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Microwave-Assisted [3+2] Cycloaddition[‡] and Suzuki–Miyaura Cross-Coupling for a Concise Access to Polyaromatic Scaffolds

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Novel 3-(prop-2-ynyl)pyrido[2,3-*d*]pyrimidin-4(3*H*)-ones and 3-(prop-2-ynyl)quinazolin-4(3*H*)-ones have been synthesized in a high-yielding microwave-assisted one-pot procedure. The one-pot sequence was conveniently extended to the synthesis of commercially unavailable 6-bromo-N^3-propargylpyrido[2,3-*d*]pyrimidinone by a regiocontrolled bromination with NBS. The synthetic scaffolds were successfully converted into triazoles by copper(I)-catalyzed [3+2] cycloaddition and substituted at the 6-position by Suzuki–Miyaura cross-coupling in high overall yields.

Introduction

As a continuation of our work on the synthesis of C,N,S-containing heterocyclic precursors of kinase inhibitors, we have reported the synthesis of various quinazoline derivatives.[1] Among the studied compounds, N^3-substituted quinazolines have been the focus of a large part of our efforts over the past 10 years.[2]

The biological activities of such derivatives[3] has encouraged us to extend recent investigations to novel pyridopyrimidine analogues. In this context, we have reported a convenient microwave-assisted one-pot sequential synthesis of the target molecules in good-to-excellent yields.[4] This reliable and convenient methodology was applied to various ring systems and aliphatic amines to form libraries of important heterocyclic scaffolds, which can be considered as precursors of novel N^3-substituted quinazolin-4(3*H*)-ones and pyrido[2,3-*d*]pyrimidin-4(3*H*)-ones (Scheme 1) showing an arrangement of cycles mimicking the structures of tris-aromatic systems including a triazole core with high biological potential.[5]

This paper relates the development of a reliable and simple synthetic method involving [3+2] cycloaddition and Suzuki–Miyaura cross-coupling reactions for the preparation of novel polyaromatic derivatives. The main part of the chemistry performed in this study was achieved under microwave irradiation as a continuation of our global strategy for the design of modified reactants and techniques with operational, economic, and environmental benefits over conventional methods.[6]

Results and Discussion

Based on our previous one-pot cyclization of anthranilic acid and various aminonicotinic acid isomers into quinazolin-4(3*H*)-ones and pyridopyrimidin-4(3*H*)-ones, respectively,[4] we wished to use amines bearing a propargyl moiety. Microwave irradiation of anthranilic acid (**1a**) or 2-aminonicotinic acid (**2**) in the presence of *N*,*N*-dimethylformamide dimethyl acetal (DMFDMA)[7] in DMF followed by irradiation with propargylamine in acetic acid gave the expected 3-(prop-2-ynyl)quinazolin-4(3*H*)-one (**3**) and 3-(prop-2-ynyl)pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (**4**) in excellent overall yields (Scheme 2).

With compounds **3** and **4** in hand, we planned to perform a copper(I)-catalyzed [3+2] cycloaddition to give easy access to triazoles **5** and **6**, which would be subsequently functionalized with a benzyl group. The absence of structure–activity relationship patterns for the studied N^3-substituted quinazolin-4(3*H*)-one and pyrido[2,3-*d*]pyrimidin-4(3*H*)-one series prompted us to employ the Topliss scheme[8] for selecting substitution patterns on the triazole. Microwave-assisted cycloaddition of the starting materials **3** and **4** in the presence of trimethylsilyl azide and copper iodide in DMF/MeOH provided triazoles **5** and **6** in good yields (70–76%).[9] Unfortunately, poor regioselectivity was

