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Modular Synthesis of Triazole-Containing Triaryl α-Helix Mimetics

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Dedicated to Professor Henning Hopf on the occasion of his 70th birthday

Keywords: Helical structures / Peptidomimetics / Click chemistry / Nitrogen heterocycles / Protein-protein interactions

We describe novel scaffold designs for nonpeptidic α-helix mimetics. The tricyclic scaffolds contain triazoles and reproduce amino acid side chains *i*, *i*+3, and *i*+7. The three different scaffolds are synthetically readily accessible, allow the introduction of further substituents to increase the versatility, and are suitable for library design. A modular synthesis route using Cu^{I}- and Ru^{II}-catalyzed azide–alkyne [3+2] cycloadditions as central steps was developed. To demonstrate the methodology, we have prepared a library of compounds containing all three scaffolds.

Introduction

It is still a challenge to mimic an extended region of a protein surface defined by secondary structure motifs. Small mimetics with geometries reproducing α-helix or β-turn conformations have been successfully developed. α-Helical regions play critical roles in many protein–protein interactions; the difficulty of developing such mimetics lies in the extended region of two to four turns of a helix that is involved in the interaction. Structural mimetics have to display the side-chain functionalities in the same spatial orientation – in terms of distances and angular relationships – as α-helixes do. Typically, one face of a helix interacts with the protein through amino acid side chains in the positions *i*, *i*+3 or *i*+4, *i*+7, and *i*+10 or *i*+11.[1] Small organic scaffolds can replace the peptide backbone and orient the side chains for recognition. A variety of terphenyl-like structures, many containing heterocycles, has recently been developed, largely due to the efforts of Hamilton and coworkers.[2] Some of these have been shown to disrupt protein interactions successfully. However, the synthesis of many of the scaffolds is elaborate and not ideally suited to the incorporation of chemical diversity.

Here we describe a new class of helix mimetics that is synthetically readily accessible through incorporation of one or two triazole rings into the scaffold design.[3] Two triazole-phenyl-triazole (**A**, **B**) and a phenyl-triazole-phenyl (**C**) core system were developed (Scheme 1, below). Four lowest-energy conformations differing in relative energies by less than 2.5 kJ mol^{-1} were calculated for the scaffolds **A**, **B**, and **C** by density functional methods (B3LYP, 6-31G**, Spartan program package; see the Supporting Information for data). In one of these conformations the scaffold side chains match the separations and relative orientations of the key positions *i*, *i*+3, and *i*+7 of an idealized peptide α-helix very well, as shown in Figure 1.

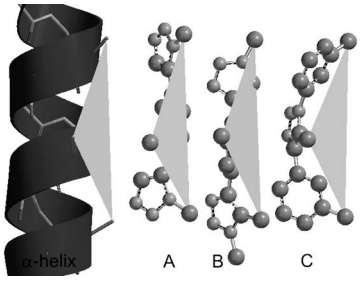

Figure 1. Orientation of the *i*, *i*+3, and *i*+7 residues in an idealized α-helix and comparison of their separations and relative orientations with the residues in the scaffolds **A**, **B**, and **C**. The triangles connect the residues to allow direct comparison of relative separations and orientations.

Retrosynthetically, we envisioned that the triazoles would be synthesized through Cu^{I}- or Ru^{II}-catalyzed [3+2] cycloadditions between azides and terminal alkynes (Scheme 1).[4] It was thought that, by starting from 4-iodoanilines, the requisite 1,4-dialkynyl-substituted benzene intermediates could be produced through Sonogashira coupling reactions, with the alkynes containing orthogonal protecting groups to allow for cleanly sequential cycloadditions. For the scaffold **C**, the alkynes would be obtained in a Colvin rearrangement from the according aldehyde.

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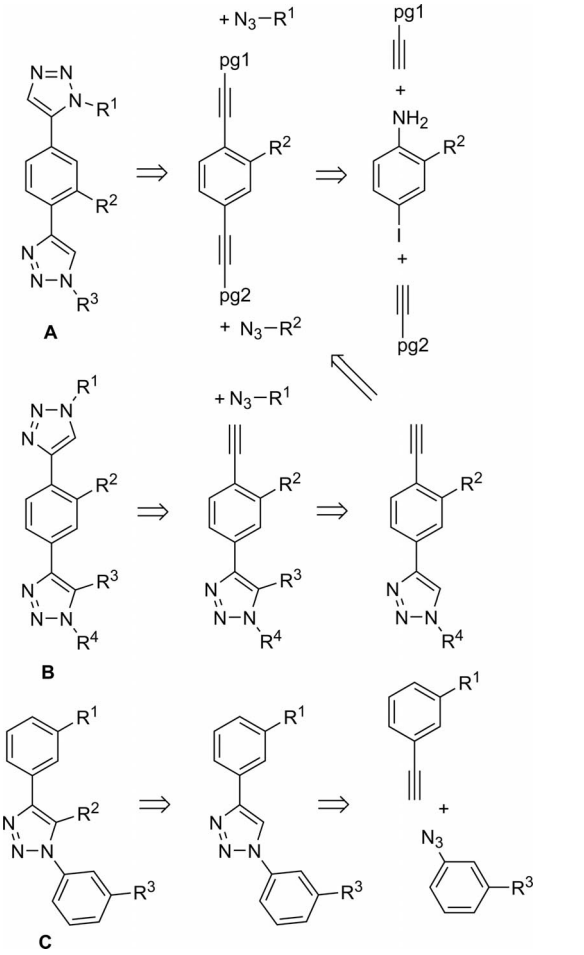


Scheme 1. Retrosynthetic approach to the scaffolds **A**, **B**, and **C**.

To demonstrate the synthesis routes, a small library containing compounds with all three scaffolds was synthesized. The individual scaffolds have distinct attributes. The scaffold **A**, for example, can be obtained by a very short synthesis through regioisomeric click reactions yielding the desired geometrical arrangement. The scaffold **B** allows the introduction of an additional substituent capable of influencing biophysical properties, of extending the binding motif to a fourth side chain in position *i*+10, or of linking two scaffolds together. Figure 2 illustrates these specific options in the case of the scaffold **B**. In the scaffold **C**, the building blocks containing the different side-chain substituents are combined in the final synthesis steps, which is advantageous for library syntheses.

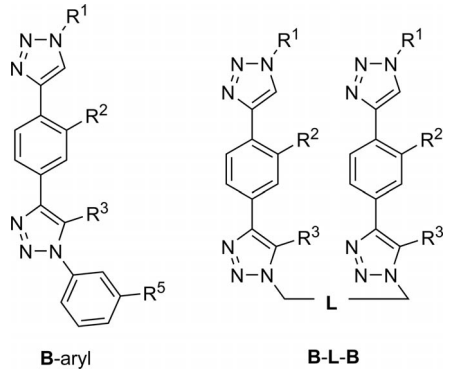


Figure 2. Extended binding motif of the scaffold **B** (left) and two helix mimetics connected by the linker **L** (right).

Results and Discussion

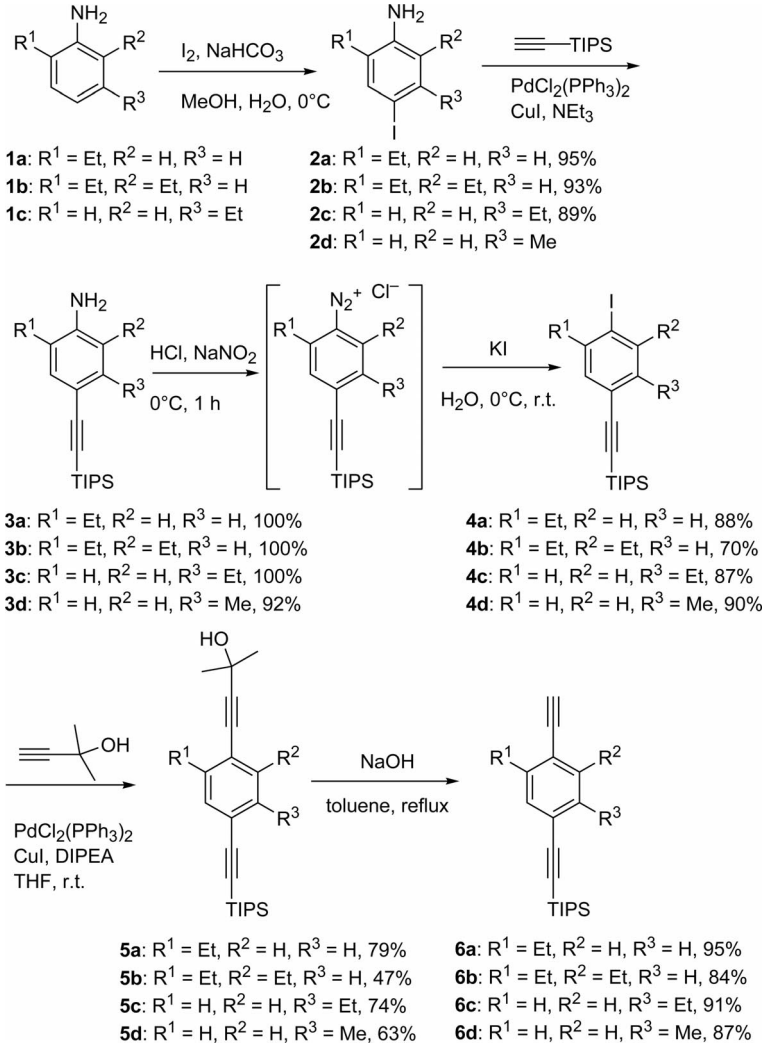
Synthesis of the 1,4-Dialkynylbenzene Intermediates

Synthesis of the 1,4-dialkynylbenzene intermediates for scaffolds **A** and **B** first entailed the selective 4-iodination of commercially available aniline derivatives by a known literature procedure (Scheme 2).[5] The aniline derivatives **1a**–**c** were thus treated with aqueous sodium hydrogencarbonate solutions and molecular iodine at 0 °C, which afforded **2a**–**c** in high yields (89–95%). The alkyne substituents were introduced through Pd-catalyzed Sonogashira reactions[6] in triethylamine. Triisopropylsilyl-protected acetylene was chosen as the first alkyne and was coupled to **2a**–**c** and to commercially available 4-iodo-3-methylaniline (**2d**). This gave the 4-alkynylanilines **3a**–**d** in quantitative yields in almost all cases. The next step was the transformation of the anilines into the iodoarenes **4a**–**d**. This was accomplished through two-step Sandmeyer-type reactions.[7] Firstly, the anilines were transformed with sodium nitrite into diazonium salts; these were found to be unstable above 0 °C. Accordingly, they were directly iodinated with potassium iodide without intermediate isolation. This two-step sequence proceeded with good yields (70–90%). Subsequent Sonogashira couplings finally concluded the syntheses of the 1,4-dialkynylbenzene intermediates **5a**–**d**. Here, the couplings were carried out with 2-methylbut-3-yn-2-ol[8] to ensure that the two alkynyl substituents in the products bore orthogonal protecting groups. Next, the alkynols were deprotected by heating at reflux with sodium hydroxide in toluene. Elimination of acetone gave the 1,4-dialkynyl-substituted benzenes **6a**–**d**, each with one deprotected alkynyl group, in good yields (84–95%).

Synthesis of Azides

For the subsequent [3+2] cycloadditions a sublibrary of azides was synthesized (Figure 3).

3-Chloropropan-1-ol (**14**) was treated with *tert*-butyl dicarbonate (Boc_2O) and magnesium perchlorate[9] to form the *tert*-butyl ether. This chloro-substituted ether was then transformed into the azide **7** by treatment with sodium azide in DMSO at 45 °C.[10] The overall yield for the two steps was 76% (Scheme 3). The azides **8**, **10**,[11] **11**,[12] and **13**[13] were prepared from the corresponding bromides by the same general procedure.



Scheme 2. Synthesis of the 1,4-dialkynylbenzene intermediates **6a**–**d**. Compound **2d** was purchased.

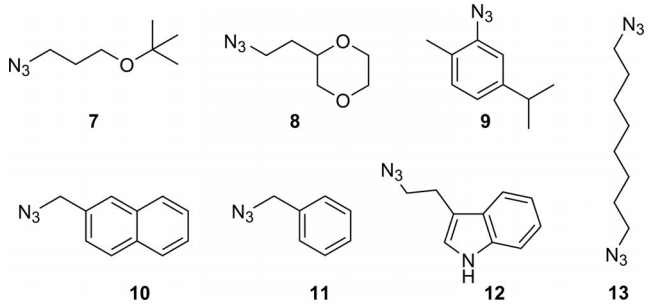
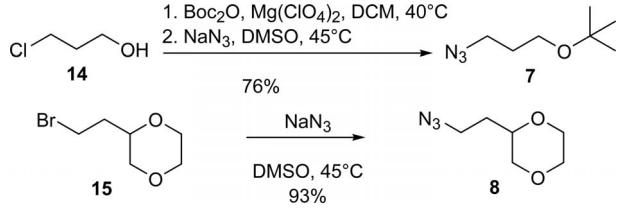
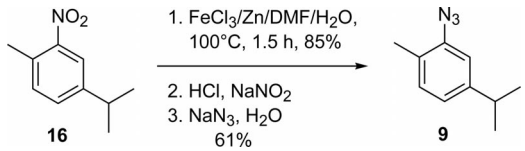


Figure 3. Synthesized azides for subsequent cycloaddition.

The azide **12** (Figure 3) was prepared by a diazo transfer reaction with use of commercially available tryptamine as starting material.[14] 2-Azido-4-isopropyl-1-methylbenzene (**9**, Scheme 4) was synthesized in a two-step procedure. Firstly, commercially available 2-nitro-*p*-cymene (**16**) was reduced to its corresponding aniline derivative by treatment with a ferric chloride/zinc/dimethyl formamide/H_2O system.[15] The aniline derivative was then treated with hydrochloric acid and sodium nitrite in an ice/salt bath. The reaction mixture was neutralized with sodium acetate, and the azide was generated by addition of sodium azide.[16] This reaction proceeded through the formation of the diazonium intermediate with an overall yield of 52% for these two steps.



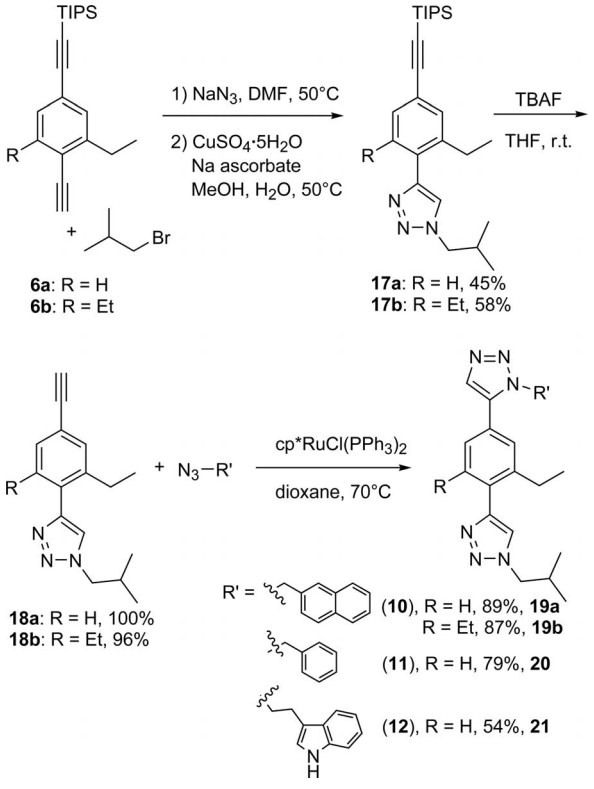
Scheme 3. Synthesis of the azides **7** and **8**.



Scheme 4. Synthesis of the azide **9**.

Scaffold A

The synthesis of compounds containing the scaffold **A** proceeded through the 1,4-dialkynylbenzene intermediates **6a** and **6b**, starting with the two-step syntheses of the 1,4-substituted 1,2,3-triazoles **17a** and **17b** (Scheme 5). In these Cu^{I}-catalyzed [3+2] cycloadditions, the *i*+7 side-chain residues were introduced. Firstly, isobutyl azide was generated from its corresponding bromide and sodium azide in DMF at 50 °C in a sealed flask for 15 h. In the next step, the alkyne, sodium ascorbate, $CuSO_4·5H_2O$, and methanol were added directly to the reaction mixtures. The cycloadditions yielded **17a** and **17b**. The triisopropylsilyl-protected alkynyl groups were deprotected with TBAF to form the unprotected alkynes **18a** and **18b**, which could then be used for the final cycloadditions. The top triazole ring in each case carries the substituent *i*. It is a 1,5-substituted triazole, formed through Ru^{II}-catalyzed [3+2] cycloadditions[17] between each alkyne and the azides **10**, **21**, and **12**; cp*$RuCl(PPh_3)_2$ was used as catalyst, in dioxane as solvent. The reactions went to completion on heating to 70 °C for 24 h, and the products **19a**, **19b**, **20**, and **21** were formed with good to moderate yields.

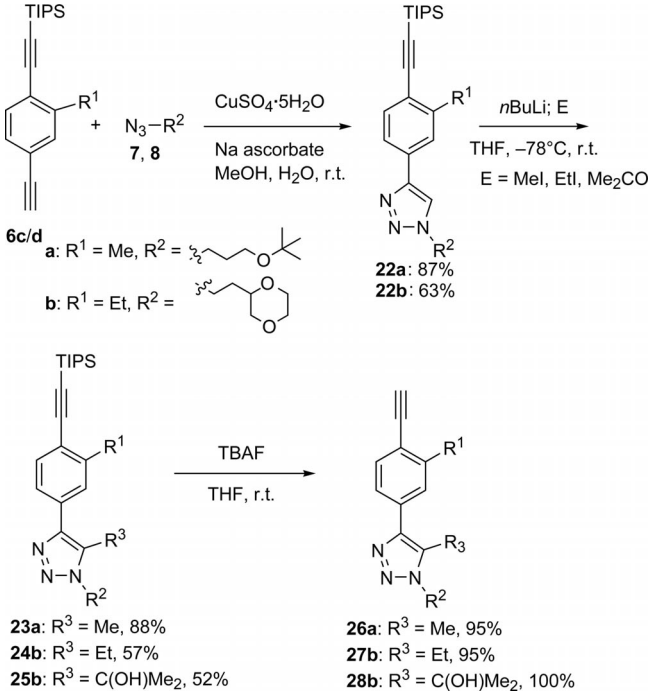


Scheme 5. Synthesis of compounds with the scaffold **A**.

