/*z* (%) = 1541 (40) $[2M + 2H]^+$, 770 (100) $[M + H]^+$, 692 (31), 311 (26). HRMS (ESI): calcd. 770.3853 ($C_{53}H_{48}N_5O$); found 770.3845. IR (ATR): $\tilde{\nu}$ = 3059 (w), 1491 (m), 1445 (m), 1409 (m), 1158 (m), 1133 (m), 1084 (m), 1036 (m), 1001 (m), 872 (m), 828 (m), 744 (s), 698 (s), 659 (s), 638 (m) cm^{-1}. UV (MeOH): λ_{max} ($lg\varepsilon$) = 203 nm (5.01).

4,4′-(1-Hydroxypropane-1,1-diyl)bis(*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide) (14): From **7** (1.90 g, 6.31 mmol), EtMgBr (2.10 mL, 6.31 mmol, 3.0 M in Et_2O) and a solution of methyl propionate (0.27 mL, 2.84 mmol) in dry CH_2Cl_2 (5 mL) which was stirred with molecular sieves (4 Å) for 2 h applying the general procedure. Column chromatography [silica, $CHCl_3$, then $CHCl_3$/MeOH (20:1)] afforded the alcohol **14** (743 mg, 64%) as colorless solid. Mp 162 °C. R_f ($CHCl_3$/MeOH, 20:1) = 0.17. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, ^4J = 1.5 Hz, 2 H, NC*H*N), 7.29 (d, ^4J = 1.4 Hz, 2 H, NC*H*CN), 3.83 (br. s, 1 H, O*H*), 2.86 (s, 12 H, NCH_3), 2.18 (q, ^3J = 7.4 Hz, 2 H, COHCH_2), 0.86 (t, ^3J = 7.4 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.8 (2 C, NCH*C*N), 136.1 (2 C, N*C*HN), 113.9 (2 C, N*C*HCN), 72.7 (*C*OH), 38.2 (4 C, NCH_3), 34.5 (COH*C*H_2), 7.8 (*C*H_3) ppm. MS (ESI^+): *m*/*z* (%) = 429 (100) $[M + Na]^+$. HRMS (ESI): calcd. 429.0985 ($C_{13}H_{22}N_6NaO_5S_2$); found 429.0986. IR (ATR): $\tilde{\nu}$ = 3259 (w), 1472 (m), 1384 (s), 1264 (m), 1174 (s), 1124 (m), 1108 (m), 1088 (m), 1071 (m), 1054 (m), 1010 (m), 987 (m), 955 (s), 910 (m), 858 (m), 847 (m), 720 (s), 617 (m), 595 (s) cm^{-1}. UV (MeOH): λ_{max} ($lg\varepsilon$) = 217 (3.89), 202 nm (3.98).

4,4′-[3-(Dibenzylamino)-1-hydroxypropane-1,1-diyl]bis(*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide) (15): From **7** (3.61 g, 12.0 mmol), EtMgBr (4.00 mL, 12.0 mmol, 3.0 M in Et_2O) and methyl 3-(dibenzylamino)propanoate (750 mg, 2.65 mmol) applying the general procedure. Column chromatography [silica, $CHCl_3$/MeOH (50:1), then $CHCl_3$/MeOH (20:1) and RP18, MeOH/H_2O (1:1), then MeOH/H_2O (2:1), then MeOH] afforded the alcohol **15** (1.15 g, 72%) as colorless solid. Mp 196 °C. R_f (RP18, MeOH/H_2O, 2:1) = 0.04. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, ^4J = 1.5 Hz, 2 H, NC*H*N), 7.34–7.25 (m, 10 H, phenyl-C*H*), 7.00 (d, ^4J = 1.5 Hz, 2 H, NC*H*CN), 3.57 (s, 4 H, CH_2NCH$_2$CH$_2$), 2.78 [s, 12 H, N(CH_3)$_2$], 2.71–2.68 (m, 2 H, CH$_2$NCH_2CH$_2$), 2.56–2.53 (m, 2 H, CH$_2$NCH$_2$CH_2), 1.71 (br. s, 1 H, O*H*) ppm. ^{13}C NMR (100 MHz,

$CDCl_3$): δ = 149.0 (2 C, NCH*C*N), 137.2 (2 C, phenyl-$C_{quart.}$) 136.2 (2 C, N*C*HN), 129.4 (4 C, phenyl-*C*H), 128.4 (4 C, phenyl-*C*H), 127.6 (2 C, phenyl-*C*H), 114.3 (2 C, N*C*HCN), 74.3 (*C*OH), 58.1 (2 C, *C*H_2NCH_2CH_2), 50.2 (COHCH_2*C*H_2), 38.1 [4 C, N(*C*H_3)$_2$], 34.1 (COH*C*H_2) ppm. MS (ESI$^+$): *m*/*z* (%) = 624 (55) [M + Na]$^+$, 602 (100) [M + H]$^+$. HRMS (ESI): calcd. 602.2214 ($C_{27}H_{36}N_7O_5S_2$); found 602.211. IR (ATR): $\tilde{\nu}$ = 3029 (w), 1456 (m), 1388 (m), 1173 (s), 1078 (m), 960 (m), 723 (s), 699 (m), 591 (s) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 203 nm (4.43).

4,4′-(1-Hydroxy-3-methoxypropane-1,1-diyl)bis(*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide) (16): From **7** (3.63 g, 12.1 mmol), EtMgBr (4.02 mL, 12.1 mmol, 3.0 M in Et_2O) and methyl 3-methoxypropanoate (0.64 mL, 5.43 mmol) applying the general procedure. Column chromatography [silica, petroleum ether/ethyl acetate (1:1), then $CHCl_3$, then $CHCl_3$/MeOH (40:1), then $CHCl_3$/MeOH (10:1)] afforded the alcohol **16** (1.68 g, 71%) as colorless solid. Mp 161 °C. R_f ($CHCl_3$/MeOH, 10:1) = 0.10. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, ^4J = 1.5 Hz, 2 H, NC*H*N), 7.29 (d, ^4J = 1.5 Hz, 2 H, NC*H*CN), 3.49 (t, ^3J = 5.6 Hz, 2 H, CH_3OCH_2), 3.29 (s, 3 H, OCH_3), 2.86 [s, 12 H, N(CH_3)$_2$], 2.54 (t, ^3J = 5.7 Hz, 2 H, $CH_3OCH_2CH_2$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.2 (2 C, NCH*C*N), 136.4 (2 C, N*C*HN), 114.2 (2 C, N*C*HCN), 73.3 (*C*OH), 70.0 (O*C*H_2), 58.9 (O*C*H_3), 39.4 (COH*C*H_2), 38.2 [4 C, N(*C*H_3)$_2$] ppm. MS (ESI$^+$): *m*/*z* (%) = 459 (100) [M + Na]$^+$. HRMS (ESI): calcd. 459.1091 ($C_{14}H_{24}N_6NaO_6S_2$); found 459.1091. IR (ATR): $\tilde{\nu}$ = 3233 (w), 1470 (m), 1380 (s), 1268 (m), 1211 (m), 1172 (s), 1117 (m), 1085 (s), 1068 (s), 1004 (m), 954 (s), 928 (m), 845 (m), 722 (s), 643 (m), 620 (m), 592 (s) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 217 (3.89), 202 nm (3.97).

4,4′-[3-(Dimethylamino)-1-hydroxypropane-1,1-diyl]bis(*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide) (17): From **7** (2.11 g, 7.00 mmol), EtMgBr (2.33 mL, 7.00 mmol, 3.0 M in Et_2O) and methyl 3-(dimethylamino)propanoate (413 mg, 3.15 mmol) applying the general procedure. Column chromatography [silica, petroleum ether/ethyl acetate (1:1), then $CHCl_3$, then $CHCl_3$/MeOH/NH_3 (90:10:1), then $CHCl_3$/MeOH/NH_3 (70:10:1)] afforded the alcohol **17** (723 mg, 51%) as colorless oil. R_f ($CHCl_3$/MeOH/NH_3, 70:10:1) = 0.43. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, ^4J = 1.5 Hz, 2 H, NC*H*N), 7.28 (d, ^4J = 0.8 Hz, 2 H, NC*H*CN), 2.86 [s, 12 H, SO_2N(CH_3)$_2$], 2.40 (br. s, 4 H, COHCH_2CH_2), 2.25 [s, 6 H, CH_2N(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.5 (2 C, NCH*C*N), 136.8 (2 C, N*C*HN), 114.7 (2 C, N*C*HCN), 74.8 (*C*OH), 56.6 (N*C*H_2), 45.4 [2 C, CH_2N(CH_3)$_2$], 38.5 [4 C, SO_2N(*C*H_3)$_2$], 35.0 (COH*C*H_2) ppm. MS (ESI$^+$): *m*/*z* (%) = 450 (100) [M + H]$^+$. HRMS (ESI): calcd. 450.1588 ($C_{15}H_{28}N_7O_5S_2$); found 450.1587. IR (ATR): $\tilde{\nu}$ = 3126 (w), 1463 (m), 1418 (m), 1386 (s), 1269 (m), 1171 (s), 1079 (s), 1054 (m), 1004 (m), 960 (s), 839 (m), 754 (m), 722 (s), 587 (s) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 216 (3.86), 202 nm (3.96).