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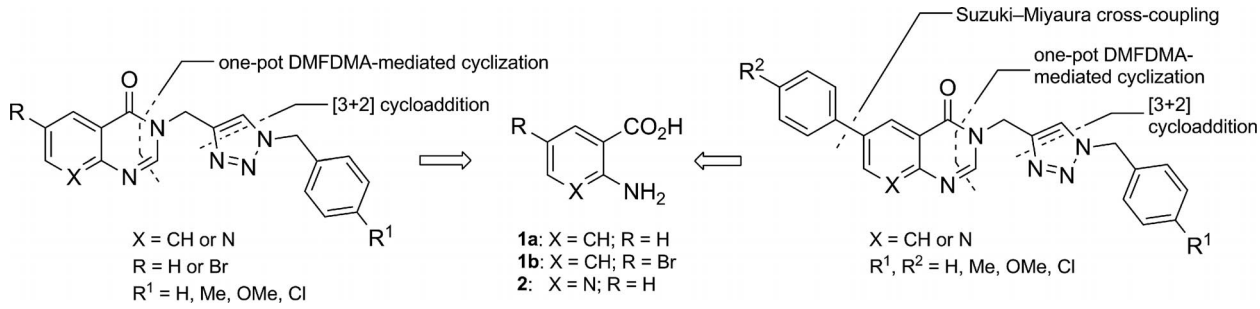
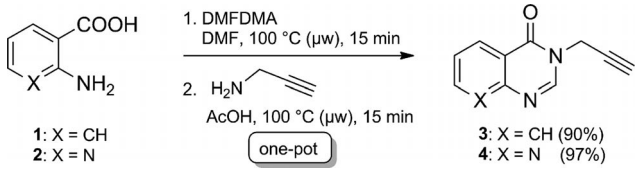
[‡] The term [3+2] cycloaddition, referring to the number of atoms implicated in the reaction, should be more formally called $[_\pi4_s+_\pi2_s]$ cycloaddition. This official IUPAC nomenclature concerns the number of π electrons participating in the cycloaddition. For convenience, the more often used [3+2] nomenclature is used in this paper.

[‡‡] These two authors contributed equally to this work.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201301014.



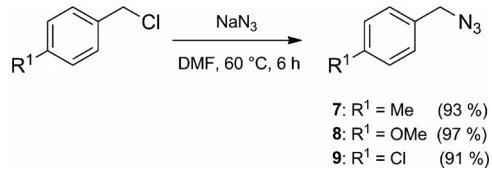
Scheme 1. Retrosynthetic pathways and access to novel N^3,6-disubstituted quinazolin-4(3*H*)-ones and pyrido[2,3-*d*]pyrimidin-4(3*H*)-ones from anthranilic acids (**1a** or **1b**) or 2-aminonicotinic acid (**2**).



Scheme 2. One-pot sequential synthesis of 3-(prop-2-ynyl)quinazolin-4(3*H*)-one (**3**) and 3-(prop-2-ynyl)pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (**4**) from anthranilic acid (**1a**) and 2-aminonicotinic acid (**2**), respectively.

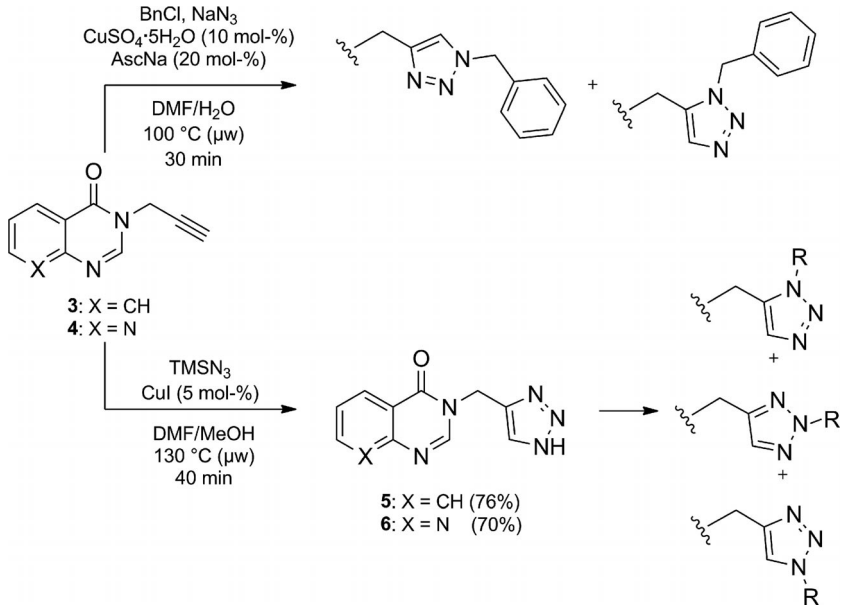
observed during alkylation reactions with alkyl iodide under basic conditions, which provided an inseparable mixture of *N*-alkylated products. Also, failure of the regioselective copper(I)-catalyzed [3+2] cycloaddition through the generation of benzyl azide in situ[10] encouraged us to study another route involving the use of substituted azides (Scheme 3).