Scaffold B

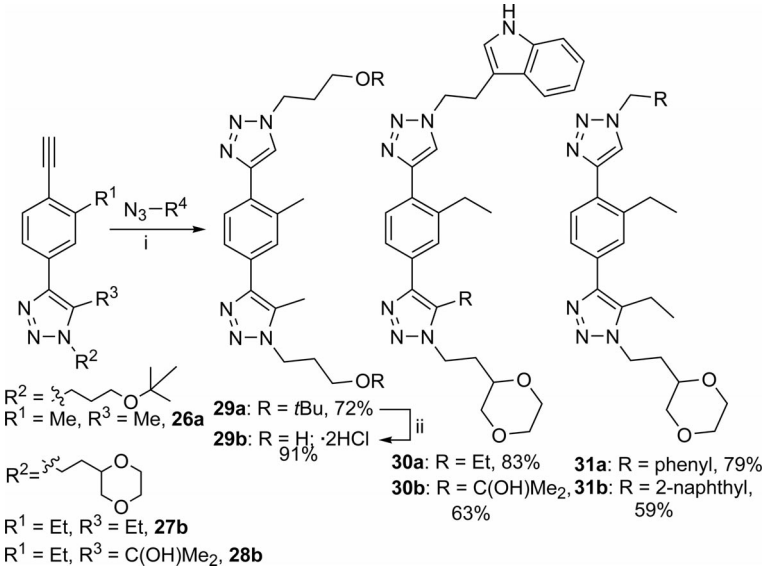
The synthesis of compounds possessing the general structure of the scaffold **B**, starting from the monoprotected 1,4-dialkynylbenzenes, required: (1) [3+2] cycloaddition to form the bottom triazole, (2) introduction of the R^3 substituent, (3) deprotection of the top alkynyl substituent, and (4) second cycloaddition to form the top triazole ring and at the same time to introduce the R^1 substituent.

Cu^{I}-catalyzed [3+2] cycloadditions[18] between the terminal alkynes **6c** and **6d** and the azides **7** or **8** selectively formed the 1,4-disubstituted triazoles **22a** and **22b** (Scheme 6). The azides each contain the additional R^4 substituent that is present in this scaffold. For this position we chose residues that should increase the polarity of the final molecules: a protected primary alcohol and a 1,4-dioxane. The reactions were carried out with $CuSO_4·5H_2O$ and sodium ascorbate as reducing agent. Next, the triazoles **22a** and **22b** were deprotonated at the 5-positions in their triazole rings with *n*BuLi. Addition of the electrophile methyl iodide or ethyl iodide resulted in alkylation, producing **23a** and **24b**, respectively.[19] The use of acetone as electrophile gave the tertiary alcohol **25b**. After this introduction of the *i*+7 substituent, the TIPS-protected alkynyl group was deprotected with TBAF solution to yield **26a**, **27b**, and **28b** in high 95–100% yields.



Scheme 6. Synthesis and modification of the bottom ring in the scaffold **B**.

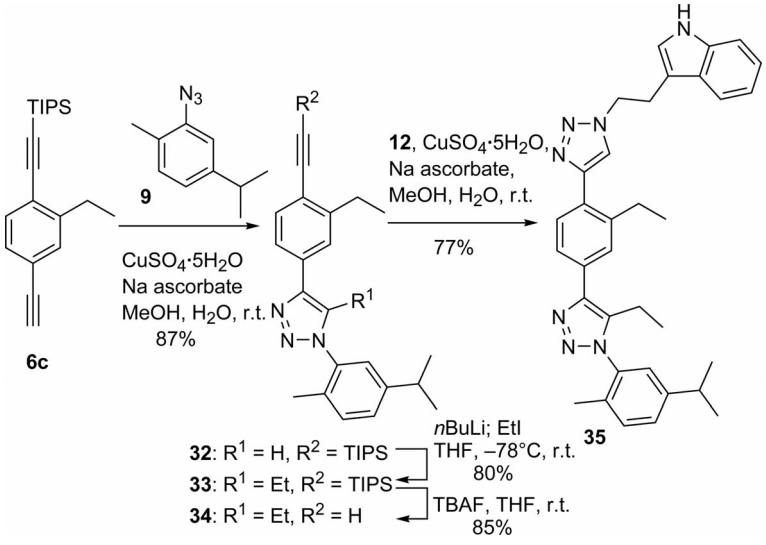
The final [3+2] cycloadditions were carried out in the same fashion as described above (Scheme 7). In this case, the azide reactants incorporate the side-chain residue *i* into the scaffold. To imitate aromatic amino acids, we used the azides **10**, **11**, and **12**, containing naphthalene, phenyl, or indole moieties, respectively. The synthesis of **30a**, **30b**, **31a**, and **31b** concluded the synthetic route to compounds with the scaffold **B**. Compound **29a** was prepared by using the azide **7**. To increase the polarity of this compound, the *tert*-butyl ethers were deprotected to yield the diol **29b**.



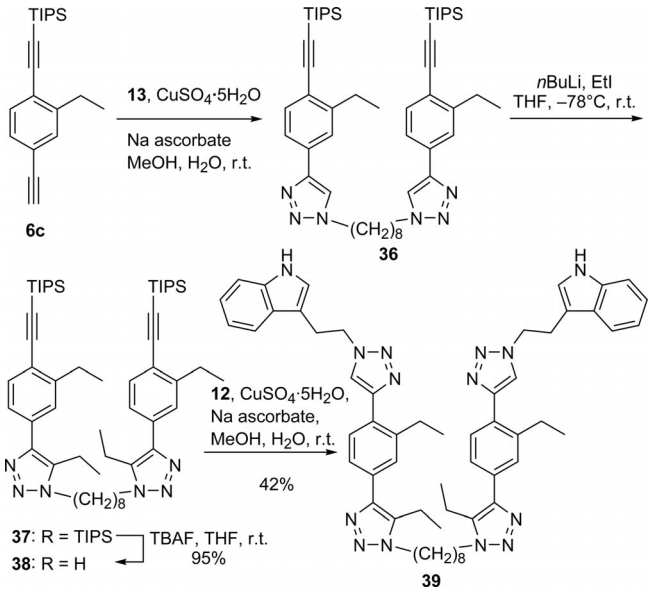
Scheme 7. Reagents and conditions. (i) Azides N_3–R^4 (**7**, **10**, **11**, **12**), $CuSO_4 \cdot 5H_2O$, sodium ascorbate or ascorbic acid, MeOH, H_2O, room temp.; (ii) HCl_{aq}, dioxane, reflux, 1.5 h.

To mimic a larger area of an α-helix, the binding motif has to be extended to a fourth side chain – either *i*+10 or *i*+11 – on the binding face of the helix. This was accomplished by extending the scaffold with an additional phenyl ring to a triazole-phenyl-triazole-phenyl system. The bottom phenyl ring orients a substituent in the *meta* position to reproduce the *i*+10 side chain correctly. The synthesis route to this extended scaffold, as depicted in Scheme 8, is similar to the previously described route. The additional phenyl ring is incorporated in the azide partner of a final Cu^I-catalyzed cycloaddition, specifically **9**, an azidobenzene carrying a *meta*-isopropyl substituent. The resulting triazole **32** was modified with ethyl iodide under basic conditions to form **33** and deprotected with TBAF solution to yield **34**. Finally, the last substituent was introduced by cycloaddition, yielding compound **35**, displaying four side chains.

Alternatively, a linker for further functionalization could be introduced. This strategy would allow incorporation of a luminescent label or the combination of two helix mimetic scaffolds in a common binding motif. We demonstrated this by using an alkyl linker to connect two triazole-phenyl-triazole structures by use of the same synthesis route as for the scaffold **B**. As linker, we used a diazido compound that reacted through both azido moieties with an alkyne intermediate. (***CAUTION:*** We suggest to treat compounds containing more than a single azide moiety as potential serious explosion hazards and to take appropriate safety measures.) In this case, **36** was prepared from 1,8-diazidooctane and subsequently treated with ethyl iodide and *n*BuLi to afford **37**; deprotection with TBAF yielded **38**. The synthesis of **39** was completed by formation of the triazoles (Scheme 9).



Scheme 8. Synthesis route to the extended scaffold **B**, which mimics side chains in the *i*, *i*+3, *i*+7, and *i*+10 positions.

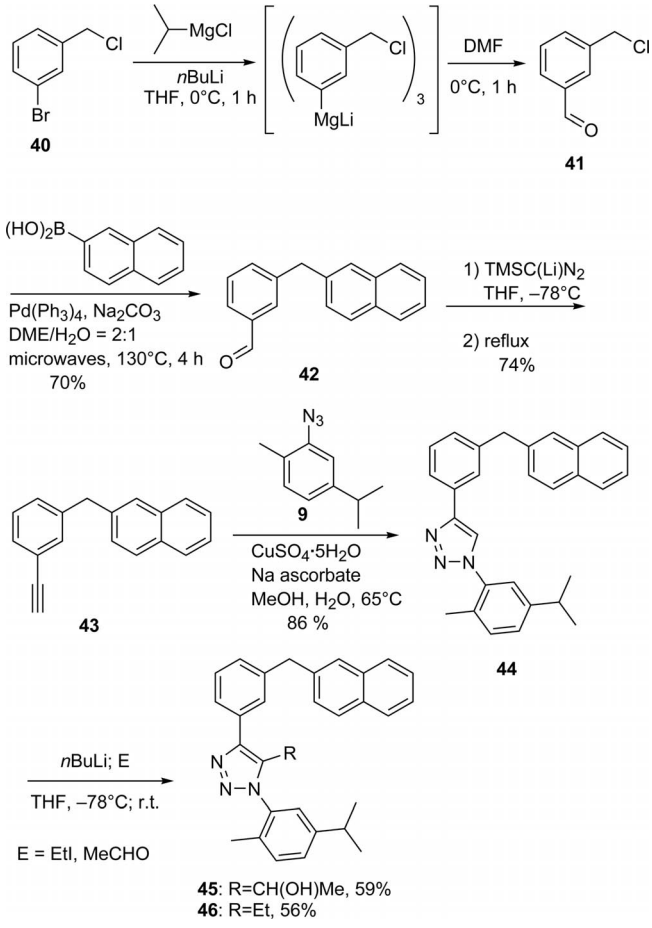


Scheme 9. Linking of two scaffolds to double the binding motif.

Scaffold C

We designed a 6-5-6 phenyl-triazole-phenyl system in which the top and bottom phenyl rings each carry a side chain at the *meta* positions to reproduce the side chains *i* and *i*+7 of a given helix target. These molecule fragments could be synthesized independently and were subsequently joined together in a triazole-forming cycloaddition to yield the complete core structure.

To allow the subsequent cycloaddition, the top phenyl fragment has to bear an alkyne substituent *meta* to the residue *i*. The commercially available 3-bromobenzyl chloride (**40**) was used as starting material and was transformed into 3-formylbenzyl chloride (**41**) through a halogen/metal exchange reaction[20] (Scheme 10). *n*BuLi was added to a solution of 3-bromobenzyl chloride and isopropylmagenesium chloride in THF at 0 °C to form a triarylmagnesiate complex. This complex was quenched with dry DMF to form the desired aldehyde **41** in quantitative yield. Naphthalene had been chosen to mimic the side chain at the position *i* of the helix, so **41** was coupled with 2-naphthylboronic acid in a Suzuki coupling reaction. This Suzuki reaction was carried out under microwave-irradiation[21] conditions with $Pd(PPh_3)_4$ as catalyst and a solvent mixture of DME/H_2O (2:1). The reaction mixture was heated in the microwave oven at 100 °C for 4 h and afforded compound **42** in 70% yield. The aldehyde **42** was transformed into its corresponding homologous alkyne **43** in 74% yield through a Colvin rearrangement.[22] This reaction used the lithium salt of trimethylsilyldiazomethane [TMSC(Li)N_2] to introduce the C_1 unit into the compound.[23] A previously synthesized azide **9** was chosen for the bottom *meta*-substituted arene designed to mimic the *i*+7 residue. The top and bottom fragments were brought together in a Cu^I-catalyzed [3+2] cycloaddition between the alkyne **43** and the azide **9** to yield compound **44** in 86% yield. In the final step, the *i*+3 residue was introduced through electrophilic attack at the 5-position in the triazole ring under basic conditions. The triazole **44** was treated with *n*BuLi, and either acetaldehyde or ethyl iodide were then used as electrophiles to form compounds **45** and **46** and to complete the synthesis route to the scaffold **C**.



Scheme 10. Synthesis route to the scaffold **C**.

Conclusions

We have developed a versatile and efficient synthetic route to different teraryl compounds that mimic the geometric arrangement of side chains in an α-helical peptide. As key steps the syntheses use azide–alkyne [3+2] cycloadditions, yielding triazoles. The three different scaffold types **A**, **B**, and **C** were produced by starting from commercially available substituted arenes. The scaffold **A** has a short synthesis route, the scaffold **B** was designed to increase the versatility by inclusion of a fourth substituent, and the scaffold **C** is especially well suited for library syntheses. The synthetic protocols allow the introduction of a wide range of different substituents as required for the development of specific protein–protein interaction inhibitors and should therefore find application in medicinal chemistry and compound library synthesis.

Experimental Section

General: Commercial reagents and starting materials were used without further purification. Solvents were dried by common procedures.[24] Flash chromatography was performed on silica gel from Merck (70–230 mesh) and Sorbent Technologies (230–400 mesh). Thin layer chromatography (TLC) was performed with alumina plates coated with silica gel (Merck silica gel 60 F_{254}, thickness 0.2 mm) or glass plates coated with silica gel (Analtech Silica Gel HLF 250 μm). Visualization was achieved with UV light (λ = 254 nm). Melting points were determined with a Stanford Research System OpitMelt melting point apparatus or a Thomas Hoover capillary melting point apparatus, are given in °C, and are uncorrected. NMR spectra were recorded with a Bruker Avance 300 (^{1}H: 300.1 MHz; ^{13}C: 75.5 MHz; T = 300 K) or a Bruker Avance 400 (^{1}H: 400.1 MHz; ^{13}C: 100.6 MHz; T = 300 K). Chemical shifts are reported in δ (ppm) relative to external standards, and coupling constants (J) are given in Hertz (Hz). Integration is determined as the relative number of protons. The solvent used for each spectrum is reported. Mass spectra were recorded with a Varian CH-5 (EI), a Finnigan MAT 95 (CI), a Finnigan MAT TSQ 7000 (ESI), or a Waters LCT Premier Micromass (ESI). IR spectra were recorded with a Bio-Rad FT-IR-FTS 155 or a Perkin–Elmer FT-IR-Spectrometer Spectrum 100. UV/Vis spectra were recorded with a Cary BIO 50 UV/Vis/NIR instrument (Varian). Elemental analyses were carried out by the Microanalytical Laboratory of the University of Regensburg.

General Procedures

GP1. Sonogashira Couplings between Aniline Derivatives and (Triisopropylsilyl)acetylene: The aniline derivative (1.0 equiv.) was dissolved at room temp. under nitrogen/argon in freshly distilled (from CaH_2) triethylamine. Bis(triphenylphosphane)palladium(II) dichloride (1 mol-%), (triisopropylsilyl)acetylene (1.0 equiv.), and copper(I) iodide (2 mol-%) were added to the stirred solution. The reaction mixture was maintained at room temp. until TLC showed full conversion of the starting material. The reaction mixture was filtered, and the filtrate was washed with saturated NH_4Cl solution (3 ×) and brine. After drying with $MgSO_4$, the solvent was evaporated under reduced pressure, and the crude product was subjected to flash column chromatography on silica gel with a hexanes/AcOEt mixture to yield the product.

GP2. Conversion of Anilines Into Iodoarenes: The aniline derivative (1.0 equiv.) was dissolved in concentrated hydrochloric acid in a three-necked round-bottomed flask with internal thermometer. The reaction mixture was cooled in an ice/NaCl bath, and a solution of sodium nitrite (1.2 equiv.) in cooled water was slowly added dropwise to keep the temperature of the reaction mixture below 3 °C. The solution was stirred at 0 °C for 1 h and was then slowly added to a stirred solution of potassium iodide (2.5 equiv.) in water, cooled in an ice bath. After the mixture had been stirred at 0 °C for 2 h, ethyl acetate was added. The phases were separated, and the aqueous phase was extracted twice with ethyl acetate. The combined organic extracts were washed with H_2O, sodium metabisulfite solution (3 ×), and brine (2 ×). After drying with $MgSO_4$, the solvent was evaporated, and the crude product was purified by flash column chromatography on silica gel with a hexanes/AcOEt mixture.

GP3. Sonogashira Coupling of Iodoarenes with 2-Methylbut-3-yn-2-ol: The iodoarene (1.0 equiv.) was dissolved in dry THF under nitrogen/argon at room temp. Freshly distilled (from CaH_2) DIPEA (4.0 equiv.), bis(triphenylphosphane)palladium(II) dichloride (2 mol-%), 2-methylbut-3-yn-2-ol (1.1 equiv.), and copper(I) iodide (4 mol-%) were added to the stirred solution. The reaction mixture was stirred until TLC showed full conversion of the starting material. The reaction mixture was then filtered, the filtrate was washed with diethyl ether, and the organic phase was washed with saturated NH_4Cl solution (3 ×) and brine. After drying with $MgSO_4$, the solvent was evaporated, and the crude product was subjected to flash column chromatography on silica gel with a hexanes/AcOEt mixture to yield the product.