4,4′-[3-(2,5-Dimethyl-1*H*-pyrrol-1-yl)-1-hydroxypropane-1,1-diyl]-bis(*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide) (18): From **7** (602 mg, 2.00 mmol), EtMgBr (0.67 mL, 2.00 mmol, 3.0 M in Et_2O) and a solution of methyl 3-(2,5-dimethyl-1*H*-pyrrol-1-yl)propanoate (163 mg, 0.90 mmol) in dry CH_2Cl_2 (10 mL) which was stirred with molecular sieves (4 Å) for 3.5 h applying the general procedure. Column chromatography [silica, petroleum ether/ethyl acetate (1:1), then $CHCl_3$, then $CHCl_3$/MeOH (20:1)] afforded **18** (341 mg, 76%) as yellow solid. Mp 221 °C (decomp.). R_f ($CHCl_3$/MeOH, 20:1) = 0.40. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, ^4J = 1.4 Hz, 2 H, NC*H*N), 7.30 (d, ^4J = 1.4 Hz, 2 H, NC*H*CN), 5.72 (s, 2 H, CH_2NCC*H*), 4.18 (br. s, 1 H, O*H*), 3.79–3.74 (m, 2 H, NCH_2), 2.86 (s, 12 H, NCH_3), 2.45–2.40 (m, 2 H, COHCH_2), 2.15 (s, 6 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.2 (2 C, NCH*C*N), 136.3 (2 C, N*C*HN), 127.2 (2 C, CH_2N*C*CH), 113.8 (2 C, N*C*HCN), 105.1 (2 C, CH_2NC*C*H), 71.3 (*C*OH), 42.1 (COH*C*H_2), 38.7 (N*C*H_2), 38.2 (4 C, N*C*H_3), 12.2 (2 C, *C*H_3) ppm. MS (ESI$^+$): *m*/*z* (%) = 500 (100) [M + H]$^+$. HRMS (ESI): calcd. 500.1744 ($C_{19}H_{30}N_7O_5S_2$); found 500.1747. IR (ATR): $\tilde{\nu}$ = 3127 (w), 1461 (m), 1416 (m), 1387 (s), 1272 (m), 1172 (s), 1086 (m), 1056 (m), 1005 (m), 960 (m), 837 (m), 724 (s), 620 (m), 590 (s) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 296 (2.85), 203 nm (4.20).

3-Phenyl-1,1-bis(1-trityl-1*H*-imidazol-4-yl)prop-2-yn-1-ol (20): To a solution of **6** (4.36 g, 10.0 mmol) in dry CH_2Cl_2 (40 mL) under Ar atmosphere was added EtMgBr (3.57 mL, 10.0 mmol, 2.8 M in Et_2O) and the solution was stirred 2 h at room temp. **19** (0.66 mL, 4.50 mmol) was added dropwise and the reaction mixture was stirred at room temp. for 45 h. After removal of the solvent under reduced pressure, column chromatography [silica, petroleum ether/ethyl acetate (3:1 to 1:1), then ethyl acetate, then $CHCl_3$, then $CHCl_3$/MeOH (20:1)] afforded **20** (2.69 g, 80%) as colorless solid. Mp 94 °C. R_f ($CHCl_3$/EtOAc, 20:1). = 0.20. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36 (d, ^4J = 1.5 Hz, 2 H, NC*H*N), 7.35–7.32 (m, 2 H, phenyl-C*H*), 7.32–7.25 (m, 18 H, phenyl-C*H*), 7.24–7.20 (m, 3 H, phenyl-C*H*), 7.14–7.08 (m, 12 H, phenyl-C*H*), 6.97 (d, ^4J = 1.5 Hz, 2 H, NC*H*CN), 4.27 (s, 1 H, O*H*) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.0 (2 C, NCH*C*N), 142.4 (6 C, phenyl-$C_{quart.}$), 138.7 (2 C, N*C*HN), 131.9 (2 C, phenyl-*C*H), 129.8 (12 C, phenyl-*C*H), 128.1 (1 C, phenyl-*C*H), 128.0 (18 C, phenyl-*C*H), 127.9 (2 C, phenyl-*C*H), 122.9 (1 C, phenyl-$C_{quart.}$), 118.7 (2 C, N*C*HCN), 90.9 (C≡*C*COH), 84.1 (*C*≡CCOH), 75.4 (2 C, *C*Ph_3), 67.0 (*C*OH) ppm. MS (ESI$^+$): *m*/*z* (%) = 1498 (41) [2M + 2H]$^+$, 749 (100) [M + H]$^+$, 507 (34) [M – CPh_3 + 2H]$^+$, 243 (18). HRMS (ESI): calcd. 749.3280 ($C_{53}H_{41}N_4O$); found 749.3278. IR (ATR): $\tilde{\nu}$ = 3335 (w), 1492 (m), 1446 (m), 1159 (m), 1130 (m), 1037 (m), 1006 (m), 943 (m), 874 (m), 832 (m), 748 (s), 699 (s), 660 (m), 640 (m) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 376 (4.36), 252 (4.29), 243 nm (2.87).

3-Phenyl-1,3-bis(1-trityl-1*H*-imidazol-4-yl)propan-1-one (22): To a solution of **6** (4.36 g, 10.0 mmol) in dry CH_2Cl_2 (40 mL) under Ar atmosphere was added EtMgBr (3.57 mL, 10.0 mmol, 2.8 M in Et_2O) and the solution was stirred for 2 h at room temp. **21** (730 mg, 4.50 mmol) was added and the reaction mixture was stirred at room temp. for 46 h. The reaction was quenched by addition of saturated aqueous NH_4Cl (50 mL). The layers were separated and the organic phase was washed with water (50 mL) and saturated aqueous NH_4Cl (50 mL). The combined water layers were extracted with CH_2Cl_2 (3 × 25 mL) and the combined organic layers were dried with $MgSO_4$. After removal of the solvent under reduced pressure, column chromatography [silica, petroleum ether/ethyl acetate (1:1), then ethyl acetate] afforded **22** (2.71 g, 80%) as colorless solid. Mp 122–124 °C. R_f (EtOAc) = 0.69. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.49 (d, ^4J = 1.4 Hz, 1 H, COCNC*H*), 7.35 (d, ^4J = 1.4 Hz, 1 H, COCC*H*), 7.34–7.18 (m, 23 H, phenyl-C*H*, CH_2CHCNC*H*), 7.16–7.03 (m, 13 H, phenyl-C*H*), 6.62 (dd, ^4J = 1.3 Hz, 1 H, CH_2CHCC*H*), 4.74 (t, ^3J = 7.4 Hz, 1 H, COCH_2C*H*), 3.72 (dd, ^3J = 6.8, ^2J = 16.4 Hz, 1 H, COCH_2CH), 3.56 (dd, ^3J = 6.8, ^2J = 16.4 Hz, 1 H, COCH_2CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 194.5 (*C*O), 144.2 (CH_2CH*C*N), 144.2 (2 C, phenyl-$C_{quart.}$), 142.5 (3 C, phenyl-$C_{quart.}$), 141.7 (3 C, phenyl-$C_{quart.}$), 140.8 (N*C*COC), 139.2 (COC*C*H), 138.5 (CH_2CHCN*C*H), 129.8 (6 C, phenyl-*C*H), 129.7 (6 C, phenyl-*C*H), 128.3 (3 C, phenyl-*C*H), 128.2 (6 C, phenyl-*C*H), 128.2 (3 C, phenyl-*C*H), 128.0 (2 C, phenyl-*C*H), 127.9 (6 C, phenyl-*C*H), 127.9 (2 C, phenyl-*C*H), 126.0 (1 C, phenyl-*C*H), 125.6 (NH*C*NCCOC), 118.3 (CH_2CHC*C*H), 76.0 (*C*Ph_3), 75.1 (*C*Ph_3), 44.8 (CO*C*H_2CH), 40.4 (COCH_2*C*H) ppm. MS (ESI): *m*/*z* (%) = 751 (25) [M + H]$^+$, 509 (9) [M – CPh_3

+ 2H]$^+$, 311 (100) [Tr-imidazole + H]$^+$, 243 (25). HRMS (ESI): calcd. 751.3437 ($C_{53}H_{43}N_4O$); found 751.3455. IR (ATR): $\tilde{\nu}$ = 1673 (m), 1529 (m), 1491 (m), 1445 (m), 1157 (m), 1131 (m), 1036 (m), 932 (m), 745 (s), 699 (s), 659 (m), 638 (m) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 259 (3.14), 203 nm (4.03).