To best direct the regioselectivity of the cycloaddition, *para*-substituted (azidomethyl)benzenes **7**–**9** were prepared in excellent yields (91–97%) by the usual methods[11] from the corresponding *para*-substituted benzyl chlorides and sodium azide in warm DMF (Scheme 4).

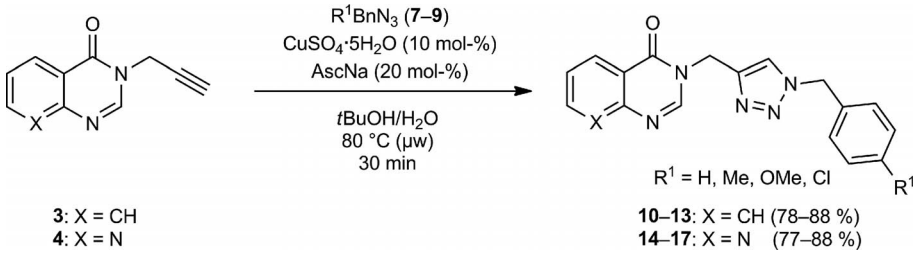


Scheme 4. Synthesis of *para*-substituted (azidomethyl)benzenes **7**–**9**.

Copper(I)-catalyzed cycloaddition was then tested with (azidomethyl)benzenes **7**–**9** and copper sulfate in the presence of sodium ascorbate at 80 °C for 30 min in *t*BuOH and water (Scheme 5). Two novel libraries of quinazolin-4(3*H*)-ones (**10–13**) and pyrido[2,3-*d*]pyrimidin-4(3*H*)-ones (**14**–



Scheme 3. Copper(I)-catalyzed [3+2] cycloaddition of azidotrimethylsilane with quinazolin-4(3*H*)-one (**3**) and pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (**4**).



Scheme 5. Optimized protocol for the microwave-assisted copper(I)-catalyzed [3+2] cycloaddition of 3-(prop-2-ynyl)quinazolin-4(3*H*)-one (**3**) and pyrido[2,3-*d*]pyrimidin-4(3*H*)-ones (**4**) with *p*-substituted (azidomethyl)benzenes **7**–**9**. For details of yields, see Table 1.

Table 1. Yields for the [3+2] cycloaddition-mediated synthesis of the 3-[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]quinazolin-4(3*H*)-ones **10**–**13** and pyrido[2,3-*d*]pyrimidin-4(3*H*)-ones **14**–**17**.

Product	R^1	Yield [%][a]
10	H	88
11	Me	78
12	OMe	85
13	Cl	88

Product	R^1	Yield [%][a]
14	H	88
15	Me	77
16	OMe	83
17	Cl	84

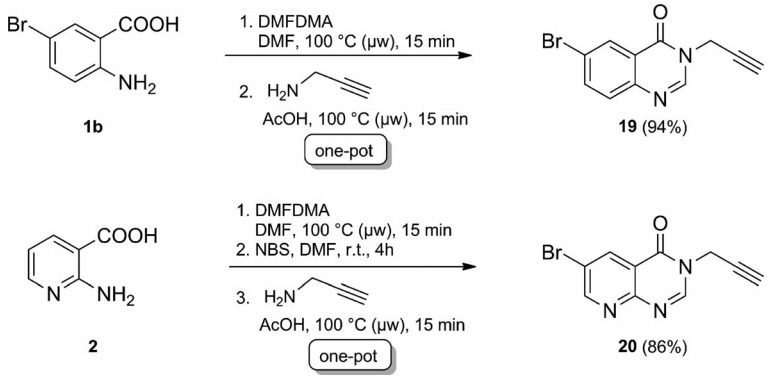
[a] Isolated yield.

17) were isolated in good yields (77–88%) with perfect control of the regioselectivity of the cycloaddition (Table 1). Given the isolated yields for the cycloaddition, the nature of the aromatic moiety, whether quinazolinic or pyrido[2,3-*d*]pyrimidinic, did not seem to affect the click reaction. Also, the yields were not affected by the nature of the *para*-substituted (azidomethyl)benzenes employed.