GP4. Deprotection of 2-Methylbut-3-yn-2-ols To Yield the Free Alkynes: Ground sodium hydroxide was added to a solution of the protected alkyne in toluene. The reaction mixture was heated at reflux for 3 h or until TLC showed complete conversion. H_2O was added, the phases were separated, and the aqueous phase was extracted twice with diethyl ether. The combined organic extracts were washed with NH_4Cl solution (2 ×) and brine and dried with $MgSO_4$. The solvent was removed in vacuo, and the crude product was purified by flash column chromatography on silica gel.

GP5. Cu^I-Catalyzed [3+2] Cycloadditions between Alkynes and Azides: The alkyne (1.0 equiv.) was dissolved in methanol, and the azide (1.1 equiv.) was added. Sodium ascorbate or ascorbic acid (0.1 equiv.) and $CuSO_4 \cdot 5H_2O$ (0.02 equiv.) were each dissolved in little H_2O and were added to the reaction mixture. The reaction mixture was stirred at room temp. overnight. If TLC showed incomplete conversion, it was heated to 65 °C. H_2O and diethyl ether were added and the phases were separated. The aqueous phase was extracted twice with diethyl ether, and the combined organic extracts were washed with a solution of NH_4Cl (2 ×) and brine (2 ×). After drying with $MgSO_4$, the solvent was evaporated. The remaining residue was purified by flash column chromatography on silica gel.

GP6. Deprotection of TIPS-Protected Alkynes: The protected alkyne (1 equiv.) was dissolved in THF, and a solution of TBAF in THF (1 M, 2 equiv.) was added. After the mixture had been stirred at room temp. for 1 h, H_2O and diethyl ether were added. The phases were separated, and the organic phase was washed with H_2O (3 ×) and brine. After drying with $MgSO_4$, the solvent was evaporated, and the crude product was purified by flash column chromatography on silica gel.

GP7. Ru^{II}-Catalyzed [3+2] Cycloadditions: The alkyne (1.0 equiv.) and the azide (1.0 equiv.) were dissolved in dioxane, and cp*$RuCl(PPh_3)_2$ (5 mol-%) was added. The reaction mixture was stirred at 70 °C for 24 h. The solvent was removed in vacuo, and the crude product was purified by flash column chromatography on silica gel.

GP8. Triazole Modification at the 5-Position: The triazole (1.0 equiv.) was dissolved in dry THF under argon in a flame-dried flask. The reaction mixture was cooled to –78 °C in an acetone/dry ice bath, and *n*BuLi (1.5 equiv.) was slowly added dropwise. After the mixture had been stirred at that temperature for 5 min, the electrophile (4.0 equiv.) was added, and the solution was stirred at –78 °C for 1 h. After the reaction mixture had been allowed to warm to room temp., it was stirred at that temperature for 1 h. H_2O was added, and the phases were separated. The aqueous phase was extracted twice with DCM, and the combined organic extracts were dried with $MgSO_4$. The solvent was evaporated under reduced pressure, and the crude product was purified by flash column chromatography on silica gel.

GP9. Cu^I-Catalyzed [3+2] Cycloadditions with Small Azides: In these two-step reactions the bromoalkane (5.0 equiv.) was dissolved in DMF. Sodium azide (6.0 equiv.) was added, and the reaction mixture was stirred at 50 °C for 15 h. The alkyne (1.0 equiv.) and

solutions of sodium ascorbate (0.10 equiv.) and $CuSO_4 \cdot 5H_2O$ (0.05 equiv.) in a little H_2O were added to the formed azide. After addition of methanol, the reaction mixtures were stirred at 50 °C for 5 d. H_2O and diethyl ether were added, and the phases were separated. The aqueous phase was extracted twice with diethyl ether, and the combined organic extracts were washed with a saturated solution of NH_4Cl and brine. After drying with $MgSO_4$, the solvent was evaporated under reduced pressure, and the crude product was purified by flash column chromatography on silica gel.

Synthesis of New Compounds

2-Ethyl-4-[(triisopropylsilyl)ethynyl]aniline (3a): Compound **3a** was synthesized according to GP1, from the 4-iodoaniline derivative **2a** (3.70 g, 15.0 mmol) in NEt_3 (70 mL), with Pd catalyst (105 mg, 0.15 mmol), (triisopropylsilyl)acetylene (3.37 mL, 15.0 mmol), and CuI (57 mg, 0.30 mmol). After the mixture had been stirred for 2 d, TLC showed full conversion of **2a**. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 2:1; R_f = 0.80), and **3a** was obtained as a brown oil (4.54 g, 100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.11–1.13 (m, 21 H, *i*Pr), 1.24 (t, ^3J = 7.57 Hz, 3 H, CH_3), 2.47 (q, ^3J = 7.57 Hz, 2 H, CH_2), 3.75 (br. s, 2 H, NH_2), 6.57 (d, ^3J = 7.83 Hz, 1 H, ArH), 7.17 (dd, ^4J = 1.38, ^3J = 8.46 Hz, 1 H, ArH), 7.18–7.19 (m, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.41, 12.78, 18.71, 23.81, 87.10 (C_{quat}), 108.24 (C_{quat}), 113.20 (C_{quat}), 114.81, 127.53 (C_{quat}), 131.03, 132.28, 144.39 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3489, 3390, 2967, 2862, 2137, 1621, 1462 cm^{-1}. HR-MS (ESI+): calcd. for $C_{19}H_{32}NSi$ $[M + H]^+$ 302.2304; found 302.2314.

2,6-Diethyl-4-[(triisopropylsilyl)ethynyl]aniline (3b): Compound **3b** was synthesized according to GP1, by dissolving the 4-iodoaniline derivative **2b** (3.70 g, 13.5 mmol) in NEt_3 (70 mL) and using Pd catalyst (95 mg, 0.14 mmol), (triisopropylsilyl)acetylene (3.24 mL, 14.4 mmol), and CuI (52 mg, 0.27 mmol). After the mixture had been stirred for 3 d, TLC showed full conversion of **2b**. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 2:1; R_f = 0.85), and **3b** was obtained as a green-brown oil (4.63 g, 100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.11–1.13 (m, 21 H, *i*Pr), 1.25 (t, ^3J = 7.45 Hz, 6 H, CH_3), 2.49 (q, ^3J = 7.49 Hz, 4 H, CH_2), 3.78 (br. s, 2 H, NH_2), 7.10 (s, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.43, 12.83, 18.72, 24.10, 86.73 (C_{quat}), 108.64 (C_{quat}), 112.59 (C_{quat}), 127.25 (C_{quat}), 130.06, 142.13 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3500, 3406, 2956, 2868, 2142, 1621, 1459 cm^{-1}. HR-MS (ESI+): calcd. for $C_{21}H_{36}NSi$ $[M + H]^+$ 330.2617; found 330.2617.

3-Ethyl-4-[(triisopropylsilyl)ethynyl]aniline (3c): Compound **3c** was synthesized according to GP1, by dissolving the 4-iodoaniline derivative **2c** (4.08 g, 16.5 mmol) in NEt_3 (70 mL) and using Pd catalyst (116 mg, 0.17 mmol), (triisopropylsilyl)acetylene (3.70 mL, 16.5 mmol), and CuI (63 mg, 0.33 mmol). After the mixture had been stirred for 3 d, TLC showed full conversion of **2c**. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 4:1; R_f = 0.58), and **3c** was obtained as a yellow oil (4.57 g, 92%). M.p. 43 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12–1.13 (m, 21 H, *i*Pr), 1.22 (t, ^3J = 7.57 Hz, 3 H, CH_3), 2.74 (q, ^3J = 7.57 Hz, 2 H, CH_2), 3.73 (br. s, 2 H, NH_2), 6.43 (dd, ^4J = 2.40, ^3J = 8.21 Hz, 1 H, ArH), 6.50 (d, ^4J = 2.27 Hz, 1 H, ArH), 7.26 (d, ^3J = 8.33 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.43, 14.90, 18.70, 27.98, 91.01 (C_{quat}), 106.26 (C_{quat}), 112.17, 112.50 (C_{quat}), 114.30, 134.09, 146.74 (C_{quat}), 148.24 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3467, 3373, 2939, 2868, 2142, 1621, 1459 cm^{-1}. HR-MS (ESI+): calcd. for $C_{19}H_{32}NSi$ $[M + H]^+$ 302.2304; found 302.2304.

3-Methyl-4-[(triisopropylsilyl)ethynyl]aniline (3d): Compound **3d** was synthesized according to GP1, from 4-iodo-3-methylaniline (500 mg, 2.15 mol), triethylamine (10 mL), $PdCl_2(PPh_3)_2$ (15 mg, 22 μmol), (triisopropylsilyl)acetylene (0.52 mL, 2.30 mmol), and CuI (8 mg, 43 μmol). TLC showed complete conversion of the starting material [petroleum ether/AcOEt, 1:1; R_f = 0.65] after stirring overnight. The product was obtained after flash column chromatography on silica gel (hexanes/AcOEt 1:1) as a brown solid (0.712 g, 100%). M.p. 52 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10–1.12 (m, 21 H, *i*Pr), 2.36 (s, 3 H, Ar-CH_3), 6.42 (dd, ^3J = 8.23, ^4J = 2.19 Hz, 1 H, ArH), 6.50 (d, ^4J = 2.19 Hz, 1 H, ArH), 7.25 (d, ^3J = 8.23 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.38, 18.70, 20.96, 91.37 (C_{quat}), 106.52 (C_{quat}), 112.07, 113.22 (C_{quat}), 115.67, 133.68, 142.08 (C_{quat}), 146.53 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2940, 2864, 2144, 1605, 1495 cm^{-1}. UV/Vis (MeCN): λ_{max} (lg ε)=280 nm (4.622). MS (EI): *m*/*z* (%) = 244.1 (100) $[M - C_3H_7]^+$, 287.2 (63) $[M]^+$. HR-MS (EI): calcd. for $C_{18}H_{29}NSi$ $[M]^+$ 287.2069; found 287.2065.

[(3-Ethyl-4-iodophenyl)ethynyl]triisopropylsilane (4a): The synthesis of **4a** was according to GP2, with the aniline derivative **3a** (4.46 g, 14.8 mmol), concentrated hydrochloric acid (15 mL), $NaNO_2$ solution (1.23 g of $NaNO_2$, 17.7 mmol; in 10 mL of H_2O), and KI solution (6.14 g of KI, 37.0 mmol; in 35 mL of H_2O). The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 10:1; R_f = 0.87), yielding **4a** as a red oil (5.39 g, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.11–1.13 (m, 21 H, *i*Pr), 1.20 (t, ^3J = 7.45 Hz, 3 H, CH_3), 2.69 (q, ^3J = 7.49 Hz, 2 H, CH_2), 6.96 (dd, ^4J = 2.02, ^3J = 8.08 Hz, 1 H, ArH), 7.29 (d, ^4J = 2.02 Hz, 1 H, ArH), 7.73 (d, ^3J = 8.08 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.28, 14.37, 18.64, 33.96, 91.67 (C_{quat}), 100.34 (C_{quat}), 106.21 (C_{quat}), 123.77 (C_{quat}), 130.82, 131.72, 139.19, 146.53 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2961, 2862, 2159, 1462 cm^{-1}. HR-MS (EI+): calcd. for $C_{19}H_{29}ISi$ $[M]^+$ 412.1083; found 412.1089.

[(3,5-Diethyl-4-iodophenyl)ethynyl]triisopropylsilane (4b): The synthesis of **4b** was according to GP2, with the aniline derivative **3b** (4.45 g, 13.5 mmol), concentrated hydrochloric acid (15 mL), $NaNO_2$ solution (1.12 g of $NaNO_2$, 16.2 mmol; in 10 mL of H_2O), and KI solution (5.60 g of KI, 33.8 mmol; in 35 mL of H_2O). The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 10:1; R_f = 0.89), yielding **4b** as a red-brown oil (4.16 g, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12–1.14 (m, 21 H, *i*Pr), 1.21 (t, ^3J = 7.45 Hz, 6 H, CH_3), 2.77 (q, ^3J = 7.49 Hz, 4 H, CH_2), 7.13 (s, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.30, 14.51, 18.67, 35.35, 91.08 (C_{quat}), 106.42 (C_{quat}), 107.30 (C_{quat}), 123.34 (C_{quat}), 129.34, 147.35 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2956, 2862, 2148, 1462 cm^{-1}. HR-MS (EI+): calcd. for $C_{21}H_{33}ISi$ $[M]^+$ 440.1396; found 440.1405.

[(2-Ethyl-4-iodophenyl)ethynyl]triisopropylsilane (4c): The synthesis of **4c** was according to GP2, from the aniline derivative **3c** (4.50 g, 14.9 mmol), concentrated hydrochloric acid (15 mL), $NaNO_2$ solution (1.24 g of $NaNO_2$, 17.9 mmol; in 10 mL of H_2O), and KI solution (6.19 g of KI, 37.3 mmol; in 35 mL of H_2O). The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 10:1; R_f = 0.89), yielding **4c** as a brown oil (5.32 g, 87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12–1.14 (m, 21 H, *i*Pr), 1.23 (t, ^3J = 7.57 Hz, 3 H, CH_3), 2.77 (q, ^3J = 7.49 Hz, 2 H, CH_2), 7.16 (d, ^3J = 8.08 Hz, 1 H, ArH), 7.46 (dd, ^4J = 1.76, ^3J = 8.08 Hz, 1 H, ArH), 7.55 (d, ^4J = 1.51 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.30, 14.72, 18.64, 27.66, 94.48 (C_{quat}), 95.83 (C_{quat}), 104.48 (C_{quat}), 122.27 (C_{quat}), 134.04, 134.61, 136.98, 148.58 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2967, 2857, 2153, 1467 cm^{-1}. HR-MS (EI+): calcd. for $C_{19}H_{29}ISi$ $[M]^+$ 412.1083; found 412.1090.

[(4-Iodo-2-methylphenyl)ethynyl]triisopropylsilane (4d): The synthesis of **4d** was according to GP2, with the aniline derivative **3d** (2.47 g, 8.58 mmol), concentrated hydrochloric acid (10 mL), $NaNO_2$ solution (710 mg of $NaNO_2$; 10.3 mmol, in 7 mL of H_2O), and KI solution (3.56 g of KI, 21.4 mmol; in 15 mL of H_2O). The crude product was purified by flash column chromatography on silica gel (petroleum ether/AcOEt, 2:1; R_f = 0.76), yielding **4d** as an orange-brown oil (3.09 g, 90%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08–1.14 (m, 21 H, *i*Pr), 2.39 (s, 3 H, $ArCH_3$), 7.15 (d, ^3J = 8.23 Hz, 1 H, ArH), 7.45 (dd, ^3J = 8.09, ^4J = 1.23 Hz, 1 H, ArH), 7.57 (d, ^4J = 0.82 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.24, 18.65, 20.56, 94.16 (C_{quat}), 96.31 (C_{quat}), 104.74 (C_{quat}), 122.98 (C_{quat}), 133.56, 134.53, 138.20, 142.54 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2941, 2865, 2154, 1473 cm^{-1}. UV/Vis ($CHCl_3$): λ_{max} (lg ε) = 265 nm (4.434). MS (CI-MS, NH_3): *m*/*z* (%) = 399.0 (100) [M + H]$^+$.

4-{2-Ethyl-4-[(triisopropylsilyl)ethynyl]phenyl}-2-methylbut-3-yn-2-ol (5a): The synthesis of **5a** was according to GP3, by dissolving the iodoarene derivative **4a** (5.32 g, 12.9 mmol) in dry THF (70 mL) and using DIPEA (9.0 mL, 51 mmol), $PdCl_2(PPh_3)_2$ (182 mg, 0.26 mmol), 2-methylbut-3-yn-2-ol (1.40 mL, 14.2 mmol), and CuI (99 mg, 0.52 mmol). The reaction was complete after the mixture had been stirred for 3 d, and the crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 4:1; R_f = 0.48). Compound **5a** was obtained as a yellow oil (3.73 g, 79%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.11–1.13 (m, 21 H, *i*Pr), 1.23 (t, ^3J = 7.57 Hz, 3 H, CH_3), 1.63 (s, 6 H, CH_3), 1.99 (br. s, 1 H, OH), 2.74 (q, ^3J = 7.57 Hz, 2 H, CH_2), 7.23 (dd, ^4J = 1.51, ^3J = 8.08 Hz, 1 H, ArH), 7.29–7.31 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.31, 14.48, 18.65, 27.50, 32.46, 65.76 (C_{quat}), 80.56 (C_{quat}), 91.92 (C_{quat}), 98.81 (C_{quat}), 106.88 (C_{quat}), 121.83 (C_{quat}), 123.45 (C_{quat}), 129.26, 131.41, 131.90, 146.10 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3346, 2967, 2862, 2153, 1459 cm^{-1}. HR-MS (EI+): calcd. for $C_{24}H_{36}OSi$ [M]$^+$ 368.2535; found 368.2526.

4-{2,6-Diethyl-4-[(triisopropylsilyl)ethynyl]phenyl}-2-methylbut-3-yn-2-ol (5b): The synthesis of **5b** was according to GP3, by dissolving the iodoarene derivative **4b** (4.06 g, 9.23 mmol) in dry THF (60 mL) and using DIPEA (6.43 mL, 36.9 mmol), $PdCl_2(PPh_3)_2$ (130 mg, 0.185 mmol), 2-methylbut-3-yn-2-ol (0.99 mL, 10.2 mmol), and CuI (70 mg, 0.37 mmol). The reaction was almost complete after the mixture had been stirred at room temp. for 3 d, and the crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 4:1; R_f = 0.76). Compound **5b** was obtained as a white solid (1.71 g, 47%). M.p. 77 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12–1.14 (m, 21 H, *i*Pr), 1.23 (t, ^3J = 7.57 Hz, 6 H, CH_3), 1.65 (s, 6 H, CH_3), 2.01 (br. s, 1 H, OH), 2.75 (q, ^3J = 7.57 Hz, 4 H, CH_2), 7.15 (s, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.32, 14.53, 18.67, 27.81, 31.48, 65.90 (C_{quat}), 78.99 (C_{quat}), 91.29 (C_{quat}), 102.68 (C_{quat}), 107.26 (C_{quat}), 121.20 (C_{quat}), 122.98 (C_{quat}), 128.87, 146.37 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3340, 2961, 2868, 2148, 1459 cm^{-1}. HR-MS (EI+): calcd. for $C_{26}H_{40}OSi$ [M]$^+$ 396.2848; found 396.2847.