(*Z*)-Methyl 3-amino-3-(1-trityl-1*H*-imidazol-4-yl)acrylate (24): To a solution of **6** (4.36 g, 10.0 mmol, 1.00 equiv.) in dry CH_2Cl_2 (40 mL) under Ar atmosphere was added EtMgBr (3.57 mL, 10.0 mmol, 2.8 M in Et_2O) and the solution was stirred 2 h at room temp. **23** (0.40 mL, 4.50 mmol) was added dropwise and the reaction mixture was stirred at room temp. for 48 h. The reaction was quenched by addition of saturated aqueous NH_4Cl (50 mL). The layers were separated and the organic phase was washed with water (50 mL) and saturated aqueous NH_4Cl (50 mL). The combined water layers were extracted with CH_2Cl_2 (3 × 25 mL) and the combined organic layers were dried with $MgSO_4$. After removal of the solvent under reduced pressure, column chromatography [silica, petroleum ether/ethyl acetate (5:1 to 1:1)] afforded the amine **24** (628 mg, 34%) as colorless solid. Mp 53–55 °C. R_f (petroleum ether/EtOAc, 5:1) = 0.10. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44 (d, ^4J = 1.3 Hz, 1 H, NC*H*N), 7.37–7.31 (m, 9 H, phenyl-C*H*), 7.20 (d, ^4J = 1.4 Hz, 1 H, NC*H*CN), 7.15–7.10 (m, 6 H, phenyl-C*H*), 4.88–4.87 (m, 1 H, COC*H*), 3.65 (s, 3 H, OCH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8 (*C*O), 153.1 (*C*NH$_2$), 141.8 (3 C, phenyl-C_{quart}), 139.0 (N*C*HN), 136.3 (NCH*C*N), 129.7 (6 C, phenyl-*C*H), 128.3 (3 C, phenyl-*C*H), 128.2 (6 C, phenyl-*C*H), 120.3 (N*C*HCN), 78.5 (CO*C*H), 75.9 (*C*Ph$_3$), 50.1 (*C*H$_3$) ppm. MS (ESI$^+$): *m*/*z* (%) = 819 (8) [2M + H]$^+$, 410 (100) [M + H]$^+$, 353 (8), 243 (16). HRMS (ESI): calcd. 410.1863 ($C_{26}H_{24}N_3O_2$); found 410.1866. IR (ATR): $\tilde{\nu}$ = 3476 (w), 3335 (w), 1660 (m), 1602 (m), 1577 (s), 1526 (m), 1491 (m), 1443 (m), 1354 (m), 1302 (m), 1219 (m), 1154 (s), 1087 (m), 1033 (m), 968 (m), 868 (m), 839 (m), 745 (s), 698 (s), 661 (m), 638 (m) cm^{-1}. UV (MeOH): λ_{max} (logε) = 306 (4.23), 237 (3.99), 204 nm (4.71).

Methyl 3-[Bis(*tert*-Butoxycarbonyl)amino]propanoate (25): To a solution of methyl 3-(*tert*-butoxycarbonylamino)propanoate (6.40 g, 31.5 mmol) in CH_3CN (100 mL) was added Boc_2O (14.7 g, 67.4 mmol) and DMAP (385 mg, 3.15 mmol). The mixture was stirred at room temp. for 5 d before water (300 mL) and EtOAc (200 mL) were added. The layers were separated and the organic phase was washed with saturated aqueous NH_4Cl (3 × 100 mL). The combined water layers were extracted with EtOAc (2 × 100 mL) and the combined organic layers were dried with $MgSO_4$. After removal of the solvent under reduced pressure, column chromatography [silica, petroleum ether/ethyl acetate (5:1)] afforded **25** (7.78 g, 81%) as colorless oil. R_f (petroleum ether/EtOAc, 5:1) = 0.55. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.89 (t, ^3J = 7.4 Hz, 2 H, NCH_2), 3.68 (s, 3 H, OCH_3), 2.61 (t, ^3J = 7.5 Hz, 2 H, COCH_2), 1.42 (s, 18 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.6 (*C*O), 152.1 (2 C, *C*O), 82.4 [2 C, *C*(CH$_3$)$_3$], 51.5 (O*C*H$_3$), 42.1 (N*C*H$_2$), 33.5 (CO*C*H$_2$), 27.9 [6 C, C(*C*H$_3$)$_3$] ppm. MS (EI): *m*/*z* (%) = 303 (0.02) [M$^+$], 147 (14) [M – Boc – C$_4$H$_9$]$^+$, 104 (16) [M – 2Boc + H]$^+$, 57 (100) [C$_4$H$_9$]$^+$. HRMS (EI): calcd. 303.1682 ($C_{14}H_{25}NO_6$); found 303.1662. IR (ATR): $\tilde{\nu}$ = 2981 (w), 1738 (s), 1695 (m), 1442 (m), 1394 (m), 1350 (s), 1323 (m), 1254 (m), 1229 (m), 1169 (s), 1135 (s), 1106 (s), 1042 (m), 854 (m), 777 (m) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 203 nm (3.42).

***Tert*-Butyl 3-Hydroxy-3,3-bis(1-trityl-1*H*-imidazol-4-yl)propylcarbamate (27) and 1,3-bis(1-trityl-1*H*-imidazol-4-yl)propan-1-one (26):** To a solution of 6 (4.36 g, 10.0 mmol) in dry CH_2Cl_2 (40 mL) under Ar atmosphere was added EtMgBr (3.33 mL, 10.0 mmol, 3.0 M in Et_2O) and the solution was stirred 2.5 h at room temp. 25 (1.36 g, 4.50 mmol) was added and the reaction mixture was stirred at room temp. for 48 h. The reaction was quenched by addition of saturated aqueous NH_4Cl (50 mL). The layers were separated and the organic phase was washed with water (50 mL) and saturated aqueous NH_4Cl (50 mL). The combined water layers were extracted with CH_2Cl_2 (3 × 25 mL) and the combined organic layers were dried with $MgSO_4$. After removal of the solvent under reduced pressure, column chromatography [silica, petroleum ether/ethyl acetate (3:1 to 1:1), then $CHCl_3$, then $CHCl_3$/MeOH (50:1 to 20:1)] afforded alcohol 27 (2.18 g, 61%) as colorless solid and ketone 26 (0.374 mg, 0.554 mmol, 12%) as yellow oil. 27: Mp 185 °C. R_f ($CHCl_3$/MeOH, 20:1) = 0.16. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (d, ^4J = 1.3 Hz, 2 H, NC*H*N), 7.30–7.20 (m, 18 H, phenyl-C*H*), 7.11–7.08 (m, 12 H, phenyl-C*H*), 6.83 (d, ^4J = 1.3 Hz, 2 H, NC*H*CN), 5.44 (br. s, 1 H, N*H*), 4.67 (br. s, 1 H, O*H*), 3.23–3.15 (m, 2 H, NHCH_2), 2.38 (t, ^3J = 6.1 Hz, 2 H, COHCH_2), 1.39 (s, 9 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.8 (*C*O), 145.7 (2 C, NCH*C*N), 142.2 (6 C, phenyl-$C_{quart.}$), 138.0 (2 C, N*C*HN), 129.5 (12 C, phenyl-*C*H), 127.8 (12 C, phenyl-*C*H), 127.8 (6 C, phenyl-*C*H), 117.8 (2 C, N*C*HCN), 78.2 [*C*(CH$_3$)$_3$], 75.1 (2 C, *C*Ph$_3$), 72.7 (*C*OH), 40.7 (C*C*H$_2$), 36.6 (NH*C*H$_2$), 28.3 (3 C, *C*H$_3$) ppm. MS (ESI$^+$): *m*/*z* (%) = 1585 (54) [2M + 2H]$^+$, 1477 (18) [2M – Boc – H$_2$O + 2H]$^+$, 792 (100) [M + H]$^+$, 243 (57). HRMS (ESI): calcd. 792.3914 ($C_{52}H_{50}N_5O_3$); found 792.3920. IR (ATR): $\tilde{\nu}$ = 3422 (w), 1705 (m), 1492 (m), 1445 (m), 1364 (m), 1229 (m), 1159 (m), 1133 (m), 1085 (m), 1036 (m), 1000 (m), 906 (m), 870 (m), 828 (m), 745 (s), 699 (s), 659 (m), 638 (m) cm^{-1}. UV (MeOH): λ_{max} (logε) = 250 (3.70), 204 nm (5.00). 26: R_f ($CHCl_3$/MeOH, 50:1) = 0.13. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 (d, ^4J = 1.4 Hz, 1 H, NC*H*N), 7.43 (d, ^4J = 1.4 Hz, 1 H, NC*H*CN), 7.34–7.27 (m, 19 H, phenyl-C*H*, NC*H*N), 7.14–7.08 (m, 12 H, phenyl-C*H*), 6.60 (d, ^4J = 1.3 Hz, 1 H, NC*H*CN), 3.33–3.29 (m, 2 H, COCH_2), 3.00–2.96 (m, 2 H, COCH$_2$CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.7 (*C*O), 142.4 (3 C, phenyl-C_{quart}), 141.6 (3 C, phenyl-C_{quart}), 140.7 (*C*CO), 140.6 (COCH$_2$CH$_2$*C*), 139.2 (N*C*HN), 138.1 (N*C*HN), 129.7 (6 C, phenyl-*C*H), 129.5 (6 C, phenyl-*C*H), 128.3 (3 C, phenyl-*C*H), 128.2 (6 C, phenyl-*C*H), 127.8 (6 C, phenyl-*C*H), 127.8 (3 C, phenyl-*C*H), 125.4 (N*C*HCN), 117.8 (N*C*HCN), 75.9 (*C*Ph$_3$), 74.9 (*C*Ph$_3$), 38.2 (CO*C*H$_2$), 22.9 (COCH$_2$*C*H$_2$) ppm. MS (ESI$^+$): *m*/*z* (%) = 1350 (68) [2M + 2H]$^+$, 675 (100) [M + H]$^+$. HRMS (ESI): calcd. 675.3118 ($C_{47}H_{38}N_4O$); found 675.3105. IR (ATR): $\tilde{\nu}$ = 1674 (m), 1570 (m), 1530 (m), 1491 (m), 1445 (s), 1157 (m), 1132 (s), 1087 (m), 1036 (m), 747 (s), 699 (s), 658 (s), 638 (m) cm^{-1}. UV (MeOH): λ_{max} (logε) = 255 (4.12), 204 nm (4.97).