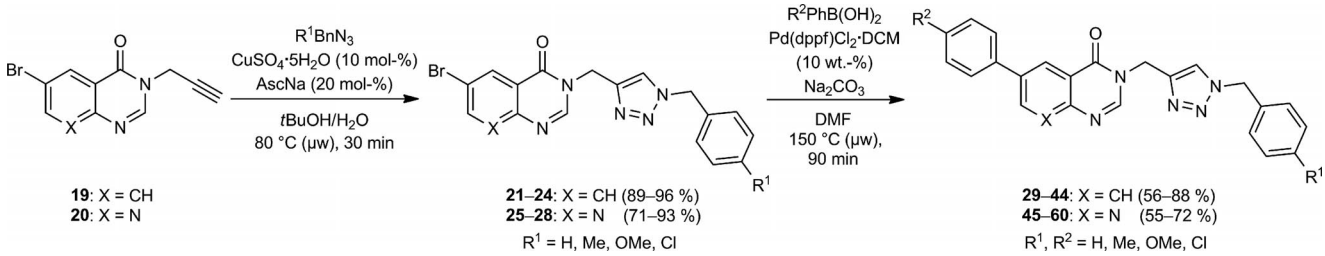
Whilst we focused on the optimization of the conditions of the [3+2] cycloaddition reaction, we envisioned extending our polycyclic scaffolds by Suzuki–Miyaura cross-coupling reaction starting from brominated intermediates. This strategy was underpinned by the commercial availability of 2-amino-5-bromobenzoic acid (**1b**). The latter was easily converted into the corresponding 6-bromo-3-(prop-2-ynyl)quinazolin-4(3*H*)-one (**19**) in an excellent 94% yield by using the one-pot sequence previously described (Scheme 6).

To obtain the 6-bromo-3-(prop-2-ynyl)pyrido[2,3-*d*]pyrimidin-4(3*H*)-one analogue **20**, a regioselective bromination of commercial 2-aminonicotinic acid was necessary. The starting compound **2** was treated with DMFDMA in the usual manner, followed by regiocontrolled bromination by the addition of NBS at room temperature. Cyclization in the presence of propargylamine in acetic acid gave the corresponding 6-bromo-3-(prop-2-ynyl)pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (**20**) in 86% overall yield (Scheme 6).

A short study of this new sequential one-pot reaction showed that bromination after the conversion of 2-aminonicotinic acid (**2**) into the amidino ester with DMFDMA was crucial, otherwise the yields were significantly reduced. By applying the procedure described above, copper(I)-catalyzed [3+2] cycloaddition of 6-bromo-3-(prop-2-ynyl)quinazolin-4(3*H*)-one (**19**) and its pyrido[2,3-*d*]pyrimidin-4(3*H*)-one analogue **20** in the presence of *para*-substituted benzyl



Scheme 6. One-pot sequential synthesis of 6-bromo-3-(prop-2-ynyl)quinazolin-4(3*H*)-one (**19**) and its pyrido[2,3-*d*]pyrimidin-4(3*H*)-one analogue **20**.



Scheme 7. Optimized sequence for the microwave-assisted [3+2] cycloaddition and Pd-catalyzed Suzuki–Miyaura cross-coupling synthesis of tris-aromatic N^3,6-disubstituted quinazolin-4(3*H*)-ones **29**–**44** and pyrido[2,3-*d*]pyrimidin-4(3*H*)-ones **45**–**60**. For the yields, see Tables 2 and 3.

Table 2. Yields for the [3+2] cycloaddition-mediated synthesis of the intermediate 3-[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-6-bromoquinazolin-4(3*H*)-ones **21**–**24** and 3-[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-6-bromopyrido[2,3-*d*]pyrimidin-4(3*H*)-ones **25**–**28**.

Product	R^1	Yield [%][a]
21	H	96
22	Me	94
23	OMe	93
24	Cl	89

Product	R^1	Yield [%][a]
25	H	93
26	Me	90
27	OMe	84
28	Cl	71

[a] Isolated yield.

azides **7**–**9** (Scheme 7) gave the expected triazole derivatives **21**–**28** in yields ranging from 71 to 96% (Table 2). Functionalization at the 6-position of the bicyclic unit by using Suzuki–Miyaura cross-coupling was best achieved with the [1,1′-bis(diphenylphosphanyl)ferrocene]dichloropalladium(II) dichloromethane complex as catalyst (Scheme 7). Irradiation of the latter in the presence of brominated derivatives **21**–**28**, sodium carbonate, and the appropriate *para*-substituted phenylboronic acid in DMF at 150 °C for 90 min gave tris-aromatic products **29**–**60** in good-to-excellent yields (Table 3). During our efforts to optimize the reaction, attempts to achieve Suzuki–Miyaura cross-coupling prior to the [3+2] cycloaddition on intermediates **19** or **20** failed to give the expected aryl derivatives.