4-{3-Ethyl-4-[(triisopropylsilyl)ethynyl]phenyl}-2-methylbut-3-yn-2-ol (5c): The synthesis of **5c** was according to GP3, by dissolving the iodoarene derivative **4c** (5.27 g, 12.8 mmol) in dry THF (70 mL) and using DIPEA (8.90 mL, 51.1 mmol), $PdCl_2(PPh_3)_2$ (180 mg, 0.256 mmol), 2-methylbut-3-yn-2-ol (2.50 mL, 25.5 mmol), and CuI (98 mg, 0.51 mmol). The reaction was complete after the mixture had been stirred at room temp. for 4 d, and the crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 4:1; R_f = 0.59). Compound **5c** was obtained as a yellow oil (3.49 g, 74%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12–1.14 (m, 21 H, *i*Pr), 1.23 (t, ^3J = 7.57 Hz, 3 H, CH_3), 1.61 (s, 6 H, CH_3), 2.00 (br. s, 1 H, OH), 2.79 (q, ^3J = 7.49 Hz, 2 H, CH_2), 7.17 (dd, ^4J = 1.51, ^3J = 7.83 Hz, 1 H, ArH), 7.26–7.27 (m, 1 H, ArH), 7.37 (d, ^3J = 7.83 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.33, 14.74, 18.64, 27.71, 31.45, 65.66 (C_{quat}), 82.12 (C_{quat}), 94.94 (C_{quat}), 95.97 (C_{quat}), 105.01 (C_{quat}), 122.58 (C_{quat}), 122.67 (C_{quat}), 128.69, 131.13, 132.57, 146.53 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3340, 2956, 2862, 2148, 1462 cm^{-1}. HR-MS (EI+): calcd. for $C_{24}H_{36}OSi$ [M]$^+$ 368.2535; found 368.2533.

2-Methyl-4-{3-methyl-4-[(triisopropylsilyl)ethynyl]phenyl}but-3-yn-2-ol (5d): The synthesis of **5d** was according to GP3, by dissolving the iodoarene derivative **4d** (498 mg, 1.25 mmol) in dry THF (7 mL) and using DIPEA (0.87 mL, 5.0 mmol), $PdCl_2(PPh_3)_2$ (17.5 mg, 0.025 mmol), 2-methylbut-3-yn-2-ol (0.14 mL, 1.4 mmol), and CuI (10 mg, 0.050 mmol). The reaction was complete after stirring overnight, and the crude product was purified by flash column chromatography on silica gel (petroleum ether/AcOEt, 4:1; R_f = 0.36). Compound **5d** was obtained as a yellow oil (282 mg, 63%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12–1.14 (m, 21 H, *i*Pr), 1.61 (s, 6 H, CH_3), 2.41 (s, 3 H, $ArCH_3$), 7.16 (dd, ^3J = 7.82, ^4J = 1.23 Hz, 1 H, ArH), 7.25–7.27 (m, 1 H, Ar2), 7.37 (d, ^3J = 7.95 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.28, 18.66, 20.68, 31.44, 65.64 (C_{quat}), 82.01 (C_{quat}), 94.97 (C_{quat}), 96.45 (C_{quat}), 105.27 (C_{quat}), 122.39 (C_{quat}), 123.37 (C_{quat}), 128.63, 132.14, 132.43, 140.47 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2941, 2864, 2150, 1491, 1461 cm^{-1}. UV/Vis ($CHCl_3$): λ_{max} (lg ε) = 280 (4.589), 290 nm (4.546). MS (CI, NH_3): *m*/*z* (%) = 337.2 (100) [M + H – H_2O]$^+$, 355.3 (6) [M + H]$^+$. HR-MS (EI): calcd. for $C_{23}H_{34}OSi$ [M]$^+$ 354.2379; found 354.2374.

[(3-Ethyl-4-ethynylphenyl)ethynyl]triisopropylsilane (6a): Compound **6a** was synthesized according to GP4. The protected alkyne **5a** (5.55 g, 15.0 mmol) was dissolved in toluene (60 mL), and sodium hydroxide (2 g) was added. TLC showed complete conversion after 3 h of heating at reflux, and the crude product was purified by flash column chromatography on silica (hexanes/AcOEt, 4:1; R_f = 0.87). As product, **6a** was obtained as a brown oil (4.45 g, 95%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.11–1.13 (m, 21 H, *i*Pr), 1.24 (t, ^3J = 7.57 Hz, 3 H, CH_3), 2.79 (q, ^3J = 7.57 Hz, 2 H, CH_2), 3.31 (s, 1 H, CH), 7.25 (dd, ^4J = 1.51, ^3J = 7.83 Hz, 1 H, ArH), 7.31 (d, ^4J = 1.01 Hz, 1 H, ArH), 7.38 (d, ^3J = 7.83 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.31, 14.62, 18.66, 27.40, 77.20, 81.99 (C_{quat}), 92.26 (C_{quat}), 106.74 (C_{quat}), 121.23 (C_{quat}), 123.98 (C_{quat}), 129.26, 131.45, 132.64, 146.74 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3296, 2945, 2862, 2148, 1618, 1456 cm^{-1}. HR-MS (EI+): calcd. for $C_{21}H_{30}Si$ [M]$^+$ 310.2117; found 310.2108.

[(3,5-Diethyl-4-ethynylphenyl)ethynyl]triisopropylsilane (6b): Compound **6b** was synthesized according to GP4. The protected alkyne **5b** (1.65 g, 4.16 mmol) was dissolved in toluene (30 mL), and sodium hydroxide (1 g) was added. TLC showed complete conversion after 3 h of heating at reflux, and the crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 10:1; R_f = 0.90). Product **6b** was obtained as a brown oil (1.18 g, 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12–1.14 (m, 21 H, *i*Pr), 1.23 (t, ^3J = 7.57 Hz, 6 H, CH_3), 2.79 (q, ^3J = 7.49 Hz, 4 H, CH_2), 3.50 (s, 1 H, CH), 7.16 (s, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.31, 14.63, 18.67, 27.73, 80.28 (C_{quat}), 85.80, 91.58 (C_{quat}), 107.12 (C_{quat}), 120.68 (C_{quat}), 123.42 (C_{quat}), 128.86, 147.16 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3307, 2967, 2868, 2148, 1459 cm^{-1}. HR-MS (EI+): calcd. for $C_{23}H_{34}Si$ [M]$^+$ 338.2430; found 338.2431.

[(2-Ethyl-4-ethynylphenyl)ethynyl]triisopropylsilane (6c): Compound **6c** was synthesized according to GP4. The protected alkyne **5c** (3.34 g, 9.07 mmol) was dissolved in toluene (40 mL), and sodium

hydroxide (1.5 g) was added. TLC showed complete conversion after 4 h of heating at reflux, and the crude product was purified by flash column chromatography on silica (hexanes/AcOEt, 10:1; R_f = 0.85). Product **6c** was obtained as a brown oil (2.56 g, 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12–1.14 (m, 21 H, *i*Pr), 1.24 (t, ^3J = 7.57 Hz, 3 H, CH_3), 2.80 (q, ^3J = 7.57 Hz, 2 H, CH_2), 3.13 (s, 1 H, CH), 7.25 (dd, ^4J = 1.76, ^3J = 7.83 Hz, 1 H, ArH), 7.33 (d, ^4J = 1.26 Hz, 1 H, ArH), 7.39 (d, ^3J = 7.83 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.31, 14.70, 18.64, 27.69, 78.28, 83.58 (C_{quat}), 96.34 (C_{quat}), 104.84 (C_{quat}), 121.90 (C_{quat}), 123.30 (C_{quat}), 129.18, 131.59, 132.60, 146.60 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3302, 2939, 2862, 2148, 1459 cm^{-1}. HR-MS (EI+): calcd. for $C_{21}H_{30}Si$ $[M]^+$ 310.2117; found 310.2106.

[(4-Ethynyl-2-methylphenyl)ethynyl]triisopropylsilane (6d): Compound **6d** was synthesized according to GP4. The protected alkyne **5d** (280 mg, 0.79 mmol) was dissolved in toluene (25 mL), and sodium hydroxide (500 mg) was added. TLC showed complete conversion after 3 h of reflux, and the crude product was purified by flash column chromatography on silica gel (petroleum ether/AcOEt, 4:1; R_f = 0.68). Product **6d** was obtained as a brown oil (205 mg, 87%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.05–1.15 (m, 21 H, *i*Pr), 2.43 (s, 3 H, $ArCH_3$), 3.12 (s, 1 H, CH), 7.24 (dd, ^4J = 0.68, ^3J = 8.09 Hz, 1 H, ArH), 7.32–7.34 (m, 1 H, ArH), 7.39 (d, ^3J = 7.95 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.27, 18.65, 20.69, 78.33, 83.46 (C_{quat}), 96.82 (C_{quat}), 105.12 (C_{quat}), 121.69 (C_{quat}), 123.99 (C_{quat}), 129.12, 132.18, 132.88, 140.55 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3309, 2942, 2865, 2152, 1489, 1463 cm^{-1}. UV/Vis ($CHCl_3$): λ_{max} (lg ε) = 275 (4.630), 285 nm (4.582). MS (EI): *m*/*z* (%) = 253.1 (100) $[M - C_3H_7]^+$, 296.2 (23) $[M]^+$. HR-MS (EI+): calcd. for $C_{20}H_{28}Si$ $[M]^+$ 296.1960; found 296.1957.

1-Azido-3-*tert*-butoxypropane (7): NaN_3 (1.66 g, 26 mmol, 1.5 equiv.) was added to a solution of 1-*tert*-butoxy-3-chloropropane (2.56 g, 17 mmol, 1 equiv.) in DMSO (10 mL), and the reaction mixture was stirred at 40 °C overnight. H_2O was added, and the solution was extracted with diethyl ether (4×). The combined organic extracts were washed with brine and dried with $MgSO_4$. The solvent was evaporated to yield product **7** as a colorless oil (2.41 g, 90%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18 (s, 9 H, *t*Bu), 1.78 (m, 2 H, CH_2), 3.36–3.44 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.43, 29.86, 48.59, 58.01, 72.77 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2975, 2088, 1363, 1195, 1094 cm^{-1}. MS (EI+): *m*/*z* = 142.1 $[M - CH_3]^+$, 114.1 $[M - C_3H_7]^+$.

2-(2-Azidoethyl)-1,4-dioxane (8): NaN_3 (488 mg, 7.5 mmol, 1.5 equiv.) was added to a solution of 2-(2-bromoethyl)-1,4-dioxane (976 mg, 1 equiv.) in DMSO (20 mL), and the reaction mixture was stirred at 45 °C overnight. H_2O was added, and the solution was extracted with diethyl ether (3×). The combined organic extracts were washed with brine and dried with $MgSO_4$. The solvent was evaporated to yield product **8** as a colorless oil (727 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.34–1.36 (m, 1 H), 1.86 (dt, ^3J = 5.22, ^3J = 6.75 Hz, 2 H, CH_2), 2.02–2.12 (m, 1 H), 3.39 (t, ^3J = 6.82 Hz, 2 H, CH_2), 3.73–3.80 (m, 2 H, CH_2), 4.08–4.12 (m, 2 H, CH_2), 4.66 (m, 1 H, CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.69, 34.46, 46.58, 66.88 (2 C), 99.42 ppm. IR: $\tilde{\nu}$ = 2961, 2857, 2093, 1138 cm^{-1}. MS (EI+): *m*/*z* (%) = 87.1 (100) $[M - C_2H_4N_3]^+$.

2-Azido-4-isopropyl-1-methylbenzene (9): 5-Isopropyl-2-methylaniline (500 mg, 3.35 mmol, 1.0 equiv.) was dissolved in a 1:1 mixture of concentrated hydrochloric acid (10 mL)/H_2O (10 mL). The solution was cooled in an ice/NaCl bath, and an aqueous $NaNO_2$ solution (347 mg, 5.03 mmol, 1.5 equiv; in 6 mL of H_2O) was slowly added dropwise. After the mixture had been stirred at that temperature for 1 h, the reaction mixture was neutralized with NaOAc (5.50 g), and an aqueous solution of NaN_3 (436 mg, 6.70 mmol, 2.0 equiv; in 7 mL of H_2O) was added dropwise over 30 min. The reaction mixture was stirred at 0 °C for an additional 30 min, allowed to warm to room temp., and stirred at that temperature for 1 h. The solution was extracted twice with AcOEt, dried with $MgSO_4$, and concentrated. Purification by flash column chromatography on silica gel (hexanes/AcOEt, 10:1; R_f = 0.76) yielded **9** as a red oil (356 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (d, ^3J = 7.07 Hz, 6 H, CH_3), 2.17 (s, 3 H, Ar-CH_3), 2.89 (sept, ^3J = 6.94 Hz, 1 H, CH), 6.91 (dd, ^4J = 1.76, ^3J = 7.83 Hz, 1 H, ArH), 6.96 (d, ^4J = 1.26 Hz, 1 H, ArH), 7.08 (d, ^3J = 7.83 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.78, 23.94, 33.85, 115.95, 122.70, 126.88 (C_{quat}), 131.01, 137.95 (C_{quat}), 148.19 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2961, 2873, 2104, 1456 cm^{-1}. HR-MS (EI+): calcd. for $C_{10}H_{13}N_3$ $[M]^+$ 175.1110; found 175.1113.

4-{2-Ethyl-4-[(triisopropylsilyl)ethynyl]phenyl}-1-isobutyl-1*H*-1,2,3-triazole (17a): Compound **17a** was synthesized according to GP9, with use of 1-bromo-2-methylpropane (685 mg, 5.0 mmol), sodium azide (390 mg, 6.0 mmol), and DMF (10 mL) to preform the azide. The next day, the alkyne **6a** (310 mg, 1.0 mmol), MeOH (2 mL), and aqueous solutions of sodium ascorbate (20 mg, 0.10 mmol) and $CuSO_4 \cdot 5H_2O$ (13 mg, 0.05 mmol) were added. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 4:1; R_f = 0.49) to yield **17a** as a white solid (185 mg, 45%). M.p. 71 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 (d, ^3J = 6.56 Hz, 6 H, CH_3), 1.13–1.15 (m, 21 H, *i*Pr), 1.20 (t, ^3J = 7.45 Hz, 3 H, CH_3), 2.26–2.28 (m, 1 H, CH), 2.81 (q, ^3J = 7.49 Hz, 2 H, CH_2), 4.21 (d, ^3J = 7.32 Hz, 2 H, CH_2), 7.36 (dd, ^4J = 1.64, ^3J = 7.95 Hz, 1 H, ArH), 7.40 (d, ^4J = 1.26 Hz, 1 H, ArH), 7.59 (s, 1 H, ArH), 7.60 (d, ^3J = 7.83 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.31, 15.04, 18.66, 19.84, 26.66, 29.74, 57.54, 90.90 (C_{quat}), 107.06 (C_{quat}), 122.06, 123.31 (C_{quat}), 129.22, 129.59, 129.56 (C_{quat}), 132.62, 141.78 (C_{quat}), 146.31 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2957, 2864, 2154, 1459 cm^{-1}. HR-MS (ESI+): calcd. for $C_{25}H_{40}N_3Si$ $[M + H]^+$ 410.2991; found 410.3017.

4-{2,6-Diethyl-4-[(triisopropylsilyl)ethynyl]phenyl}-1-isobutyl-1*H*-1,2,3-triazole (17b): Compound **17b** was synthesized according to GP9, with use of 1-bromo-2-methylpropane (1.01 g, 7.39 mmol), sodium azide (576 mg, 8.86 mmol), and DMF (10 mL) to preform the azide. The next day, the alkyne **6b** (500 mg, 1.48 mmol), MeOH (2 mL), and aqueous solutions of sodium ascorbate (29 mg, 0.15 mmol) and $CuSO_4 \cdot 5H_2O$ (18 mg, 0.07 mmol) were added. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 4:1; R_f = 0.42) to yield **17b** as a yellow solid (377 mg, 58%). M.p. 76 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (d, ^3J = 6.56 Hz, 6 H, CH_3), 1.03 (t, ^3J = 7.45 Hz, 6 H, CH_3), 1.14–1.15 (m, 21 H, *i*Pr), 2.27–2.29 (m, 1 H, CH), 2.37 (q, ^3J = 7.57 Hz, 4 H, CH_2), 4.24 (d, ^3J = 7.32 Hz, 2 H, CH_2), 7.24 (s, 2 H, ArH), 7.40 (s, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.38, 15.44, 18.70, 19.76, 26.81, 29.82, 57.52, 90.28 (C_{quat}), 107.36 (C_{quat}), 122.83, 123.90 (C_{quat}), 129.45, 129.63 (C_{quat}), 144.31 (C_{quat}), 144.35 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2967, 2862, 2153, 1459 cm^{-1}. HR-MS (ESI+): calcd. for $C_{27}H_{43}N_3SiNa$ $[M + Na]^+$ 460.3124; found 460.3149.