***tert*-Butyl 3,3-Bis(1-trityl-1*H*-imidazol-4-yl)allylcarbamate (28):** To a solution of **27** (300 mg, 0.38 mmol) in dry CH_2Cl_2 (15 mL) was added MsCl (0.12 mL, 1.52 mmol) and Et_3N (0.32 mL, 2.27 mmol). The mixture was stirred at room temp. for 7 h before DBU (0.23 mL, 1.52 mmol, 4.00 equiv.) was added. The mixture was stirred for another 16 h and then quenched with aqueous NH_4Cl solution (25 mL). The mixture was extracted with diethyl ether (6 × 25 mL). The combined ether extracts were dried with $MgSO_4$ and then concentrated under reduced pressure. Column chromatography [silica, $CHCl_3$/MeOH (30:1) and RP18, MeOH/H_2O/0.5% TFA, 5:1] afforded **28** (225 mg, 76%) as colorless solid. Mp 214 °C. R_f (RP18, MeOH/H_2O, 5:1) = 0.12. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 (d, ^4J = 1.4 Hz, 1 H, NC*H*N), 7.38 (d, ^4J = 1.2 Hz, 1 H, NC*H*N), 7.34–7.18 (m, 18 H, phenyl-C*H*), 7.15–7.04 (m, 12 H, phenyl-C*H*), 6.72 (br. s, 1 H, NC*H*CN), 6.60 (d, ^4J = 1.2 Hz, 1 H, NC*H*CN), 6.52 (t, ^3J = 7.5 Hz, 1 H, C*H*CH$_2$), 5.61 (t, ^3J = 5.1 Hz, 1 H, N*H*), 4.03 (dd, ^3J = 6.4, 7.3 Hz, 2 H, CH_2), 1.42 (s, 9 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.8 (*C*O), 142.2 (3 C, phenyl-$C_{quart.}$), 142.1 (3 C, phenyl-$C_{quart.}$),

141.4 (NCH*C*N), 138.6 (N*C*HN), 138.3 (NCH*C*N), 138.1 (N*C*HN), 129.5 (*C*CHCH$_2$), 129.4 (6 C, phenyl-*C*H), 129.4 (6 C, phenyl-*C*H), 127.9 (6 C, phenyl-*C*H), 127.9 (6 C, phenyl-*C*H), 127.8 (3 C, phenyl-*C*H), 127.8 (3 C, phenyl-*C*H), 123.4 (*C*HCH$_2$), 121.4 (N*C*HCN), 119.7 (N*C*HCN), 78.4 (*C*CH$_3$), 75.2 (*C*Ph$_3$), 75.1 (*C*Ph$_3$), 38.5 (NH*C*H$_2$), 28.4 (3 C, *C*H$_3$) ppm. MS (ESI$^+$): *m*/*z* (%) = 1549 (32) [2M + 2H]$^+$, 1450 (26) [2M – Boc + 4H]$^+$, 774 (100) [M + H]$^+$, 675 (20) [M Boc + 2H]$^+$. HRMS (ESI): calcd. 774.3808 ($C_{52}H_{48}N_5O_2$); found 774.3823. IR (ATR): $\tilde{\nu}$ = 1705 (m), 1491 (m), 1445 (m), 1229 (m), 1159 (m), 1133 (m), 1086 (m), 1037 (m), 868 (m), 831 (m), 745 (s), 699 (s), 658 (s), 639 (m) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 255 (4.19), 204 nm (4.98).

3,3-Bis(1*H*-imidazol-4-yl)prop-2-en-1-amine (29): To a solution of **28** (294 mg, 0.38 mmol) in MeOH (5 mL) was added H$_2$O/0.5% TFA (10 mL) and the mixture was stirred at room temp. for 5 h. After removal of the solvent under reduced pressure, column chromatography (RP18, MeOH/H$_2$O/0.5% TFA, 1:2) afforded **29** (71.0 mg, 99%) as colorless oil. R_f (RP18, MeOH/H$_2$O, 1:2) = 0.15. ^{1}H NMR (400 MHz, CD$_3$OD): δ = 8.89 (d, ^4J = 1.3 Hz, 1 H, NC*H*N), 8.75 (d, ^4J = 1.4 Hz, 1 H, NC*H*N), 7.74 (d, ^4J = 1.3 Hz, 1 H, NC*H*CN), 7.59 (d, ^4J = 1.4 Hz, 1 H, NC*H*CN), 6.56 (t, ^3J = 7.1 Hz, 1 H, C*H*CH$_2$), 3.88 (d, ^3J = 7.1 Hz, 2 H, CHC*H*$_2$) ppm. ^{13}C NMR (100 MHz, CD$_3$OD): δ = 137.3 (N*C*HN), 137.1 (N*C*HN), 133.0 (NCH*C*N), 129.2 (NCH*C*N), 127.6 (*C*HCH$_2$), 122.0 (*C*CHCH$_2$), 121.8 (N*C*HCN), 119.9 (N*C*HCN), 39.0 (*C*H$_2$) ppm. MS (ESI$^+$): *m*/*z* (%) = 190 (100) [M + H]$^+$, 165 (16), 105 (2). HRMS (ESI): calcd. 190.1087 ($C_9H_{12}N_5$); found 190.1068. IR (ATR): $\tilde{\nu}$ = 3118 (m), 3016 (m), 2836 (m), 2634 (m), 1660 (s), 1429 (m), 1178 (s), 1124 (s), 833 (s), 796 (s), 720 (s), 625 (m), 597 (m) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 202 (3.55), 261 nm (3.56).

2-Azido-*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide (30): To a solution of *N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide (1.75 g, 10.0 mmol) in dry THF (100 mL) under argon atmosphere at –78 °C was added *n*BuLi (4.80 mL, 12.0 mmol, 2.5 M solution in hexane) and the solution was stirred 1 h at room temp. TosN$_3$ (1.97 g, 10.0 mmol) was added dropwise and the reaction mixture was allowed to reach room temp. The reaction mixture was stirred for additional 18 h and the reaction was quenched by addition of saturated aqueous NH$_4$Cl (50 mL) and H$_2$O (60 mL). The layers were separated and the water layer was extracted with CH$_2$Cl$_2$ (5 × 100 mL). The combined organic layers were dried with MgSO$_4$ and the solvent was removed under reduced pressure. Column chromatography [silica, petroleum ether/EtOAc (5:1), then petroleum ether/EtOAc (3:1)] afforded the azide **30** (859 mg, 40%) as yellow solid. Mp 75 °C. R_f (petroleum ether/EtOAc, 3:1) = 0.19. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.12 (d, ^3J = 1.8 Hz, 1 H, NCN$_3$NCHC*H*), 6.84 (d, ^3J = 1.8 Hz, 1 H, NCN$_3$NC*H*), 2.98 [s, 6 H, N(C*H*$_3$)$_2$] ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 140.4 (*C*N$_3$), 126.3 (NCN$_3$NC*H*), 119.5 (NCN$_3$NCH*C*H), 38.4 [2 C, N(*C*H$_3$)$_2$] ppm. MS (ESI$^+$): *m*/*z* (%) = 278 (100), 253 (55), 239 (39) [M + Na]$^+$, 217 (65) [M + H]$^+$, 194 (96). HRMS (ESI): calcd. 217.0502 ($C_5H_9N_6O_2S$); found 217.0509. IR (ATR): $\tilde{\nu}$ = 2166 (s), 2145 (m), 1524 (m), 1493 (m), 1388 (s), 1306 (m), 1280 (m), 1244 (m), 1166 (s), 1138 (s), 1103 (m), 1035 (m), 966 (s), 909 (m), 720 (s), 678 (s), 570 (s), 555 (s) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 259 (3.90), 202 nm (3.77).

2-Amino-*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide (31): Azide **30** (288 mg, 1.33 mmol) was reduced to the corresponding amine by dissolving it in EtOH (15 mL) in presence of Lindlar catalyst (Pd/CaCO$_3$ with 5% Pb, 5% Pd, 566 mg, 0.266 mmol Pd) and stirring the reaction mixture at room temp. under 1 atm H$_2$ (balloon) overnight. The reaction mixture was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified by column chromatography (silica, CHCl$_3$/MeOH, 30:1) to give amine **31** (210 mg, 83%) as a colorless solid. Mp 139 °C. R_f (CHCl$_3$/MeOH, 30:1) = 0.09. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.77 (d, ^3J = 1.9 Hz, 1 H, NCNH$_2$NCHC*H*), 6.59 (d, ^3J = 2.0 Hz, 1 H, NCNH$_2$NC*H*), 5.43 (br. s, 2 H, NH$_2$), 2.92 [s, 6 H, N(CH$_3$)$_2$] ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 148.9 (*C*NH$_2$), 125.8 (NCNH$_2$N*C*H), 113.6 (NCNH$_2$NCH*C*H), 38.9 [2 C, N(*C*H$_3$)$_2$] ppm. MS (ESI$^+$): *m*/*z* (%) = 191 (100) [M + H]$^+$. HRMS (ESI): calcd. 191.0597 ($C_5H_{11}N_4O_2S$); found 191.0605. IR (ATR): $\tilde{\nu}$ = 3455 (w), 3117 (m), 1639 (m), 1562 (m), 1453 (m), 1373 (m), 1268 (m), 1188 (m), 1160 (s), 1136 (m), 1046 (s), 963 (s), 758 (m), 704 (s), 593 (s) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 232 (3.76), 201 nm (3.53).

2-Azido-1*H*-imidazole (32): To a solution of the protected azide **30** (57.0 mg, 0.264 mmol) in MeOH (2 mL) was added an excess of concd. HCl (5 mL) and the reaction mixture was refluxed for 2 h. The reaction mixture was concentrated and the residue was purified by column chromatography (silica, CHCl$_3$/MeOH/NH$_3$, 40:10:1) to give the deprotected azide **32** (28.0 mg, 97%) as a colorless solid. Mp 135–136 °C (decomp.). R_f (CHCl$_3$/MeOH, 20:1) = 0.43. ^{1}H NMR (400 MHz, CD$_3$OD): δ = 6.87 (s, 2 H, NHCHC*H*N, NHC*H*CHN) ppm. $'^{13}$C NMR (100 MHz, CD$_3$OD): δ = 142.1 (*C*N$_3$), 122.2 (2C, NH*C*HCHN, NHCH*C*HN) ppm. MS (EI): *m*/*z* (%) = 171 (6), 155 (7), 109 (64) [M$^+$], 91 (18), 83 (27), 81 (35), 54 (100), 53 (31). HRMS (EI): calcd. 109.0383 ($C_3H_3N_5$); found 109.0380. IR (ATR): $\tilde{\nu}$ = 2741 (m), 2123 (s), 1578 (m), 1485 (s), 1305 (m), 1231 (m), 1150 (m), 1097 (m), 989 (m), 861 (m), 829 (m), 775 (m), 736 (s), 690 (s), 539 (m) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 254 (3.83), 202 nm (3.68).

4,4′-(Prop-1-ene-1,1-diyl)bis(*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide) (34): To a solution of **14** (1.47 g, 3.62 mmol) in dry CH$_2$Cl$_2$ (45 mL) was added MsCl (2.24 mL, 29.0 mmol) and Et$_3$N (6.00 mL, 43.4 mmol). The mixture was stirred at room temp. for 7.5 h before DBU (4.33 mL, 29.0 mmol) was added. The mixture was stirred for another 5 h and then quenched with aqueous NH$_4$Cl solution (50 mL). The mixture was extracted with CH$_2$Cl$_2$ (3 × 30 mL). The combined organic layers were dried with MgSO$_4$ and then concentrated under reduced pressure. Column chromatography [silica, CHCl$_3$/MeOH (50:1)] afforded **34** (1.39 g, 99%) as yellow oil. R_f (CHCl$_3$/MeOH, 50:1) = 0.09. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.96 (d, ^4J = 1.3 Hz, 1 H, NC*H*N), 7.85 (d, ^4J = 1.4 Hz, 1 H, NC*H*N), 7.30 (d, ^4J = 1.4 Hz, 1 H, NC*H*CN), 7.24 (d, ^4J = 1.3 Hz, 1 H, NC*H*CN), 6.80 (q, ^3J = 7.3 Hz, 1 H, C*H*CH$_3$), 2.91 [s, 6 H, N(C*H*$_3$)$_2$], 2.86 [s, 6 H, N(C*H*$_3$)$_2$], 1.97 (d, ^3J = 7.3 Hz, 3 H, CHC*H*$_3$) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 142.9 (NCH*C*N), 139.1 (NCH*C*N), 136.0 (N*C*HN), 135.8 (N*C*HN), 127.2 (*C*HCH$_3$), 124.9 (*C*CHCH$_3$), 116.6 (NC*H*CN), 114.0 (NC*H*CN), 38.0 [2 C, N(*C*H$_3$)$_2$], 38.0 [2 C, N(*C*H$_3$)$_2$], 15.0 (CH*C*H$_3$) ppm. MS (ESI$^+$): *m*/*z* (%) = 411 (74) [M + Na]$^+$, 399 (100), 389 (62) [M + H]$^+$. HRMS (ESI): calcd. 411.0880 ($C_{13}H_{20}N_6NaO_4S_2$); found 411.0880. IR (ATR): $\tilde{\nu}$ = 1462 (m), 1419 (m), 1386 (s), 1267 (m), 1206 (m), 1171 (s), 1115 (m), 1077 (s), 1004 (m), 960 (s), 934 (m), 835 (m), 722 (s), 592 (s) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 230 (4.14), 202 nm (4.19).

4,4′-(Propane-1,1-diyl)bis(*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide) (36): Alkene **34** (407 mg, 1.05 mmol) was reduced to the corresponding alkane by dissolving it in EtOH (5 mL) in presence of Pd/C (Pd/C with 5% Pd, 782 mg, 0.37 mmol Pd) and stirring the reaction mixture at room temp. under 1 atm H$_2$ (balloon) overnight. The reaction mixture was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified by column chromatography (silica, CHCl$_3$/MeOH, 40:1) to give alkane

36 (317 mg, 77%) as a colorless solid. Mp 135 °C. R_f ($CHCl_3$/MeOH, 20:1) = 0.21. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, ^4J = 1.4 Hz, 2 H, NC*H*N), 7.08 (dd, ^4J = 1.2, 0.6 Hz, 2 H, NC*H*CN), 3.83 (t, ^3J = 7.5 Hz, 1 H, C*H*CH_2), 2.85 [s, 12 H, N(CH_3)$_2$], 2.06 (quint, ^3J = 7.4 Hz, 2 H, CHC*H*$_2$), 0.90 (^3J = 7.3 Hz, 3 H, C*H*$_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.4 (2 C, NCH*C*N), 136.3 (2 C, N*C*HN), 114.2 (2 C, N*C*HCN), 40.3 (*C*HCH$_2$), 38.2 (CH*C*H$_2$), 27.5 [4 C, N(*C*H$_3$)$_2$], 12.1 (*C*H$_3$) ppm. MS (ESI$^+$): *m*/*z* (%) = 391 (100) [M + H]$^+$. HRMS (ESI): calcd. 391.1217 ($C_{13}H_{23}N_6O_4S_2$); found 391.1214. IR (ATR): $\tilde{\nu}$ = 1378 (s), 1270 (m), 1212 (w), 1168 (s), 1091 (m), 1072 (s), 1005 (m), 957 (s), 759 (m), 721 (s), 592 (s) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 274 (3.06), 219 (3.88), 202 nm (3.97).