4-(2-Ethyl-4-ethynylphenyl)-1-isobutyl-1*H*-1,2,3-triazole (18a): The synthesis of compound **18a** was according to GP6, by dissolving **17a** (156 mg, 0.38 mmol) in THF (15 mL) and adding TBAF solution (1 M in THF, 0.76 mL, 0.76 mmol). After the mixture had been stirred at room temp. for 1 h, TLC showed full conversion, and the reaction mixture was worked up. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 4:1;

R_f = 0.27) to yield **18a** (105 mg, 100%) as a white solid. M.p. 64 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 (d, ^3J = 6.56 Hz, 6 H, CH_3), 1.20 (t, ^3J = 7.57 Hz, 3 H, CH_3), 2.27 (sept, ^3J = 6.82 Hz, 1 H, CH), 2.81 (q, ^3J = 7.49 Hz, 2 H, CH_2), 3.10 (s, 1 H, CH), 4.22 (d, ^3J = 7.07 Hz, 2 H, CH_2), 7.38 (dd, ^4J = 1.64, ^3J = 7.95 Hz, 1 H, ArH), 7.44 (d, ^4J = 1.26 Hz, 1 H, ArH), 7.60 (s, 1 H, ArH), 7.62 (d, ^3J = 8.08 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.91, 19.83, 26.59, 29.74, 57.56, 77.44, 83.66 (C_{quat}), 121.85 (C_{quat}), 122.11, 129.35, 129.58, 130.14 (C_{quat}), 132.73, 141.92 (C_{quat}), 146.17 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3283, 2968, 2875, 1450 cm^{-1}. HR-MS (ESI+): calcd. for $C_{16}H_{20}N_3$ [M + H]$^+$ 254.1657; found 254.1663.

4-(2,6-Diethyl-4-ethynylphenyl)-1-isobutyl-1*H*-1,2,3-triazole (18b): The synthesis of compound **18b** was according to GP6, by dissolving **17b** (350 mg, 0.80 mmol) in THF (20 mL) and adding TBAF solution (1 M in THF, 1.6 mL, 1.6 mmol). After the mixture had been stirred at room temp. for 1 h, TLC showed full conversion, and the reaction mixture was worked up. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 4:1; R_f = 0.31) to yield **18b** (209 mg, 96%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 (d, ^3J = 6.82 Hz, 6 H, CH_3), 1.04 (t, ^3J = 7.57 Hz, 6 H, CH_3), 2.24–2.32 (m, 1 H, CH), 2.38 (q, ^3J = 7.49 Hz, 4 H, CH_2), 3.08 (s, 1 H, CH), 4.25 (d, ^3J = 7.32 Hz, 2 H, CH_2), 7.28 (s, 2 H, ArH), 7.42 (s, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.30, 19.76, 26.75, 29.81, 57.54, 77.20, 83.92 (C_{quat}), 122.41 (C_{quat}), 122.81, 129.48, 129.66 (C_{quat}), 144.15 (C_{quat}), 144.45 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3285, 2967, 2873, 1465 cm^{-1}. HR-MS (ESI+): calcd. for $C_{18}H_{24}N_3$ [M + H]$^+$ 282.1970; found 282.1969.

4-{2-Ethyl-4-[3-(naphthalen-2-ylmethyl)-3*H*-1,2,3-triazol-4-yl]-phenyl}-1-isobutyl-1*H*-1,2,3-triazole (19a): Compound **19a** was synthesized according to GP7, from the alkyne **18a** (100 mg, 0.39 mmol), the azide **10** (73 mg, 0.39 mmol), cp*RuCl(PPh$_3$)$_2$ (16 mg, 20 μmol), and dioxane (2.5 mL). Purification by flash column chromatography on silica gel (hexanes/AcOEt, 1:1; R_f = 0.31) yielded **19a** as a slightly orange solid (160 mg, 89%). M.p. 139 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.99 (d, ^3J = 6.56 Hz, 6 H, CH_3), 1.05 (t, ^3J = 7.57 Hz, 3 H, CH_3), 2.28 (sept, ^3J = 6.82 Hz, 1 H, CH), 2.75 (q, ^3J = 7.57 Hz, 2 H, CH_2), 4.24 (d, ^3J = 7.32 Hz, 2 H, CH_2), 5.72 (s, 2 H, CH_2), 7.15 (d, ^4J = 1.51 Hz, 1 H, ArH), 7.18 (dd, ^4J = 1.89, ^3J = 7.95 Hz, 1 H, ArH), 7.30 (dd, J = 1.76, J = 8.58 Hz, 1 H, ArH), 7.44–7.49 (m, 2 H, ArH), 7.52 (s, 1 H, ArH), 7.60 (s, 1 H, ArH), 7.70 (d, ^3J = 7.83 Hz, 1 H, ArH), 7.72–7.73 (m, 1 H, ArH), 7.79–7.82 (m, 2 H, ArH), 7.80 (s, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.80, 19.84, 26.65, 29.76, 52.09, 57.61, 122.20, 124.70, 126.30, 126.34, 126.35, 126.47, 127.66, 127.89, 128.80, 126.68 (C_{quat}), 129.55, 129.96, 130.86 (C_{quat}), 132.91 (C_{quat}), 132.98 (C_{quat}), 133.16 (C_{quat}), 133.29, 138.05 (C_{quat}), 142.64 (C_{quat}), 145.85 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2953, 2872, 1466, 1427 cm^{-1}. HR-MS (ESI+): calcd. for $C_{27}H_{29}N_6$ [M + H]$^+$ 437.2454; found 437.2456.

4-{2,6-Diethyl-4-[3-(naphthalen-2-ylmethyl)-3*H*-1,2,3-triazol-4-yl]phenyl}-1-isobutyl-1*H*-1,2,3-triazole (19b): Compound **19b** was synthesized according to GP7, from the alkyne **18b** (89 mg, 0.33 mmol), the azide **10** (61 mg, 0.33 mmol), cp*RuCl(PPh$_3$)$_2$ (13 mg, 17 μmol), and dioxane (2.5 mL). Purification by flash column chromatography on silica gel (hexanes/AcOEt, 1:1; R_f = 0.31) yielded **19b** as a white solid (130 mg, 87%). M.p. 101 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 (d, ^3J = 6.82 Hz, 6 H, CH_3), 0.91 (t, ^3J = 7.45 Hz, 6 H, CH_3), 2.17–2.30 (m, 1 H, CH), 2.34 (q, ^3J = 7.57 Hz, 4 H, CH_2), 4.26 (d, ^3J = 7.07 Hz, 2 H, CH_2), 5.71 (s, 2 H, CH_2), 7.00 (s, 2 H, ArH), 7.32 (dd, J = 1.89, J = 8.46 Hz, 1 H, ArH), 7.43 (s, 1 H, ArH), 7.45–7.49 (m, 2 H, ArH), 7.54 (s, 1 H, ArH), 7.72–7.74 (m, 1 H, ArH), 7.78 (s, 1 H, ArH), 7.79–7.81 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.20, 19.74, 26.81, 29.80, 52.12, 57.56, 122.82, 126.37, 127.34 (C_{quat}), 124.79, 126.33, 126.37, 126.41, 126.46, 127.66, 127.88, 128.77, 130.60 (C_{quat}), 132.92 (C_{quat}), 133.06 (C_{quat}), 133.16 (C_{quat}), 143.84 (C_{quat}), 145.11 (C_{quat}), 145.15 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2967, 2873, 1462, 1454 cm^{-1}. HR-MS (ESI+): calcd. for $C_{29}H_{33}N_6$ [M + H]$^+$ 465.2767; found 465.2759.

4-[4-(3-Benzyl-3*H*-1,2,3-triazol-4-yl)-2-ethylphenyl]-1-isobutyl-1*H*-1,2,3-triazole (20): Compound **20** was synthesized according to GP7, from the alkyne **18a** (100 mg, 0.39 mmol), the azide **11** (53 mg, 0.39 mmol), cp*RuCl(PPh$_3$)$_2$ (16 mg, 20 μmol), and dioxane (2.5 mL). Purification by flash column chromatography on silica gel (hexanes/AcOEt, 1:1; R_f = 0.40) yielded **20** as a brown viscous oil (119 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.00 (d, ^3J = 6.82 Hz, 6 H, CH_3), 1.12 (t, ^3J = 7.57 Hz, 3 H, CH_3), 2.29 (sept, ^3J = 6.82 Hz, 1 H, CH), 2.80 (q, ^3J = 7.49 Hz, 2 H, CH_2), 4.24 (d, ^3J = 7.32 Hz, 2 H, CH_2), 5.57 (s, 2 H, CH_2), 7.11–7.13 (m, 2 H, ArH), 7.15–7.18 (m, 2 H, ArH), 7.29–7.30 (m, 3 H, ArH), 7.62 (s, 1 H, ArH), 7.72 (d, ^3J = 7.83 Hz, 1 H, ArH), 7.77 (s, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.80, 19.82, 26.65, 29.73, 51.84, 57.57, 122.21, 126.30, 126.62 (C_{quat}), 127.05, 128.11, 128.80, 129.45, 129.90, 130.81 (C_{quat}), 133.22, 135.59 (C_{quat}), 137.93 (C_{quat}), 142.57 (C_{quat}), 145.82 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2961, 2868, 1454 cm^{-1}. HR-MS (ESI+): calcd. for $C_{23}H_{27}N_6$ [M + H]$^+$ 387.2297; found 387.2303.

3-(2-{5-[3-Ethyl-4-(1-isobutyl-1*H*-1,2,3-triazol-4-yl)phenyl]-1*H*-1,2,3-triazol-1-yl}ethyl)-1*H*-indole (21): Compound **21** was synthesized according to GP7, from the alkyne **18a** (100 mg, 0.39 mmol), the azide **12** (74 mg, 0.39 mmol), cp*RuCl(PPh$_3$)$_2$ (16 mg, 20 μmol), and dioxane (2.5 mL). Purification by flash column chromatography on silica gel (hexanes/AcOEt, 1:1; R_f = 0.21) yielded **21** as a brown viscous oil (91 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.00 (d, ^3J = 6.82 Hz, 6 H, CH_3), 1.10 (t, ^3J = 7.57 Hz, 3 H, CH_3), 2.29 (sept, ^3J = 6.82 Hz, 1 H, CH), 2.68 (q, ^3J = 7.49 Hz, 2 H, CH_2), 3.37 (t, ^3J = 7.19 Hz, 2 H, CH_2), 4.24 (d, ^3J = 7.32 Hz, 2 H, CH_2), 4.63 (t, ^3J = 7.19 Hz, 2 H, CH_2), 6.79 (d, $^3J_{CH,NH}$ = 2.27 Hz, 1 H, ArH), 6.88 (d, ^4J = 1.51 Hz, 1 H, ArH), 6.94 (dd, ^4J = 1.76, ^3J = 7.83 Hz, 1 H, ArH), 7.01 (dd, ^3J = 7.07, ^3J = 7.32 Hz, 1 H, ArH), 7.12 (dd, ^3J = 7.07, ^3J = 7.32 Hz, 1 H, ArH), 7.25 (d, ^3J = 7.07 Hz, 1 H, ArH), 7.30 (d, ^3J = 8.08 Hz, 1 H, ArH), 7.60 (d, ^3J = 7.83 Hz, 1 H, ArH), 7.60 (s, 1 H, ArH), 7.65 (s, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.16, 19.85, 26.43, 26.68, 29.77, 48.79, 57.61, 111.17, 111.25 (C_{quat}), 118.14, 119.60, 122.09, 122.17, 122.45, 126.20, 126.83 (C_{quat}), 127.00 (C_{quat}), 129.30, 129.87, 130.46 (C_{quat}), 132.85, 136.08 (C_{quat}), 138.10 (C_{quat}), 142.61 (C_{quat}), 145.93 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3390, 2961, 2873, 1456, 1226 cm^{-1}. HR-MS (ESI+): calcd. for $C_{26}H_{30}N_7$ [M + H]$^+$ 440.2563; found 440.2560.

1-(3-*tert*-Butoxypropyl)-4-{3-methyl-4-[(triisopropylsilyl)ethynyl]-phenyl}-1*H*-1,2,3-triazole (22a): The synthesis of compound **22a** was according to GP5, by dissolving the alkyne **6d** (720 mg, 2.43 mmol) in methanol (15 mL) and using the azide **29** (420 mg, 2.67 mmol) and aqueous solutions of ascorbic acid (43 mg, 0.24 mmol) and $CuSO_4 \cdot 5H_2O$ (12 mg, 0.049 mmol). TLC (hexanes/AcOEt, 2:1; R_f = 0.43) showed complete conversion after stirring at room temp. overnight. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 2:1). As product, **22a** was obtained as a yellow oil (960 mg, 87%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14–1.16 (m, 21 H, *i*Pr), 1.18 (s, 9 H, *t*Bu), 2.16 (tt, ^3J = 6.17, ^3J = 6.26 Hz, 2 H, CH_2), 2.50 (s, 3 H, $ArCH_3$),

3.38 (t, ^3J = 5.62 Hz, 2 H, CH_2), 4.50 (t, ^3J = 6.86 Hz, 2 H, CH_2), 7.49 (d, ^3J = 7.95 Hz, 1 H, ArH), 7.55 (dd, ^4J = 1.23, ^3J = 8.09 Hz, 1 H, ArH), 7.71–7.73 (m, 1 H, ArH), 7.78 (s, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.30, 18.67, 20.95, 27.48, 30.96, 47.59, 57.58, 72.96 (C_{quat}), 95.32 (C_{quat}), 105.62 (C_{quat}), 120.22, 122.58, 122.98 (C_{quat}), 126.37, 130.41 (C_{quat}), 132.80, 141.14 (C_{quat}), 147.01 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2941, 2865, 2152, 1462, 1363, 1196 cm^{-1}. UV/Vis ($CHCl_3$): λ_{max} (lgε) = 285 nm (4.618). MS (EI): *m*/*z* (%) = 410.3 (100) [M – C_3H_7]$^+$, 453.3 (45) [M]$^+$. HR-MS (EI): calcd. for $C_{27}H_{43}N_3OSi$ [M]$^+$ 453.3175; found 453.3171. $C_{27}H_{43}N_3OSi$ (453.7): calcd. C 71.47, H 9.55, N 9.26; found C 70.72, H 9.80, N 9.09.

1-[2-(1,4-Dioxan-2-yl)ethyl]-4-{3-ethyl-4-[(triisopropylsilyl)ethynyl]phenyl}-1*H*-1,2,3-triazole (22b): The synthesis of compound **37** was according to GP5, by dissolving the alkyne **6c** (1.86 g, 6.00 mmol) and the azide **8** (1.04 g, 6.60 mmol) in methanol (50 mL) and using aqueous solutions of sodium ascorbate (119 mg, 0.60 mmol) and $CuSO_4 \cdot 5H_2O$ (30 mg, 0.12 mmol). TLC showed complete conversion after the mixture had been stirred at room temp. overnight followed by at 60 °C for 3 h. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 2:1; R_f = 0.28). Product **22b** was obtained as a white solid (2.66 g, 95%). M.p. 56 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.14–1.15 (m, 21 H, *i*Pr), 1.28 (t, ^3J = 7.45 Hz, 3 H, CH_3), 1.35 (m, 1 H), 2.02–2.14 (m, 1 H), 2.23 (dt, ^3J = 4.80, ^3J = 7.07 Hz, 2 H, CH_2), 2.88 (q, ^3J = 7.57 Hz, 2 H, CH_2), 3.71–3.77 (m, 2 H, CH_2), 4.08–4.14 (m, 2 H, CH_2), 4.53 (t, ^3J = 7.19 Hz, 2 H, CH_2), 4.57 (t, ^3J = 4.92 Hz, 1 H, CH), 7.49 (d, ^3J = 8.08 Hz, 1 H, ArH), 7.56 (dd, ^4J = 1.76, ^3J = 8.08 Hz, 1 H, ArH), 7.72 (d, ^4J = 1.26 Hz, 1 H, ArH), 7.76 (s, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.36, 14.96, 18.66, 25.62, 28.03, 35.39, 45.44, 66.86, 94.87 (C_{quat}), 98.92, 105.32 (C_{quat}), 120.09, 122.33 (C_{quat}), 122.73, 125.13, 130.59 (C_{quat}), 133.22 (C_{quat}), 147.27 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2956, 2862, 2148, 1462, 1144 cm^{-1}. HR-MS (ESI+): calcd. for $C_{27}H_{42}N_3O_2Si$ [M + H]$^+$ 468.3100; found 497.3129.

1-(3-*tert*-Butoxypropyl)-5-methyl-4-{3-methyl-4-[(triisopropylsilyl)-ethynyl]-phenyl}-1*H*-1,2,3-triazole (23a): The synthesis was according to GP8, by dissolving the triazole **22a** (910 mg, 2.01 mmol) in dry THF (32 mL) under N_2 and using *n*BuLi (1.6 M solution in hexanes, 1.89 mL, 3.02 mmol) and iodomethane (0.50 mL, 8.0 mmol). Purification by flash column chromatography on silica gel (petroleum ether/AcOEt, 2:1; R_f = 0.32) yielded **23a** as a white solid (832 mg, 88%). M.p. 79 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13–1.15 (m, 21 H, *i*Pr), 1.17 (s, 9 H, *t*Bu), 2.13 (m, 2 H, CH_2), 2.47 (s, 3 H, Ar-CH_3), 2.51 (s, 3 H, Ar-CH_3), 3.38 (t, ^3J = 5.76 Hz, 2 H, CH_2), 4.38 (t, ^3J = 6.99 Hz, 2 H, CH_2), 7.43 (dd, ^4J = 1.23, ^3J = 8.09 Hz, 1 H, ArH), 7.52 (d, ^3J = 7.95 Hz, 1 H, ArH), 7.60–7.61 (m, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.22, 11.30, 18.67, 21.00, 27.48, 30.73, 45.00 57.64, 72.93 (C_{quat}), 95.16 (C_{quat}), 105.66 (C_{quat}), 122.47 (C_{quat}), 123.89, 127.88, 129.23 (C_{quat}), 131.64 (C_{quat}), 132.56, 140.94 (C_{quat}), 143.77 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2937, 2863, 2148, 1362, 1199 cm^{-1}. UV/Vis ($CHCl_3$): λ_{max} (lgε) = 280 nm (4.405). MS (EI-MS): *m*/*z* (%) = 424.3 (100) [M – C_3H_7]$^+$, 467.3 (50) [M]$^+$. HR-MS (EI+): calcd. for $C_{28}H_{45}N_3OSi$ [M]$^+$ 467.3332; found 467.3171. $C_{28}H_{45}N_3OSi$ (467.7): calcd. C 71.90, H 9.70, N 8.98; found C 71.61, H 9.82, N 8.73.