4,4′-(Propane-1,1-diyl)bis(2-azido-*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide) (37): To a solution of **36** (260 mg, 0.666 mmol) in dry THF (15 mL) under argon atmosphere at –78 °C was added *n*BuLi (0.930 mL, 2.33 mmol, 2.5 M solution in hexane) and the solution was stirred 1.25 h at room temp. $TosN_3$ (486 mg, 2.46 mmol) was added dropwise and the reaction mixture was allowed to reach room temp. The reaction mixture was stirred for additional 2 h and the reaction was quenched by addition of saturated aqueous NH_4Cl (20 mL) and H_2O (10 mL). The reaction mixture was extracted with EtOAc (3 × 60 mL). The combined organic layers were dried with $MgSO_4$ and the solvent was removed under reduced pressure. Column chromatography [silica, hexane/EtOAc (3:1)] afforded the diazide **37** (125 mg, 40%) as brown oil. R_f (hexane/EtOAc, 1:1) = 0.37. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.91 (d, ^4J = 0.7 Hz, 2 H, NC*H*CN), 3.57 (t, ^3J = 7.4 Hz, 1 H, C*H*CH_2), 2.98 [s, 12 H, N(CH_3)$_2$], 1.94 (quint, ^3J = 7.4 Hz, 2 H, CHC*H*$_2$), 0.90 (t, ^3J = 7.3 Hz, 3H CH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.8 (2 C, NCH*C*N), 139.4 (2 C, *C*N$_3$), 115.8 (2 C, CN$_3$N*C*HC), 40.4 (*C*HCH$_2$), 38.4 [4 C, N(*C*H$_3$)$_2$], 26.8 (CH*C*H$_2$), 12.1 (*C*H$_3$) ppm. MS (ESI$^+$): *m*/*z* (%) = 967 (100) [2M + Na]$^+$, 945 (24) [2M + H]$^+$, 495 (25) [M + Na]$^+$, 473 (36) [M + H]$^+$. HRMS (ESI): calcd. 473.1245 ($C_{13}H_{21}N_{12}O_4S_2$); found 473.1243. IR (ATR): $\tilde{\nu}$ = 2140 (s), 1510 (m), 1386 (s), 1238 (m), 1171 (m), 1126 (m), 1072 (m), 966 (s), 856 (m), 723 (s), 577 (s) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 265 (4.17), 203 nm (4.12).

4,4′-(Prop-1-ene-1,1-diyl)bis(2-azido-*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide) (38): To a solution of **34** (426 mg, 1.10 mmol) in dry THF (10 mL) under argon atmosphere at –78 °C was added *n*BuLi (1.54 mL, 3.85 mmol, 2.5 M solution in hexane) and the solution was stirred 1 h at room temp. $TosN_3$ (803 mg, 4.07 mmol) was added dropwise and the reaction mixture was allowed to reach room temp. The reaction mixture was stirred for additional 2 h and the reaction was quenched by addition of saturated aqueous NH_4Cl (20 mL) and H_2O (10 mL). The reaction mixture was extracted with EtOAc (3 × 60 mL). The combined organic layers were dried with $MgSO_4$ and the solvent was removed under reduced pressure. Column chromatography [silica, hexane/EtOAc (3:1)] afforded the diazide **38** (284 mg, 54%) as brown oil. R_f (hexane/EtOAc, 3:1) = 0.65. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.10 (s, 1 H, NC*H*CN), 7.06 (s, 1 H, NC*H*CN), 6.70 (q, ^3J = 7.3 Hz, 1 H, C*H*CH_3), 3.03 [s, 6 H, N(CH_3)$_2$], 2.97 [s, 6 H, N(CH_3)$_2$], 1.95 (d, ^3J = 7.3 Hz, 3 H, CHC*H*$_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.9 (*C*N$_3$), 139.7 (*C*N$_3$), 138.4 (NCH*C*N), 134.7 (NCH*C*N), 127.7 (*C*HCH$_3$), 124.3 (*C*CHCH$_3$), 118.4 (NC*H*CN), 115.8 (NC*H*CN), 38.5 [2 C, N(*C*H$_3$)$_2$], 38.5 [2 C, N(*C*H$_3$)$_2$], 15.2 (CH*C*H$_3$) ppm. MS (ESI$^+$): *m*/*z* (%) = 471 (100) [M + H]$^+$. HRMS (ESI): calcd. 471.1088 ($C_{13}H_{19}N_{12}O_4S_2$); found 471.1085. IR (ATR): $\tilde{\nu}$ = 2141 (s), 1511 (m), 1420 (m), 1389 (s), 1239 (m), 1173 (s), 1130 (s), 1076 (s), 967 (s), 871 (m), 724 (s), 663 (m), 575 (s) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 251 (4.30), 201 nm (4.24).

4,4′-(3-Methoxyprop-1-ene-1,1-diyl)bis(*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide) (35): To a solution of **16** (1.66 g, 3.80 mmol) in dry CH_2Cl_2 (40 mL) was added MsCl (2.35 mL, 30.4 mmol) and Et_3N (6.34 mL, 45.6 mmol). The mixture was stirred at room temp. for 6 h before DBU (4.54 mL, 30.4 mmol) was added. The mixture was stirred for another 16 h and then quenched with aqueous NH_4Cl solution (50 mL). The mixture was extracted with CH_2Cl_2 (4 × 35 mL). The combined organic layers were dried with $MgSO_4$ and then concentrated under reduced pressure. Column chromatography [silica, $CHCl_3$ then $CHCl_3$/MeOH (40:1)] afforded **35** (1.56 g, 98%) as colorless solid. Mp 136 °C. R_f ($CHCl_3$/MeOH, 15:1) = 0.21. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, ^4J = 1.3 Hz, 1 H, NC*H*N), 7.89 (d, ^4J = 1.4 Hz, 1 H, NC*H*N), 7.44 (d, ^4J = 1.4 Hz, 1 H, NC*H*CN), 7.37 (d, ^4J = 1.9 Hz, 1 H, NC*H*CN), 6.74 (t, ^3J = 6.6 Hz, 1 H, C*H*CH_2), 4.27 (d, ^3J = 6.6 Hz, 2 H, CHC*H*$_2$), 3.38 (s, 3 H, OC*H*$_3$), 2.92 [s, 6 H, N(CH_3)$_2$], 2.87 [s, 6 H, N(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.0 (NCH*C*N), 138.6 (NCH*C*N), 136.0 (N*C*HN), 135.9 (N*C*HN), 127.7 (*C*HCH$_2$), 126.7 (*C*CHCH$_2$), 117.1 (NC*H*CN), 115.2 (NC*H*CN), 69.2 (O*C*H$_2$), 57.8 (O*C*H$_3$), 37.9 [2 C, N(*C*H$_3$)$_2$], 37.9 [2 C, N(*C*H$_3$)$_2$] ppm. MS (ESI$^+$): *m*/*z* (%) = 419 (100) [M + H]$^+$, 387 (72) [M – OMe]$^+$, 171 (20). HRMS (ESI): calcd. 419.1166 ($C_{14}H_{23}N_6O_5S_2$); found 419.1164. IR (ATR): $\tilde{\nu}$ = 1463 (m), 1419 (m), 1387 (s), 1269 (m), 1172 (s), 1076 (s), 1005 (m), 959 (s), 915 (m), 832 (m), 722 (s), 589 (s) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 233 (4.11), 202 nm (4.15).