1-[2-(1,4-Dioxan-2-yl)ethyl]-5-ethyl-4-{3-ethyl-4-[(triisopropylsilyl)-ethynyl]-phenyl}-1*H*-1,2,3-triazole (24b): The synthesis was according to GP8, by dissolving the triazole **22b** (486 mg, 1.0 mmol) in dry THF (20 mL) and using *n*BuLi (2.5 M solution in hexanes, 0.60 mL, 1.5 mmol) and iodoethane (0.33 mL, 4.0 mmol). Purification by flash column chromatography on silica gel (hexanes/AcOEt, 2:1; R_f = 0.34) yielded **24b** as a white solid (282 mg, 57%). M.p. 67 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.14–1.15 (m, 21 H, *i*Pr), 1.25 (t, ^3J = 7.57 Hz, 3 H, CH_3), 1.29 (t, ^3J = 7.45 Hz, 3 H, CH_3), 1.33–1.37 (m, 1 H), 2.02–2.14 (m, 1 H), 2.25 (dt, ^3J = 5.05, ^3J = 7.19 Hz, 2 H, CH_2), 2.87 (q, ^3J = 7.57 Hz, 2 H, CH_2), 2.89 (q, ^3J = 7.57 Hz, 2 H, CH_2), 3.71–3.78 (m, 2 H, CH_2), 4.08–4.14 (m, 2 H, CH_2), 4.39 (t, ^3J = 7.19 Hz, 2 H, CH_2), 4.62 (t, ^3J = 4.92 Hz, 1 H, CH), 7.43 (dd, ^4J = 1.76, ^3J = 7.83 Hz, 1 H, ArH), 7.52 (d, ^3J = 7.83 Hz, 1 H, ArH), 7.62 (d, ^4J = 1.51 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.36, 13.39, 14.92, 16.40, 18.67, 25.65, 28.02, 35.34, 42.76, 66.84 (2 C), 94.74 (C_{quat}), 99.07, 105.41 (C_{quat}), 121.86 (C_{quat}), 123.83, 126.60, 131.85 (C_{quat}), 133.03, 134.74 (C_{quat}), 143.42 (C_{quat}), 147.02 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2935, 2863, 2153, 1462, 1144 cm^{-1}. HR-MS (ESI+): calcd. for $C_{29}H_{46}N_3O_2Si$ [M + H]$^+$ 496.3359; found 496.3362.

2-(3-[2-(1,4-Dioxan-2-yl)ethyl]-5-{3-ethyl-4-[(triisopropylsilyl)-ethynyl]phenyl}-3*H*-1,2,3-triazol-4-yl)propan-2-ol (25b): The synthesis was according to GP8, by dissolving the triazole **22b** (351 mg, 0.75 mmol) in dry THF (20 mL) and using *n*BuLi (2.5 M solution in hexanes, 0.45 mL, 1.2 mmol) and dry acetone (0.22 mL, 3.0 mmol). Purification by flash column chromatography on silica gel (hexanes/AcOEt, 2:1; R_f = 0.16) yielded **25b** as a white solid (204 mg, 52%). M.p. 112 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.14–1.15 (m, 21 H, *i*Pr), 1.24 (t, ^3J = 7.57 Hz, 3 H, CH_3), 1.33–1.37 (m, 1 H), 1.48 (s, 6 H, CH_3), 2.02–2.15 (m, 1 H), 2.32 (dt, ^3J = 4.88, ^3J = 7.13 Hz, 2 H, CH_2), 2.53 (br. s, 1 H, OH), 2.85 (q, ^3J = 7.57 Hz, 2 H, CH_2), 3.73–3.80 (m, 2 H, CH_2), 4.08–4.12 (m, 2 H, CH_2), 4.70 (t, J = 4.80 Hz, 1 H, CH), 4.78 (t, ^3J = 7.19 Hz, 2 H, CH_2), 7.12 (dd, ^4J = 1.76, ^3J = 7.83 Hz, 1 H, ArH), 7.21 (d, $^4J_{2,6}$ = 1.51 Hz, 1 H, ArH), 7.47 (d, ^3J = 7.83 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.35, 14.86, 18.66, 25.62, 27.85, 31.65, 35.80, 45.72, 66.86 (2 C), 69.36 (C_{quat}), 94.95 (C_{quat}), 99.81, 105.17 (C_{quat}), 122.64 (C_{quat}), 127.45, 129.93, 132.42, 133.41 (C_{quat}), 138.58 (C_{quat}), 143.40 (C_{quat}), 146.40 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3224, 2958, 2864, 2151, 1461, 1148 cm^{-1}. HR-MS (ESI+): calcd. for $C_{30}H_{48}N_3O_3Si$ [M + H]$^+$ 526.3465; found 526.3473.

1-(3-*tert*-Butoxypropyl)-4-(4-ethynyl-3-methylphenyl)-5-methyl-1*H*-1,2,3-triazole (26a): The synthesis of compound **26a** was according to GP6, by dissolving **23a** (780 mg, 1.67 mmol) in THF (50 mL) and adding TBAF solution (1 M in THF, 3.34 mL, 3.34 mmol). After the mixture had been stirred at room temp. for 1.5 h, TLC (petroleum ether/AcOEt, 1:1; R_f = 0.46) showed full conversion, and the reaction mixture was worked up. The crude product was purified by flash column chromatography on silica gel (see TLC) to yield **26a** (493 mg, 95%) as a red-brown oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.17 (s, 9 H, *t*Bu), 2.13 (m, 2 H, CH_2), 2.48 (s, 3 H, Ar-CH_3), 2.50 (s, 3 H, Ar-CH_3), 3.31 (s, 1 H, CH), 3.37 (t, ^3J = 5.62 Hz, 2 H, CH_2), 4.38 (t, ^3J = 6.99 Hz, 2 H, CH_2), 7.44 (dd, ^4J = 1.37, ^3J = 7.95 Hz, 1 H, ArH), 7.52 (d, ^3J = 7.95 Hz, 1 H, ArH), 7.61–7.63 (m, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.22, 20.67, 27.48, 30.71, 45.01, 57.62, 72.95 (C_{quat}), 81.42, 82.43 (C_{quat}), 120.98 (C_{quat}), 123.96, 127.99, 129.32, 132.16 (C_{quat}), 132.75, 141.19 (C_{quat}), 143.62 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2971, 2153, 1362, 1195, 1072 cm^{-1}. UV/Vis ($CHCl_3$): λ_{max} (lgε) = 270 nm (4.253). MS (ESI): *m*/*z* (%) = 312.0 (61) [M + H]$^+$, 623.3.5 (100) [2 M + H]$^+$. HR-MS (EI+): calcd. for $C_{19}H_{25}N_3O$ [M]$^+$ 311.1998; found 311.1993.

1-[2-(1,4-Dioxan-2-yl)ethyl]-5-ethyl-4-(3-ethyl-4-ethynylphenyl)-1*H*-1,2,3-triazole (27b): The synthesis of compound **27b** was according to GP6, by dissolving **24b** (260 mg, 0.52 mmol) in THF (15 mL) and adding TBAF solution (1 M in THF, 1.0 mL, 1.0 mmol). After the mixture had been stirred at room temp. for

1.5 h, TLC showed full conversion, and the reaction mixture was worked up. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 1:1; R_f = 0.33) to yield **27b** (167 mg, 95%) as a white solid. M.p. 102 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26 (t, ^3J = 7.57 Hz, 3 H, CH_3), 1.29 (t, ^3J = 7.45 Hz, 3 H, CH_3), 1.33–1.37 (m, 1 H), 2.02–2.14 (m, 1 H), 2.26 (dt, ^3J = 4.88, ^3J = 7.26 Hz, 2 H, CH_2), 2.87 (m, 4 H), 3.29 (s, 1 H, CH), 3.71–3.78 (m, 2 H, CH_2), 4.08–4.12 (m, 2 H, CH_2), 4.39 (t, ^3J = 7.19 Hz, 2 H, CH_2), 4.61 (t, ^3J = 4.80 Hz, 1 H, CH), 7.44 (dd, ^4J = 1.76, ^3J = 7.83 Hz, 1 H, ArH), 7.52 (d, ^3J = 7.83 Hz, 1 H, ArH), 7.62 (d, ^4J = 1.26 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.39, 14.70, 16.38, 25.63, 27.62, 35.31, 42.75, 66.83 (2 C), 81.04, 82.21 (C_{quat}), 99.04, 120.39 (C_{quat}), 123.87, 126.59, 132.35 (C_{quat}), 133.13, 134.81 (C_{quat}), 143.26 (C_{quat}), 147.22 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3280, 2972, 2851, 1459, 1144 cm^{-1}. HR-MS (ESI+): calcd. for $C_{20}H_{26}N_3O_2$ $[M + H]^+$ 340.2014; found 340.2014.

2-{3-[2-(1,4-Dioxan-2-yl)ethyl]-5-(3-ethyl-4-ethynylphenyl)-3*H*-1,2,3-triazol-4-yl}propan-2-ol (28b): The synthesis of compound **28b** was according to GP6, by dissolving **25b** (191 mg, 0.36 mmol) in THF (10 mL) and adding TBAF solution (1 M in THF, 0.72 mL, 0.72 mmol). After the mixture had been stirred at room temp. for 1.5 h, TLC showed full conversion, and the reaction mixture was worked up. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 1:1; R_f = 0.20) to yield **28b** (133 mg, 100%) as a white solid. M.p. 138 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, ^3J = 7.57 Hz, 3 H, CH_3), 1.34–1.38 (m, 1 H), 1.48 (s, 6 H, CH_3), 2.04–2.15 (m, 1 H), 2.33 (dt, ^3J = 5.05, ^3J = 7.19 Hz, 2 H, CH_2), 2.49 (br. s, 1 H, OH), 2.84 (q, ^3J = 7.57 Hz, 2 H, CH_2), 3.29 (s, 1 H, CH), 3.74–3.80 (m, 2 H, CH_2), 4.09–4.13 (m, 2 H, CH_2), 4.71 (t, ^3J = 4.92 Hz, 1 H, CH), 4.79 (t, ^3J = 7.32 Hz, 2 H, CH_2), 7.14 (dd, ^4J = 1.76, ^3J = 7.83 Hz, 1 H, ArH), 7.23 (d, ^4J = 1.51 Hz, 1 H, ArH), 7.48 (d, ^3J = 7.83 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.64, 25.61, 27.45, 31.64, 35.80, 45.72, 66.88 (2 C), 69.36 (C_{quat}), 81.24, 81.98 (C_{quat}), 99.81, 121.25 (C_{quat}), 127.55, 129.96, 132.53, 133.94 (C_{quat}), 138.60 (C_{quat}), 143.29 (C_{quat}), 146.63 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3423, 3204, 2962, 2866, 1461, 1135 cm^{-1}. HR-MS (ESI+): calcd. for $C_{21}H_{28}N_3O_3$ $[M + H]^+$ 370.2131; found 370.2121.

1-(3-*tert*-Butoxypropyl)-4-{4-[1-(3-*tert*-butoxypropyl)-1*H*-1,2,3-triazol-4-yl]-3-methylphenyl}-5-methyl-1*H*-1,2,3-triazole (29a): The synthesis of compound **29a** was according to GP5, by dissolving the alkyne **26a** (447 mg, 1.43 mmol) in methanol (25 mL) and using the azide **7** (248 mg, 1.58 mmol) and aqueous solutions of ascorbic acid (25 mg, 0.14 mol) and $CuSO_4{\cdot}5H_2O$ (9 mg, 0.03 mmol). TLC (AcOEt, R_f = 0.42) showed complete conversion after the mixture had been stirred at room temp. overnight and at 40 °C for 2 h. The crude product was purified by flash column chromatography on silica gel (AcOEt). Product **29a** was obtained as a white solid (482 mg, 72%). M.p. 139 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18, 1.19 (2 s, 18 H, 2 *t*Bu), 2.10–2.23 (m, 4 H), 2.51, 2.53 (2 s, 6 H, 2 ArCH_3), 3.27–3.42 (m, 4 H), 4.40, 4.54 (2 t, J = 6.99, J = 6.86 Hz, 4 H, 2 H_2), 7.55 (dd, ^4J = 1.37, ^3J = 7.95 Hz, 1 H, ArH), 7.69–7.70 (m, 1 H, ArH), 7.71 (s, 1 H), 7.90 (d, ^3J = 7.95 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.21, 21.57, 27.49, 30.73, 30.99, 44.99, 47.46, 57.59, 57.65, 72.93 (C_{quat}), 72.95 (C_{quat}), 122.19, 124.54, 128.95, 129.17 (C_{quat}), 129.24 (C_{quat}), 129.54, 131.36 (C_{quat}), 135.68 (C_{quat}), 143.89 (C_{quat}), 146.43 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2972, 1361, 1197, 1076 cm^{-1}. UV/Vis (MeCN): λ_{max} (lgε) = 270 nm (4.415). MS (ESI): *m*/*z* (%) = 469.1 (100) $[M + H]^+$, 937.5 (27) $[2 M + H]^+$. HR-MS (EI+): calcd. for $C_{26}H_{40}N_6O_2$ $[M]^+$ 468.3213; found 468.3206. $C_{26}H_{40}N_6O_2$ (468.6): calcd. C 66.64, H 8.60, N 17.93; found C 66.64, H 8.73, N 17.94.

3-(4-{4-[1-(3-Hydroxypropyl)-1*H*-1,2,3-triazol-4-yl]-3-methylphenyl}-5-methyl-1*H*-1,2,3-triazol-1-yl)propan-1-ol (29b): Compound **29a** (100 mg, 0.205 mmol) was dissolved in dioxane (7 mL), and HCl (4 N, 1.1 mL) was added. The reaction mixture was heated at reflux for 1.5 h. The solvent was evaporated to yield the diprotonated chloride salt **29b** as a white solid (80 mg, 91%). M.p. 148 °C. ^{1}H NMR (300 MHz, CD_3OD): δ = 2.24–2.28 (m, 4 H), 2.60 (s, 3 H, Ar-CH_3), 2.70 (s, 3 H, Ar-CH_3), 3.69–3.70 (m, 4 H), 4.72–4.80 (m, 4 H), 7.71–7.76 (m, 2 H, ArH), 7.92 (d, ^3J = 7.95 Hz, 1 H, ArH), 8.76–8.82 (m, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, CD_3OD): δ = 9.48, 21.28, 32.78, 33.74, 49.49, 51.04, 59.41, 59.60, 127.54, 127.63, 128.11 (C_{quat}), 129.84 (C_{quat}), 131.68, 132.11, 136.30 (C_{quat}), 139.72 (C_{quat}), 140.68 (C_{quat}), 144.29 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3379, 2188, 1866 cm^{-1}. UV/Vis (H_2O): λ_{max} (lgε) = 256 nm (4.355). MS (ESI): *m*/*z* (%) = 357.0 (100) $[M + H]^+$, 713.3 (30) $[2 M + H]^+$. HR-MS (EI+): calcd. for $C_{18}H_{24}N_6O_2$ $[M]^+$ 356.1961; found 356.1958. $C_{18}H_{26}N_6O_2Cl_2$, (429.34): calcd. C 50.35, H 6.10, N 19.57; found C 50.07, H 5.85, N 19.39.

3-{2-[4-(4-{1-[2-(1,4-Dioxan-2-yl)ethyl]-5-ethyl-1*H*-1,2,3-triazol-4-yl}-2-ethyl-phenyl)-1*H*-1,2,3-triazol-1-yl]ethyl}-1*H*-indole (30a): The synthesis of compound **30a** was according to GP5, by dissolving the alkyne **27b** (100 mg, 0.29 mmol) and the azide **12** (61 mg, 0.32 mmol) in methanol (5 mL) and using aqueous solutions of sodium ascorbate (6 mg, 0.03 mmol) and $CuSO_4{\cdot}5H_2O$ (2 mg, 6 μmol). TLC showed complete conversion after the mixture had been stirred at room temp. overnight. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEtm, 1:4; R_f = 0.42). Product **30a** was obtained as a white solid (126 mg, 83%). M.p. 61 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12 (t, ^3J = 7.57 Hz, 3 H, CH_3), 1.27 (t, ^3J = 7.57 Hz, 3 H, CH_3), 1.34–1.38 (m, 1 H), 2.05–2.14 (m, 1 H), 2.27 (dt, ^3J = 4.80, ^3J = 7.19 Hz, 2 H, CH_2), 2.68 (q, ^3J = 7.49 Hz, 2 H, CH_2), 2.89 (q, ^3J = 7.66 Hz, 2 H, CH_2), 3.44 (t, ^3J = 6.69 Hz, 2 H, CH_2), 3.72–3.79 (m, 2 H, CH_2), 4.09–4.13 (m, 2 H, CH_2), 4.40 (t, ^3J = 7.32 Hz, 2 H, CH_2), 4.62 (t, ^3J = 4.92 Hz, 1 H, CH), 4.75 (t, ^3J = 6.82 Hz, 2 H, CH_2), 6.89 (d, $^3J_{CH,NH}$ = 2.27 Hz, 1 H, CH), 7.14 (t, ^3J = 7.45 Hz, 1 H, Ar), 7.22 (t, ^3J = 7.70 Hz, 1 H, ArH), 7.24 (s, 1 H, ArH), 7.39 (d, ^3J = 8.08 Hz, 1 H, ArH), 7.50 (dd, ^4J = 1.76, ^3J = 8.08 Hz, 1 H, ArH), 7.57 (d, ^3J = 7.57 Hz, 1 H, ArH), 7.63 (d, ^3J = 8.08 Hz, 1 H, ArH), 7.67 (d, ^4J = 1.51 Hz, 1 H, ArH), 8.08 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.44, 15.07, 16.37, 25.63, 26.62, 26.71, 35.32, 42.76, 50.74, 66.83 (2 C), 99.08, 111.25 (C_{quat}), 111.44, 118.20, 119.76, 122.36 (2 C), 122.71, 124.25, 126.78 (C_{quat}), 127.67, 128.81 (C_{quat}), 129.68, 131.59 (C_{quat}), 134.71 (C_{quat}), 136.31 (C_{quat}), 142.17 (C_{quat}), 143.56 (C_{quat}), 146.14 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3263, 2967, 2862, 1456, 1144 cm^{-1}. HR-MS (ESI+): calcd. for $C_{30}H_{36}N_7O_2$ $[M + H]^+$ 526.2930; found 526.2919.

2-[3-[2-(1,4-Dioxan-2-yl)ethyl]-5-(4-{1-[2-(1*H*-indol-3-yl)ethyl]-1*H*-1,2,3-triazol-4-yl}-3-ethylphenyl)-3*H*-1,2,3-triazol-4-yl]propan-2-ol (30b): Compound **30b** was synthesized according to GP5, by dissolving the alkyne **28b** (148 mg, 0.40 mmol) and the azide **12** (82 mg, 0.44 mmol) in methanol (10 mL) and using aqueous solutions of sodium ascorbate (8 mg, 0.04 mmol) and $CuSO_4{\cdot}5H_2O$ (2 mg, 8 μmol). TLC showed complete conversion after the mixture had been stirred at room temp. overnight. The crude product was purified by flash column chromatography on silica (hexanes/AcOEt, 1:4; R_f = 0.20). Product **30b** was obtained as a white solid (138 mg, 63%). M.p. 131 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (t, ^3J = 7.45 Hz, 3 H, CH_3), 1.30–1.34 (m, 1 H), 1.41 (s, 6 H, CH_3), 2.01–2.11 (m, 1 H), 2.27–2.32 (m, 2 H, CH_2), 2.55 (q, ^3J = 7.41 Hz, 2 H, CH_2), 3.36 (t, ^3J = 6.44 Hz, 2 H, CH_2), 3.71–3.76 (m, 2 H, CH_2), 4.05–4.09 (m, 3 H, CH_2, OH), 4.67–4.71 (m, 3 H, CH, CH_2), 4.76 (t, ^3J = 7.19 Hz, 2 H, CH_2), 6.72 (d, $^3J_{CH,NH}$ =

2.02 Hz, 1 H, ArH), 7.04–7.10 (m, 2 H, ArH), 7.13–7.17 (m, 3 H, ArH), 7.35 (d, ^3J = 8.08 Hz, 1 H, ArH), 7.44 (d, ^3J = 7.83 Hz, 1 H, ArH), 7.52 (d, ^3J = 7.83 Hz, 1 H, ArH), 9.05 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.95, 25.58, 26.31, 26.64, 31.48, 35.75, 45.83, 50.70, 66.75 (2 C), 68.94 (C_{quat}), 99.78, 110.56 (C_{quat}), 111.60, 117.97, 119.41, 121.98, 122.70, 123.06, 126.65 (C_{quat}), 127.69, 129.12, 129.34 (C_{quat}), 130.76, 133.76 (C_{quat}), 136.37 (C_{quat}), 139.06 (C_{quat}), 141.61 (C_{quat}), 143.19 (C_{quat}), 145.81 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3396, 3289, 2963, 2865, 1457, 1143 cm^{-1}. HR-MS (ESI+): calcd. for $C_{31}H_{38}N_7O_3$ $[M + H]^+$ 556.3036; found 556.3029.

4-[4-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)-3-ethylphenyl]-1-[2-(1,4-dioxan-2-yl)ethyl]-5-ethyl-1*H*-1,2,3-triazole (31a): The synthesis of compound **31a** was according to GP5, by dissolving the alkyne **27b** (97 mg, 0.28 mmol) and the azide **11** (42 mg, 0.31 mmol) in methanol (3 mL) and using aqueous solutions of sodium ascorbate (6 mg, 0.03 mmol) and $CuSO_4 \cdot 5H_2O$ (2 mg, 6 μmol). TLC showed complete conversion after the mixture had been stirred at room temp. overnight. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 1:4; R_f = 0.52). Product **31a** was obtained as a white solid (104 mg, 79%). M.p. 117 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22 (t, ^3J = 7.45 Hz, 3 H, CH_3), 1.27 (t, ^3J = 7.57 Hz, 3 H, CH_3), 1.34–1.37 (m, 1 H), 2.04–2.16 (m, 1 H), 2.26 (dt, ^3J = 4.88, ^3J = 7.19 Hz, 2 H, CH_2), 2.85 (q, ^3J = 7.41 Hz, 2 H, CH_2), 2.89 (q, ^3J = 7.49 Hz, 2 H, CH_2), 3.71–3.78 (m, 2 H, CH_2), 4.08–4.12 (m, 2 H, CH_2), 4.40 (t, ^3J = 7.19 Hz, 2 H, CH_2), 4.62 (t, ^3J = 4.80 Hz, 1 H, CH), 5.61 (s, 2 H, CH_2), 7.30–7.33 (m, 2 H, ArH), 7.36–7.42 (m, 3 H, ArH), 7.52 (dd, ^4J = 1.89, ^3J = 7.95 Hz, 1 H, ArH), 7.57 (s, 1 H, ArH), 7.68 (d, ^3J = 8.33 Hz, 1 H, ArH), 7.70 (d, ^4J = 1.76 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.44, 15.11, 16.39, 25.64, 26.82, 35.34, 42.75, 54.16, 66.83 (2 C), 99.09, 121.61, 124.30, 127.77, 127.96, 128.73, 129.14, 128.63 (C_{quat}), 129.72, 131.82 (C_{quat}), 134.70 (C_{quat}), 134.78 (C_{quat}), 142.30 (C_{quat}), 143.56 (C_{quat}), 147.31 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2967, 2854, 1457, 1126 cm^{-1}. HR-MS (ESI+): calcd. for $C_{27}H_{33}N_6O_2$ $[M + H]^+$ 473.2665; found 473.2666.

1-[2-(1,4-Dioxan-2-yl)ethyl]-5-ethyl-4-{3-ethyl-4-[1-(naphthalen-2-ylmethyl)-1*H*-1,2,3-triazol-4-yl]phenyl}-1*H*-1,2,3-triazole (31b): The synthesis of compound **31b** was according to GP5, by dissolving the alkyne **27b** (75 mg, 0.22 mmol) and the azide **10** (45 mg, 0.24 mmol) in methanol (3 mL) and using aqueous solutions of sodium ascorbate (5 mg, 0.02 mmol) and $CuSO_4 \cdot 5H_2O$ (1 mg, 4 μmol). TLC showed complete conversion after the mixture had been stirred at room temp. overnight. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 1:4; R_f = 0.49). Product **31b** was obtained as a white viscous oil (66 mg, 59%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22 (t, ^3J = 7.57 Hz, 3 H, CH_3), 1.26 (t, ^3J = 7.57 Hz, 3 H, CH_3), 1.35 (m, 1 H), 2.02–2.14 (m, 1 H), 2.26 (dt, ^3J = 4.96, ^3J = 7.26 Hz, 2 H, CH_2), 2.85 (q, ^3J = 7.49 Hz, 2 H, CH_2), 2.89 (q, ^3J = 7.57 Hz, 2 H, CH_2), 3.71–3.78 (m, 2 H, CH_2), 4.08–4.12 (m, 2 H, CH_2), 4.40 (t, ^3J = 7.19 Hz, 2 H, CH_2), 4.62 (t, ^3J = 4.80 Hz, 1 H, CH), 5.78 (s, 2 H, CH_2), 7.41 (dd, ^4J = 1.76, ^3J = 8.33 Hz, 1 H, ArH), 7.50–7.53 (m, 3 H, ArH), 7.61 (s, 1 H, ArH), 7.67–7.70 (m, 2 H, ArH), 7.79 (s, 1 H, ArH), 7.82–7.88 (m, 3 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.41, 15.09, 16.36, 25.61, 26.81, 35.32, 42.72, 54.33, 66.80 (2 C), 99.05, 121.70, 124.27, 125.21, 127.24, 126.68, 126.72, 127.72, 127.77, 127.90, 129.16, 128.60 (C_{quat}), 129.71, 131.79 (C_{quat}), 132.12 (C_{quat}), 133.21 (C_{quat}), 133.21 (C_{quat}), 134.68 (C_{quat}), 142.28 (C_{quat}), 143.52 (C_{quat}), 147.35 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2967, 2851, 1454, 1138 cm^{-1}. HR-MS (ESI+): calcd. for $C_{31}H_{35}N_6O_2$ $[M + H]^+$ 523.2821; found 523.2822.

4-{3-Ethyl-4-[(triisopropylsilyl)ethynyl]phenyl}-1-(5-isopropyl-2-methylphenyl)-1*H*-1,2,3-triazole (32): Compound **32** was synthesized according to GP5, by dissolving the alkyne **6c** (124 mg, 0.40 mmol) and the azide **9** (84 mg, 0.48 mmol) in methanol (6 mL) and using aqueous solutions of sodium ascorbate (8 mg, 0.04 mmol) and $CuSO_4 \cdot 5H_2O$ (2 mg, 8 μmol). TLC showed complete conversion after the mixture had been stirred at room temp. overnight. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 2:1; R_f = 0.67). Product **32** was obtained as a yellow oil (170 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15–1.16 (m, 21 H, *i*Pr), 1.27 (d, ^3J = 7.07 Hz, 6 H, CH_3), 1.31 (t, ^3J = 7.57 Hz, 3 H, CH_3), 2.22 (s, 3 H, Ar-CH_3), 2.91 (q, ^3J = 7.49 Hz, 2 H, CH_2), 2.94 (sept, ^3J = 6.97 Hz, 1 H, CH), 7.23 (s, 1 H, ArH), 7.29–7.30 (m, 2 H, ArH), 7.54 (d, ^3J = 7.83 Hz, 1 H, ArH), 7.65 (dd, ^4J = 1.64, ^3J = 7.95 Hz, 1 H, ArH), 7.82 (d, ^4J = 1.26 Hz, 1 H, ArH), 7.97 (s, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.35, 14.98, 17.42, 18.66, 23.83, 28.04, 33.53, 95.00 (C_{quat}), 105.31 (C_{quat}), 121.39, 122.51 (C_{quat}), 122.84, 123.92, 125.25, 128.10, 130.31 (C_{quat}), 130.81 (C_{quat}), 131.35, 133.29, 136.28 (C_{quat}), 147.12 (C_{quat}), 147.35 (C_{quat}), 147.98 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2956, 2862, 2142, 1459 cm^{-1}. HR-MS (ESI+): calcd. for $C_{31}H_{44}N_3Si$ $[M + H]^+$ 486.3304; found 486.3306.

5-Ethyl-4-{3-ethyl-4-[(triisopropylsilyl)ethynyl]phenyl}-1-(5-isopropyl-2-methylphenyl)-1*H*-1,2,3-triazole (33): The synthesis was according to GP8, by dissolving the triazole **32** (150 mg, 0.31 mmol) in dry THF (10 mL) and using *n*BuLi (1.6 M solution in hexanes, 0.30 mL, 0.47 mmol) and iodoethane (0.10 mL, 1.24 mmol). Purification by flash column chromatography on silica gel (hexanes/AcOEt, 4:1; R_f = 0.65) yielded **33** as a yellow oil (128 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (t, ^3J = 7.57 Hz, 3 H, CH_3), 1.15–1.16 (m, 21 H, *i*Pr), 1.27 (d, ^3J = 7.07 Hz, 6 H, CH_3), 1.31 (t, ^3J = 7.45 Hz, 3 H, CH_3), 2.04 (s, 3 H, Ar-CH_3), 2.72 (q, ^3J = 7.49 Hz, 2 H, CH_2), 2.92 (q, ^3J = 7.66 Hz, 2 H, CH_2), 2.95 (sept, ^3J = 7.01 Hz, 1 H, CH), 7.13 (s, 1 H, ArH), 7.32–7.33 (m, 2 H, ArH), 7.54–7.55 (m, 2 H, ArH), 7.74 (d, $^4J_{2,6}$ = 1.01 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.38, 12.96, 14.96, 16.83, 18.69 (2 C), 23.86, 28.07, 33.49, 94.84 (C_{quat}), 105.41 (C_{quat}), 121.98 (C_{quat}), 123.80, 125.39, 126.58, 128.62, 131.10, 131.66 (C_{quat}), 132.88 (C_{quat}), 133.11, 135.11 (C_{quat}), 136.17 (C_{quat}), 147.13 (C_{quat}), 147.88 (C_{quat}), 148.01 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2956, 2862, 2148, 1459 cm^{-1}. HR-MS (ESI+): calcd. for $C_{33}H_{48}N_3Si$ $[M + H]^+$ 514.3618; found 497.3607.

5-Ethyl-4-(3-ethyl-4-ethynylphenyl)-1-(5-isopropyl-2-methylphenyl)-1*H*-1,2,3-triazole (34): The synthesis of compound **34** was according to GP6, by dissolving **33** (112 mg, 0.22 mmol) in THF (15 mL) and adding TBAF solution (1 M in THF, 0.44 mL, 0.44 mmol). After the mixture had been stirred at room temp. for 1 h, TLC showed full conversion, and the reaction mixture was worked up. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 4:1; R_f = 0.66) to yield **34** (67 mg, 85%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (t, ^3J = 7.50 Hz, 3 H, CH_3), 1.26 (d, ^3J = 6.82 Hz, 6 H, CH_3), 1.31 (t, ^3J = 7.57 Hz, 3 H, CH_3), 2.03 (s, 3 H, Ar-CH_3), 2.73 (q, ^3J = 7.66 Hz, 2 H, CH_2), 2.90 (q, ^3J = 7.41 Hz, 2 H, CH_2), 2.93 (sept, ^3J = 6.86 Hz, 1 H, CH), 3.03 (s, 1 H, CH), 7.13 (s, 1 H, ArH), 7.31–7.32 (m, 2 H, ArH), 7.55–7.56 (m, 2 H, ArH), 7.75–7.76 (m, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.93, 14.72, 16.75, 17.65, 23.79, 27.63, 33.43, 81.11, 82.16 (C_{quat}), 120.49 (C_{quat}), 123.79, 125.29, 126.52, 128.61, 131.06, 132.11 (C_{quat}), 132.79 (C_{quat}), 133.16, 135.00 (C_{quat}), 136.22 (C_{quat}), 142.86 (C_{quat}), 147.27 (C_{quat}), 147.83 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3285, 2956, 2873, 1456 cm^{-1}. HR-MS (ESI+): calcd. for $C_{24}H_{28}N_3$ $[M + H]^+$ 358.2283; found 358.2279.

3-[2-(4-{2-Ethyl-4-[5-ethyl-1-(5-isopropyl-2-methylphenyl)-1*H*-1,2,3-triazol-4-yl]phenyl}-1*H*-1,2,3-triazol-1-yl)ethyl]-1*H*-indole (35): Compound **35** was synthesized according to GP5, by dissolving the alkyne **34** (55 mg, 0.15 mmol) and the azide **12** (31 mg, 0.17 mmol) in methanol (3 mL) and using aqueous solutions of sodium ascorbate (3 mg, 15 μmol) and $CuSO_4 \cdot 5H_2O$ (1 mg, 3 μmol). TLC showed complete conversion after the mixture had been stirred at room temp. overnight. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 1:1; R_f = 0.46). Product **35** was obtained as a white solid (63 mg, 77%). M.p. 161 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.07 (t, ^3J = 7.45 Hz, 3 H, CH_3), 1.13 (t, ^3J = 7.57 Hz, 3 H, CH_3), 1.27 (d, ^3J = 6.82 Hz, 6 H, CH_3), 2.04 (s, 3 H, CH_3), 2.69 (q, ^3J = 7.49 Hz, 2 H, CH_2), 2.74 (q, ^3J = 7.49 Hz, 2 H, CH_2), 2.95 (sept, ^3J = 6.88 Hz, 1 H, CH), 3.43 (t, ^3J = 6.69 Hz, 2 H, CH_2), 4.75 (t, ^3J = 6.82 Hz, 2 H, CH_2), 6.87 (d, $^3J_{CH,NH}$ = 2.27 Hz, 1 H, ArH), 7.11–7.15 (m, 2 H, ArH), 7.20 (t, ^3J = 7.07 Hz, 1 H, ArH), 7.27 (s, 1 H, ArH), 7.30–7.32 (m, 2 H, ArH), 7.38 (d, ^3J = 8.08 Hz, 1 H, ArH), 7.56 (d, ^3J = 7.83 Hz, 1 H, ArH), 7.60 (dd, ^4J = 1.76, ^3J = 8.08 Hz, 1 H, ArH), 7.67 (d, ^3J = 8.08 Hz, 1 H, ArH), 7.78 (d, ^4J = 1.26 Hz, 1 H, ArH), 8.47 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.99, 15.10, 16.76, 16.79, 23.82, 26.64, 26.70, 33.45, 50.75, 111.09 (C_{quat}), 111.49, 118.14, 119.67, 122.26, 122.41, 122.79, 124.20, 125.34, 126.76 (C_{quat}), 127.63, 128.59, 128.92 (C_{quat}), 129.74, 131.07, 131.37 (C_{quat}), 132.84 (C_{quat}), 135.11 (C_{quat}), 136.12 (C_{quat}), 136.33 (C_{quat}), 142.26 (C_{quat}), 143.21 (C_{quat}), 146.08 (C_{quat}), 147.84 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3263, 2961, 2868, 1456 cm^{-1}. HR-MS (ESI+): calcd. for $C_{34}H_{38}N_7$ $[M + H]^+$ 544.3189; found 544.3153.