4,4′-(3-Methoxyprop-1-ene-1,1-diyl)bis(2-azido-*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide) (39): To a solution of **35** (800 mg, 1.91 mmol) in dry THF (60 mL) under argon atmosphere at –78 °C was added *n*BuLi (2.68 mL, 6.69 mmol, 2.5 M solution in hexane) and the solution was stirred 2.5 h at room temp. $TosN_3$ (1.39 g, 7.07 mmol) was added dropwise and the reaction mixture was allowed to reach room temp. The reaction mixture was stirred for additional 3 h and the reaction was quenched by addition of saturated aqueous NH_4Cl (20 mL) and H_2O (10 mL). The reaction mixture was extracted with EtOAc (3 × 60 mL). The combined organic layers were dried with $MgSO_4$ and the solvent was removed under reduced pressure. Column chromatography [silica, $CHCl_3$, then $CHCl_3$/MeOH (3:1) and RP18, H_2O/MeOH (1:1), then H_2O/MeOH (1:3)] afforded the diazide **39** (586 mg, 61%) as brown oil. R_f ($CHCl_3$/EtOAc, 3:1) = 0.27. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.20 (s, 1 H, NC*H*CN), 7.18 (s, 1 H, NC*H*CN), 6.66 (t, ^3J = 6.6 Hz, 1 H, CC*H*CH_2), 4.27 (d, ^3J = 6.6 Hz, 2 H, CCHC*H*$_2$), 3.39 (s, 3 H, OC*H*$_3$), 3.03 [s, 6 H, N(CH_3)$_2$], 2.99 [s, 6 H, N(CH_3)$_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.1 (*C*N$_3$), 139.9 (*C*N$_3$) 137.5 (NCH*C*N), 134.3 (NCH*C*N), 128.3 (C*C*HCH$_2$), 125.8 (*C*CHCH$_2$), 118.8 (N*C*HCN), 117.0 (N*C*HCN), 69.5 (O*C*H$_2$), 58.1 (O*C*H$_3$), 38.5 [2 C, N(*C*H$_3$)$_2$], 38.4 [2 C, N(*C*H$_3$)$_2$] ppm. MS (ESI$^+$): *m*/*z* (%) = 1023 (4) [2M + Na]$^+$, 523 (100) [M + Na]$^+$, 467 (63), 277 (44). HRMS (ESI): calcd. 523.1013 ($C_{14}H_{20}N_{12}NaO_5S_2$); found 523.1016. IR (ATR): $\tilde{\nu}$ = 2144 (s), 1513 (m), 1392 (s), 1177 (m), 1132 (m), 1076 (s), 967 (m), 870 (w), 725 (s), 666 (m), 576 (s) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 255 (4.22), 203 nm (4.16).

4,4′-(3-Methoxyprop-1-ene-1,1-diyl)bis(2-amino-*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide) (40): Alkene **39** (56.0 mg, 0.112 mmol) was reduced to the corresponding alkane by dissolving it in EtOH (15 mL) in presence of Lindlar catalyst (Pd/$CaCO_3$ with 5% Pb, 5% Pd, 96 mg, 0.045 mmol Pd) and stirring the reaction mixture at room temp. under 1 atm H_2 (balloon) overnight. The reaction mixture was filtered through a pad of celite and the filtrate was concentrated. The residue was purified by column chromatography (silica, $CHCl_3$/MeOH/NH_3, 70:10:1) to give **40** (28.0 mg, 56%) as a yellow oil. R_f ($CHCl_3$/MeOH/NH_3, 70:10:1) = 0.44. ^1H NMR (600 MHz, $CDCl_3$): δ = 6.85 (s, 1 H, NC*H*CN), 6.84 (s, 1 H, NC*H*CN), 6.50

(t, ^3J = 6.8 Hz, 1 H, CC*H*CH$_2$), 5.13 (br. s, 4 H, N*H*$_2$), 4.21 (d, ^3J = 6.8 Hz, 2 H, CCHC*H*$_2$), 3.35 (s, 3 H, OC*H*$_3$), 2.97 [s, 6 H, N(C*H*$_3$)$_2$], 2.92 [s, 6 H, N(C*H*$_3$)$_2$] ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 147.8 (*C*NH$_2$), 147.5 (*C*NH$_2$), 137.0 (NCH*C*N), 133.6 (NCH*C*N), 127.6 (*C*CHCH$_2$), 126.3 (C*C*HCH$_2$), 112.9 (N*C*HCN), 111.6 (N*C*HCN), 69.5 (O*C*H$_2$), 58.0 (O*C*H$_3$), 38.7 [2 C, N(*C*H$_3$)$_2$], 38.7 [2 C, N(*C*H$_3$)$_2$] ppm. MS (ESI$^+$): *m*/*z* (%) = 471 (100) [M + Na]$^+$, 449 (53) [M + H]$^+$, 417 (80) [M – OCH$_3$]$^+$. HRMS (ESI): calcd. 449.1384 ($C_{14}H_{25}N_8O_5S_2$); found 449.1380. IR (ATR): $\tilde{\nu}$ = 3441 (w), 2922 (w), 1636 (m), 1379 (m), 1266 (w), 1172 (m), 1053 (m), 964 (m), 717 (s), 600 (s) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 260 (3.85), 213 (4.17), 203 nm (4.23).

4,4′-(3-Methoxyprop-1-ene-1,1-diyl)bis(2-azido-1*H*-imidazole) (41): To a solution of the protected azide **39** (396.0 mg, 0.791 mmol) in MeOH (10 mL) was added an excess of concd. HCl (5 mL) and the reaction mixture was refluxed for 3 h. The reaction mixture was concentrated and the residue was purified by column chromatography (silica, $CHCl_3$/MeOH/NH_3, 90:10:1) to give the deprotected azide **41** (163.0 mg, 72%) as a colorless solid. R_f ($CHCl_3$/MeOH/NH_3, 90:10:1) = 0.34. ^{1}H NMR (400 MHz, CD_3OD): δ = 6.91 (s, 1 H, NHC*H*), 6.73 (s, 1 H, NHC*H*), 6.28 (br. s, 1 H, CC*H*), 4.16 (d, ^3J = 4.5 Hz, 2 H, C*H*$_2$), 3.33 (s, 3 H, OC*H*$_3$) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 144.1 (*C*N$_3$), 142.5 (*C*N$_3$), 130.5 (NHCH*C*N), 127.3 (*C*CHCH$_2$), 127.2 (NHCH*C*N), 124.3 (C*C*HCH$_2$), 116.8 (NH*C*HCN), 115.5 (NH*C*HCN), 70.7 (*C*H$_2$), 58.2 (O*C*H$_3$) ppm. MS (ESI$^+$): *m*/*z* (%) = 309 (100) [M + Na]$^+$, 595 (28) [2M + Na]$^+$. HRMS (ESI): calcd. 309.0931 ($C_{10}H_{10}N_{10}NaO$); found 309.0930. IR (ATR): $\tilde{\nu}$ = 3133 (w), 2124 (s), 1524 (m), 1498 (w), 1459 (w), 1148 (m), 1076 (m), 771 (m) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 272 (4.23), 202 nm (4.04).

4,4′-(3-Methoxyprop-1-ene-1,1-diyl)bis(1*H*-imidazol-2-amine) (42): Diazide **41** (137.0 mg, 0.479 mmol) was dissolved in MeOH (5 mL) in presence of Lindlar catalyst (Pd/$CaCO_3$ with 5% Pb, 5% Pd, 102 mg, 0.048 mmol Pd). After stirring at room temp. under 1 atm H_2 for 4 h, the reaction mixture was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified by column chromatography (RP18, MeOH/H_2O/0.5% TFA, 1:6) to give diamine **42** (97.0 mg, 86%) as a yellow oil. R_f (RP18, MeOH/H_2O, 1:6) = 0.50. ^{1}H NMR (600 MHz, CD_3OD): δ = 6.94 (s, 1 H, NH$_2$CNC*H*), 6.78 (s, 1 H, NH$_2$CNHC*H*), 6.31 (t, ^3J = 6.6 Hz, 1 H, C*H*CH$_2$OCH$_3$), 4.11 (d, ^3J = 6.6 Hz, 2 H, C*H*$_2$OCH$_3$), 3.36 (s, 3 H, OC*H*$_3$) ppm. ^{13}C NMR (150 MHz, CD_3OD): δ = 149.9 (*C*NH$_2$), 149.4 (*C*NH$_2$), 129.7 (*C*HCH$_2$OCH$_3$), 127.5 (CH$_2$CH*C*), 121.7 (CH$_2$CH*C*C), 120.5 (CH$_2$CH*C*C), 115.3 (NH$_2$CN*C*H), 113.6 (NH$_2$CNH*C*H), 69.7 (*C*H$_2$OCH$_3$), 58.6 (O*C*H$_3$) ppm. MS (ESI$^+$): *m*/*z* (%) = 235 (13) [M + H]$^+$, 203 (100), 201 (30). HRMS (ESI): calcd. 235.1302 ($C_{10}H_{15}N_6O$); found 235.1302. IR (ATR): $\tilde{\nu}$ = 3153 (m), 1669 (s), 1181 (s), 1129 (s), 837 (m), 799 (m), 720 (m) cm^{-1}. UV (MeOH): λ_{max} (lgε) = 354 (2.97), 265 (3.48), 203 nm (3.76).

Supporting Information (see also the footnote on the first page of this article)**:** NMR spectra of compounds **8**–**18**, **20**, **22**, **24**–**32**, **34**–**43**, NOESY spectra of compounds **29**, **42**.

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[1] A. Al-Mourabit, P. Potier, *Eur. J. Org. Chem.* **2001**, 237–243.
[2] Reviews on the synthesis of the pyrrole-imidazole alkaloids: a) H. Hoffmann, T. Lindel, *Synthesis* **2003**, 1753–1783; b) D. E. N. Jacquot, T. Lindel, *Curr. Org. Chem.* **2005**, *9*, 1551–1565; c) S. M. Weinreb, *Nat. Prod. Rep.* **2007**, *24*, 931–948; d) B. Forte, B. Malgesini, C. Piutti, F. Quartieri, A. Scolaro, G. Papeo, *Mar. Drugs* **2009**, *7*, 705–753.
[3] a) T. Lindel, H. Hoffmann, M. Hochgürtel, J. R. Pawlik, *J. Chem. Ecol.* **2000**, *26*, 1477–1496; b) U. Bickmeyer, C. Drechsler, M. Köck, M. Assmann, *Toxicon* **2004**, *44*, 45–51.
[4] T. E. Ballard, J. J. Richards, A. Aquino, C. S. Reed, C. Melander, *J. Org. Chem.* **2009**, *74*, 1755–1758 and references cited therein.
[5] T. Endo, M. Tsuda, T. Okada, S. Mitsuhashi, H. Shima, K. Kikuchi, Y. Mikami, J. Fromont, J. Kobayashi, *J. Nat. Prod.* **2004**, *67*, 1262–1267.
[6] J. Appenzeller, S. Tilvi, M.-T. Martin, J.-F. Gallard, H. El-bitar, E. Tran Huu Dau, C. Debitus, D. Laurent, C. Moriou, A. Al-Mourabit, *Org. Lett.* **2009**, *11*, 4874–4877.
[7] A. Arrki, M. Tsuda, T. Kubota, Y. Mikami, J. Fromont, J. Kobayashi, *Org. Lett.* **2007**, *9*, 2369–2371.
[8] a) R. Sivappa, N. M. Hernandez, Y. He, C. J. Lovely, *Org. Lett.* **2007**, *9*, 3861–3864; b) D. P. O'Malley, K. Li, M. Maue, A. L. Zografos, P. S. Baran, *J. Am. Chem. Soc.* **2007**, *129*, 4762–4775; c) D. P. O′Malley, J. Yamaguchi, I. S. Young, I. B. Seiple, P. S. Baran, *Angew. Chem. Int. Ed.* **2008**, *47*, 3581–3583; d) S. Su, I. B. Seiple, I. S. Young, P. S. Baran, *J. Am. Chem. Soc.* **2008**, *130*, 16490–16491.
[9] a) S. Urban, P. A. Leone, A. R. Carrol, G. A. Fechner, J. Smith, J. N. A. Hooper, R. J. Quinn, *J. Org. Chem.* **1999**, *64*, 731–735; b) S. Nishimura, S. Matsunaga, M. Shibazaki, K. Suzuki, K. Furihata, R. W. M. van Soest, N. Fusetani, *Org. Lett.* **2003**, *5*, 2255–2257; c) A. Grube, S. Immel, P. S. Baran, M. Köck, *Angew. Chem. Int. Ed.* **2007**, *46*, 6721–6724.
[10] C. Pöverlein, N. Jacobi, T. Lindel, *Synthesis* **2007**, 3620–3626.
[11] M. R. Bhandari, R. Sivappa, C. J. Lovely, *Org. Lett.* **2009**, *11*, 1535–1538.
[12] a) R. M. Turner, S. D. Lindell, S. V. Ley, *J. Org. Chem.* **1991**, *56*, 5739–5740; b) R. M. Turner, S. V. Ley, S. D. Lindell, *Synlett* **1993**, 748–750; c) D. S. Carver, S. D. Lindell, E. A. Saville-Stones, *Tetrahedron* **1997**, *42*, 14481–14496; d) R. H.-J. Butz, S. D. Lindell, *J. Org. Chem.* **2002**, *67*, 2699–2701; e) M. Abarbri, F. Dehmel, P. Knochel, *Tetrahedron Lett.* **1999**, *40*, 7449–7453; f) F. Dehmel, M. Abarbri, P. Knochel, *Synlett* **2000**, 345–346; g) M. Abarbri, J. Thibonnet, L. Bérillon, F. Dehmel, M. Rottländer, P. Knochel, *J. Org. Chem.* **2000**, *65*, 4618–4634; h) P. Knochel, W. Dohle, N. Gommermann, F. Kneisel, F. Kopp, T. Korn, I. Sapountzis, V. A. Vu, *Angew. Chem. Int. Ed.* **2003**, *42*, 4302–4320; i) C. J. Lovely, H. du, R. Sivappa, M. R. Bhandari, Y. He, H. V. R. Dias, *J. Org. Chem.* **2007**, *72*, 3741–3749; j) C. J. Lovely, H. Du, H. V. R. Dias, *Org. Lett.* **2001**, *3*, 1319–1322.
[13] M. P. Groziak, L. Wei, *J. Org. Chem.* **1991**, *56*, 4296–4300.
[14] R. Breslow, J. T. Hunt, R. Smiley, T. Tarnowski, *J. Am. Chem. Soc.* **1983**, *105*, 5337–5342.
[15] A. R. Katritzky, J. J. Slawinski, F. J. Brunner, *J. Chem. Soc. Perkin Trans. 1* **1989**, 1139–1145.
[16] Y. Hari, S. Obika, M. Sakaki, K. Morio, Y. Yamagata, T. Imanishi, *Tetrahedron* **2002**, *58*, 3051–3063.
[17] a) J. Volkman, K. M. Nicholas, *Org. Lett.* **2004**, *6*, 4301–4302; b) L. Zhou, K. M. Nicholas, *Inorg. Chem.* **2008**, *47*, 4356–4367.
[18] M. C. Jetter, R. E. Boyd, A. B. Reitz, *Org. Prep. Proced. Int.* **1996**, *28*, 709–710.
[19] R. Aslanian, M. W. Mutahi, N.-Y. Shih, K. D. McCormick, J. J. Piwinski, P. C. Ting, M. M. Albanese, M. Y. Berlin, X. Zhu, S.-C. Wong, S. B. Rosenblum, Y. Jiang, R. West, S. She,

S. M. Williams, M. Bryant, J. A. Hey, *Bioorg. Med. Chem. Lett.* **2002**, *12*, 937–941.

[20] J. P. Collman, M. Zhong, Z. Wang, *Org. Lett.* **1999**, *1*, 949–951.

[21] R. E. Boyd, C. R. Rasmussen, J. B. Press, R. B. Raffa, E. E. Codd, C. D. Connelly, Q. S. Li, R. P. Martinez, M. A. Lewis, H. R. Almond, A. B. Reitz, *J. Med. Chem.* **2001**, *44*, 863–872.

[22] K. L. Kirk, *J. Heterocycl. Chem.* **1985**, *22*, 57–59.

[23] L. Bhagavatula, R. H. Premchandran, D. J. Plata, S. A. King, H. E. Morton, *Heterocycles* **2000**, *53*, 729–732.

[24] a) S. P. Breukelman, G. D. Meakins, M. D. Tirel, *J. Chem. Soc., Chem. Commun.* **1982**, *14*, 800–801; b) B. L. Chenard, *J. Org. Chem.* **1984**, *49*, 1224–1227.

[25] G. Breckle, K. Polborn, T. Lindel, *Z. Naturforsch., B: Chem. Sci.* **2003**, *58*, 451–456.

[26] a) S. Daninos-Zeghal, A. Al-Mourabit, A. Ahond, C. Poupat, P. Potier, *Tetrahedron* **1997**, *53*, 7605–7614; b) T. Lindel, M. Hochgürtel, *Tetrahedron Lett.* **1998**, *39*, 2541–2544; c) T. Lindel, M. Hochgürtel, *J. Org. Chem.* **2000**, *65*, 2806–2809.

[27] a) I. Kawasaki, N. Sakaguchi, N. Fukushima, N. Fujioka, F. Nikaido, M. Yamashita, S. Ohta, *Tetrahedron Lett.* **2002**, *43*, 4377–4380; b) I. Kawasaki, N. Sakaguchi, A. Khadeer, M. Yamashita, S. Ohta, *Tetrahedron* **2006**, *62*, 10182–10192.

[28] S. Mukherjee, R. Sivappa, M. Yousufuddin, C. J. Lovely, *Synlett* **2010**, 817–821.

[29] a) A. Batch, R. H. Dodd, *J. Org. Chem.* **1998**, *63*, 872–877; b) T. Ankner, G. Hilmersson, *Org. Lett.* **2009**, *11*, 503–506.

[30] T. Lindel, G. Breckle, M. Hochgürtel, C. Volk, A. Grube, M. Köck, *Tetrahedron Lett.* **2004**, *45*, 8149–8152.

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