1,8-Bis(4-{3-ethyl-4-[(triisopropylsilyl)ethynyl]phenyl}-1*H*-1,2,3-triazol-1-yl)octane (36): Compound **36** was synthesized according to GP5, by dissolving the alkyne **6c** (280 mg, 0.90 mmol, 2.1 equiv.) and the azide **13** (83 mg, 0.42 mmol, 1.0 equiv.) in methanol (5 mL) and using aqueous solutions of sodium ascorbate (16 mg, 0.08 mmol, 0.2 equiv.) and $CuSO_4 \cdot 5H_2O$ (4 mg, 17 μmol, 0.04 equiv.). TLC showed complete conversion after the mixture had been stirred at room temp. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 2:1; R_f = 0.31). Product **36** was obtained as a white solid (266 mg, 78%). M.p. 119 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.13 (m, 42 H, *i*Pr), 1.27 (t, J = 7.57 Hz, 6 H, CH_3), 1.30–1.33 (m, 8 H, CH_2), 1.88–1.94 (m, 4 H, CH_2), 2.87 (q, J = 7.57 Hz, 4 H, CH_2), 4.35 (t, J = 7.07 Hz, 4 H, NCH_2), 7.49 (d, ^3J = 7.83 Hz, 2 H, ArH), 7.56 (dd, ^4J = 1.76, ^3J = 8.08 Hz, 2 H, ArH), 7.72 (d, ^4J = 1.26 Hz, 2 H, ArH), 7.75 (s, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.31, 14.94, 18.62, 27.99, 26.18, 28.59, 30.15, 50.26, 94.86 (C_{quat}), 105.28 (C_{quat}), 119.67, 122.27 (C_{quat}), 122.67, 125.06, 130.54 (C_{quat}), 133.18, 147.24 (C_{quat}), 147.27 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2939, 2857, 2148, 1459 cm^{-1}. HR-MS (ESI+): calcd. for $C_{50}H_{76}N_6Si_2Na$ $[M + Na]^+$ 839.5568; found 839.5545.

1,8-Bis(5-ethyl-4-{3-ethyl-4-[(triisopropylsilyl)ethynyl]phenyl}-1*H*-1,2,3-triazol-1-yl)octane (37): The synthesis was according to GP8, by dissolving the triazole **36** (220 mg, 0.27 mmol) in dry THF (20 mL) and using *n*BuLi (1.6 M solution in hexanes, 0.51 mL, 0.81 mmol) and iodoethane (0.20 mL, 2.16 mmol). Purification by flash column chromatography on silica gel (hexane/AcOEt, 2:1; R_f = 0.44) yielded **37** as an orange oil (130 mg, 56%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.14–1.15 (m, 42 H, *i*Pr), 1.24 (t, ^3J = 7.57 Hz, 6 H, CH_3), 1.28 (t, ^3J = 7.57 Hz, 6 H, CH_3), 1.35–1.40 (m, 8 H), 1.91–1.95 (m, 4 H), 2.85 (q, ^3J = 7.49 Hz, 4 H, CH_2), 2.88 (q, ^3J = 7.49 Hz, 4 H, CH_2), 4.25 (t, ^3J = 7.32 Hz, 4 H, NCH_2), 7.42 (dd, ^4J = 1.76, ^3J = 7.83 Hz, 2 H, ArH), 7.52 (d, ^3J = 7.83 Hz, 2 H, ArH), 7.61 (d, ^4J = 1.26 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.34, 13.42, 14.91, 16.57, 18.65, 28.01, 26.50, 28.85, 30.27, 47.82, 94.74 (C_{quat}), 105.37 (C_{quat}), 121.85 (C_{quat}), 123.80, 126.57, 131.82 (C_{quat}), 133.02, 134.39 (C_{quat}), 143.46 (C_{quat}), 147.01 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 2934, 2868, 2148, 1462 cm^{-1}. HR-MS (ESI+): calcd. for $C_{54}H_{85}N_6Si_2$ $[M + H]^+$ 873.6374; found 873.6404.

1,8-Bis[5-ethyl-4-(3-ethyl-4-ethynylphenyl)-1*H*-1,2,3-triazol-1-yl]-octane (38): The synthesis of compound **38** was according to GP6, by dissolving **37** (114 mg, 0.13 mmol) in THF (10 mL) and adding TBAF solution (1 M in THF, 0.26 mL, 0.26 mmol). After the mixture had been stirred at room temp. for 1 h, TLC showed full conversion, and the reaction mixture was worked up. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 2:1; R_f = 0.31) to yield **38** (99 mg, 95%) as an orange oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, ^3J = 7.70 Hz, 6 H, CH_3), 1.27 (t, ^3J = 7.57 Hz, 6 H, CH_3), 1.33–1.37 (m, 8 H), 1.90–1.97 (m, 4 H), 2.85 (q, ^3J = 7.41 Hz, 4 H, CH_2), 2.86 (q, ^3J = 7.41 Hz, 4 H, CH_2), 3.28 (s, 2 H, CH), 4.22–4.29 (m, 4 H), 7.42 (dd, ^4J = 1.51, ^3J = 8.08 Hz, 2 H, ArH), 7.51 (d, ^3J = 7.83 Hz, 2 H, ArH), 7.62 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.39, 14.66, 16.51, 27.56, 26.43, 28.84, 30.19, 47.78, 81.05, 82.13 (C_{quat}), 120.35 (C_{quat}), 123.79, 126.50, 132.82 (C_{quat}), 133.07, 134.44 (C_{quat}), 143.24 (C_{quat}), 147.16 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3285, 2967, 2857, 1456 cm^{-1}. HR-MS (ESI+): calcd. for $C_{36}H_{45}N_6$ $[M + H]^+$ 561.3706; found 561.3707.

1,8-Bis[4-(4-{1-[2-(1*H*-indol-3-yl)ethyl]-1*H*-1,2,3-triazol-4-yl}-3-ethylphenyl)-5-ethyl-1*H*-1,2,3-triazol-1-yl]octane (39): Compound **39** was synthesized according to GP5, by dissolving the alkyne **38** (85 mg, 0.11 mmol, 1.0 equiv.) and the azide **12** (44 mg, 0.23 mmol, 2.2 equiv.) in methanol (5 mL) and using aqueous solutions of sodium ascorbate (5 mg, 0.02 mmol, 0.2 equiv.) and $CuSO_4 \cdot 5H_2O$ (2 mg, 5 μmol, 0.04 equiv.). TLC showed complete conversion after the mixture had been stirred at room temp. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 1:2; R_f = 0.10). Product **39** was obtained as a green-brown oil (42 mg, 42%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.07 (t, J = 7.45 Hz, 6 H, CH_3), 1.24 (t, ^3J = 7.45 Hz, 6 H, CH_3), 1.33–1.38 (m, 8 H, CH_2), 1.89–1.96 (m, 4 H, CH_2), 2.63 (q, ^3J = 7.57 Hz, 4 H, CH_2), 2.85 (q, ^3J = 7.41 Hz, 4 H, CH_2), 3.40 (t, ^3J = 6.56 Hz, 4 H, CH_2), 4.25 (t, ^3J = 7.19 Hz, 4 H, NCH_2), 4.72 (t, ^3J = 6.56 Hz, 4 H, NCH_3), 6.83 (d, $^3J_{N,H}$ = 1.76 Hz, 2 H, ArH), 7.11 (dd, ^3J = 6.94, ^3J = 7.45 Hz, 2 H, ArH), 7.18 (dd, ^3J = 7.45, ^3J = 7.78 Hz, 2 H, ArH), 7.23 (s, 2 H, ArH), 7.36 (d, ^3J = 8.08 Hz, 2 H, ArH), 7.47 (dd, ^4J = 1.38, ^3J = 7.95 Hz, 2 H, ArH), 7.53 (d, ^3J = 7.83 Hz, 2 H, ArH), 7.61 (d, ^3J = 8.08 Hz, 2 H, ArH), 7.64 (m, 2 H, ArH), 8.70 (br. s, 2 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.46, 15.02, 16.50, 26.43, 26.57, 26.67, 28.78, 30.20, 47.81, 50.72, 110.91 (C_{quat}), 111.52, 118.08, 119.55, 122.14, 122.43, 122.86, 124.19, 126.73 (C_{quat}), 127.59, 128.80 (C_{quat}), 129.65, 131.53 (C_{quat}), 134.40 (C_{quat}) 136.34 (C_{quat}), 142.16 (C_{quat}), 143.59 (C_{quat}), 146.02 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3258, 2967, 2857, 1454 cm^{-1}. HR-MS (ESI+): calcd. for $C_{56}H_{65}N_{14}$ $[M + H]^+$ 933.5517; found 933.5461.

3-(Naphthalen-2-ylmethyl)benzaldehyde (42): In a microwave vial, containing a stirring bar, Na_2CO_3 (1.21 g, 11.4 mmol, 2.1 equiv.) was dissolved in H_2O (5.5 mL). The benzyl chloride derivative **41** (852 mg, 5.44 mmol, 1.0 equiv.) and DME (11.0 mL) were added, followed by 2-naphthylboronic acid (1.12 g, 6.53 mmol, 1.2 equiv.) and $Pd(PPh_3)_4$ (126 mg, 0.109 mmol, 2 mol-%). The reaction mixture was heated in a microwave oven at 130 °C for 4 h. H_2O was added to the solution, and the phases were separated. The aqueous phase was extracted twice with AcOEt, and the combined organic extracts were dried with $MgSO_4$. The solvent was evaporated, and the crude product was purified by flash column chromatography

on silica gel (hexanes/AcOEt, 8:1; R_f = 0.50). Compound **42** was obtained as a yellow oil (937 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.22 (s, 2 H, CH_2), 7.30 (dd, ^4J = 1.64, ^3J = 8.46 Hz, 1 H, ArH), 7.44–7.52 (m, 4 H, ArH), 7.64–7.65 (m, 1 H, ArH), 7.72–7.82 (m, 5 H, ArH), 9.98 (s, 1 H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.45, 125.59, 126.16, 127.24, 127.33, 127.53, 127.64, 127.87, 128.36, 129.18, 129.98, 132.16 (C_{quat}), 133.56 (C_{quat}), 135.14, 136.67 (C_{quat}), 137.55 (C_{quat}), 142.15 (C_{quat}), 192.42 ppm. IR: $\tilde{\nu}$ = 3049, 2824, 1695 cm^{-1}. HR-MS (EI+): calcd. for $C_{18}H_{14}O$ [M]$^+$ 246.1045; found 246.1039.

2-(3-Ethynylbenzyl)naphthalene (43): Diisopropylamine (0.62 mL, 4.34 mmol, 1.2 equiv.) was dissolved in dry THF (30 mL) under argon in a flame-dried flask. The solution was cooled to –78 °C, and *n*BuLi (1.6 M solution in hexanes, 2.72 mL, 4.34 mmol, 1.2 equiv.) was slowly added dropwise. After the mixture had been stirred at that temp. for 10 min, $TMSCHN_2$ (2 M solution in hexanes, 2.17 mL, 4.34 mmol, 1.2 equiv.) was slowly added. The reaction mixture was stirred at –78 °C for 30 min, and a solution of the aldehyde **42** (890 mg, 3.61 mmol, 1.0 equiv.) in dry THF (8 mL) was added dropwise. After stirring at –78 °C for 1 h, the reaction mixture was heated at reflux for 3 h. H_2O was added, and the phases were separated. The aqueous phase was extracted twice with diethyl ether. The combined organic extracts were dried with $MgSO_4$ and concentrated. Purification of the crude product by flash column chromatography (hexanes/AcOEt, 10:1; R_f = 0.62) yielded **43** as a white solid (650 mg, 74%). M.p. 56 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.05 (s, 1 H, CH), 4.13 (s, 2 H, CH_2), 7.22–7.49 (m, 7 H, ArH), 7.64–7.65 (m, 1 H, ArH), 7.77–7.83 (m, 3 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.47, 77.07, 83.69 (C_{quat}), 122.17 (C_{quat}), 125.45, 126.04, 127.16, 127.46, 127.53, 127.61, 128.20, 128.46, 129.61, 129.98, 132.10 (C_{quat}), 132.63, 133.55 (C_{quat}), 137.88 (C_{quat}), 141.18 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3289, 3054, 2906, 1599, 1480 cm^{-1}. HR-MS (EI+): calcd. for $C_{19}H_{14}$ [M]$^+$ 242.1096; found 242.1095.

1-(5-Isopropyl-2-methylphenyl)-4-[3-(naphthalen-2-ylmethyl)phenyl]-1*H*-1,2,3-triazole (44): Compound **44** was synthesized according to GP5, by dissolving the alkyne **43** (600 mg, 2.47 mmol) and the azide **9** (477 mg, 2.72 mmol) in methanol (40 mL) and using aqueous solutions of sodium ascorbate (49 mg, 0.25 mmol) and $CuSO_4 \cdot 5H_2O$ (13 mg, 49 μmol). TLC showed complete conversion after the mixture had been stirred at room temp. overnight and at 65 °C for additional 2 h. The crude product was purified by flash column chromatography on silica gel (hexanes/AcOEt, 6:1; R_f = 0.46). Product **44** was obtained as a viscous colorless oil (888 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26 (d, ^3J = 6.56 Hz, 6 H, CH_3), 2.20 (s, 3 H, CH_3), 2.94 (sept, ^3J = 6.94 Hz, 1 H, CH), 4.22 (s, 2 H, CH_2), 7.22–7.25 (m, 2 H, ArH), 7.28–7.29 (m, 2 H, ArH), 7.35–7.45 (m, 4 H, ArH), 7.68–7.69 (m, 1 H, ArH), 7.75–7.81 (m, 4 H, ArH), 7.84–7.85 (m, 1 H, ArH), 7.91 (s, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.40, 23.84, 33.52, 42.10, 121.23, 123.74, 123.96, 125.37, 125.98, 126.47, 127.13, 127.56 (2×), 127.59, 128.04, 128.13, 129.06, 129.09, 130.63 (C_{quat}), 130.85 (C_{quat}), 131.32, 132.09 (C_{quat}), 133.59 (C_{quat}), 136.33 (C_{quat}), 138.37 (C_{quat}), 141.72 (C_{quat}), 147.48 (C_{quat}), 147.95 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3051, 2961, 1508, 1457 cm^{-1}. HR-MS (ESI+): calcd. for $C_{29}H_2N_3$ [M + H]$^+$ 418.2283; found 418.2300.

1-{3-(5-Isopropyl-2-methylphenyl)-5-[3-(naphthalen-2-ylmethyl)-phenyl]-3*H*-1,2,3-triazol-4-yl}ethanol (45): The synthesis was according to GP8, by dissolving the triazole **44** (150 mg, 0.36 mmol) in dry THF (15 mL) and using *n*BuLi (1.6 M solution in hexanes, 0.34 mL, 0.54 mmol) and acetaldehyde (0.10 mL, 1.4 mmol). Purification by flash column chromatography on silica gel (hexanes/AcOEt, 4:1; R_f = 0.30) yielded **45** as a colorless oil (97 mg, 59%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.23–1.25 (m, 9 H), 1.86 (br. s, 1 H, OH), 2.04 (s, 3 H, CH_3), 2.92 (sept, ^3J = 6.88 Hz, 1 H, CH), 4.22 (s, 2 H, CH_2), 4.90–4.97 (m, 1 H, CH), 7.18–7.19 (m, 1 H, ArH), 7.27–7.32 (m, 3 H, ArH), 7.35–7.46 (m, 4 H, ArH), 7.69–7.71 (m, 2 H, ArH), 7.74–7.80 (m, 4 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.93, 23.79, 23.82, 33.42, 42.04, 61.01, 125.35, 125.71, 125.98, 126.55, 127.24, 127.52, 127.58, 127.72, 128.09, 128.69 (2×), 128.84, 129.47, 131.01, 131.24 (C_{quat}), 132.05 (C_{quat}), 133.03 (C_{quat}), 133.57 (C_{quat}), 135.49 (C_{quat}), 136.35 (C_{quat}), 138.45 (C_{quat}), 141.42 (C_{quat}), 144.79 (C_{quat}), 147.69 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3307, 2962, 2927, 1508, 1454 cm^{-1}. HR-MS (ESI+): calcd. for $C_{31}H_{32}N_3O$ [M + H]$^+$ 462.2545; found 462.2527.

5-Ethyl-1-(5-isopropyl-2-methylphenyl)-4-[3-(naphthalen-2-ylmethyl)phenyl]-1*H*-1,2,3-triazole (46): The synthesis was according to GP8, by dissolving the triazole **44** (150 mg, 0.36 mmol) in dry THF (15 mL) and using *n*BuLi (1.6 M solution in hexanes, 0.34 mL, 0.54 mmol) and iodoethane (0.12 mL, 1.4 mmol). Purification by flash column chromatography on silica gel (hexanes/AcOEt, 6:1; R_f = 0.34) yielded **46** as a colorless oil (87 mg, 56%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (t, ^3J = 7.57 Hz, 3 H, CH_3), 1.25 (d, ^3J = 7.07 Hz, 6 H, CH_3), 2.01 (s, 3 H, Ar-CH_3), 2.62 (q, ^3J = 7.57 Hz, 2 H, CH_2), 2.94 (sept, ^3J = 6.88 Hz, 1 H, CH), 4.24 (s, 2 H, CH_2), 7.11–7.12 (m, 1 H, ArH), 7.25–7.30 (m, 3 H, ArH), 7.36–7.47 (m, 4 H, ArH), 7.64–7.66 (m, 1 H, ArH), 7.70–7.71 (m, 2 H, ArH), 7.63–7.80 (m, 3 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.91, 16.68, 16.78, 23.82, 33.45, 42.07, 124.73, 125.34, 125.36, 125.95, 127.22, 127.52, 127.58, 127.67, 127.69, 128.10, 128.36, 128.52, 128.86, 131.02, 131.77 (C_{quat}), 132.08 (C_{quat}), 132.85 (C_{quat}), 133.60 (C_{quat}), 135.14 (C_{quat}), 135.94 (C_{quat}), 138.40 (C_{quat}), 141.56 (C_{quat}), 143.42 (C_{quat}), 147.78 (C_{quat}) ppm. IR: $\tilde{\nu}$ = 3051, 2962, 2871, 1508, 1457 cm^{-1}. HR-MS (ESI+): calcd. for $C_{31}H_{32}N_3$ [M + H]$^+$ 446.2596; found 446.2604.

Supporting Information (see footnote on the first page of this article): Proton and carbon NMR spectra of selected compounds.

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