In addition to the spectral characterization, the three-dimensional structure of compound **44** was confirmed by single-crystal X-ray diffraction. A single crystal of **44** was obtained from methanol/diethyl ether/dichloromethane (1:1:1, v/v/v). The ORTEP representation is displayed in Figure 1. Analysis revealed the perfectly planar structure of

Table 3. Yields for the Pd-catalyzed Suzuki–Miyaura cross-coupled synthesis of tris-aromatic N^3,6-disubstituted quinazolin-4(3*H*)-ones **29**–**44** and pyrido[2,3-*d*]pyrimidin-4(3*H*)-ones **45**–**60**.

Product	R^1	R^2	Yield [%][a]
29	H	H	86
30	H	Me	88
31	H	OMe	84
32	H	Cl	56
33	Me	H	79
34	Me	Me	81
35	Me	OMe	74
36	Me	Cl	72
37	OMe	H	77
38	OMe	Me	73
39	OMe	OMe	65
40	OMe	Cl	75
41	Cl	H	67
42	Cl	Me	66
43	Cl	OMe	69
44	Cl	Cl	67

Product	R^1	R^2	Yield [%][a]
45	H	H	68
46	H	Me	64
47	H	OMe	66
48	H	Cl	61
49	Me	H	56
50	Me	Me	63
51	Me	OMe	61
52	Me	Cl	64
53	OMe	H	72
54	OMe	Me	62
55	OMe	OMe	71
56	OMe	Cl	69
57	Cl	H	72
58	Cl	Me	67
59	Cl	OMe	66
60	Cl	Cl	55

[a] Isolated yield.

the quinazolinone core and the aromatic moiety at the 6-position. The presence of the methylene group at N-3 leads to the 1,4-disubstituted triazole moiety being almost orthogonal to the quinazolin-4(3*H*)-one ring, with the second methylene group promoting a stair-like three-dimensional structure of the molecule.

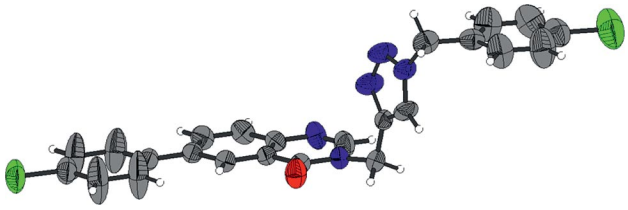


Figure 1. ORTEP diagram of **44** (for details, see the Exp. Sect. and additional data).

Some comments can be made concerning the microwave procedure as well as the technical and practical aspects. In the case of our microwave-assisted synthesis, DMF and acetic acid have the advantage of good dielectric properties, thus enabling an efficient heating of the reaction mixture.[12] The one-pot reactions and [3+2] cycloadditions (with the exception of compounds **5** and **6**) were carried out at amospheric pressure in a multimode cavity, and Suzuki–Miyaura cross-coupling reactions were performed in pressurized vials in a single-mode reactor (for details see Exp. Sect.).

Conclusions

An innovative synthetic methodology for the rapid synthesis of N^3-substituted quinazolin-4(3*H*)-ones and pyrido[2,3-*d*]pyrimidin-4(3*H*)-ones in a one-pot sequence has been achieved. This one-pot sequential reaction was extended to the synthesis of variously functionalized pyrido[2,3-*d*]pyrimidinones by including a regioselective bromination step. Copper(I)-catalyzed [3+2] cycloaddition and Suzuki–Miyaura cross-coupling were optimized and perfectly controlled to provide novel 3-[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-6-phenylquinazolin-4(3*H*)-ones **29**–**44** and phenylpyrido[2,3-*d*]pyrimidin-4(3*H*)-ones **45**–**60**. Microwave technology proved to be a versatile tool allowing rapid and clean reactions in all steps of the syntheses. This approach is coherent with our overall strategy for the design of new molecules with operational, economic, and environmental benefits.

Experimental Section

General: All reactions were carried out under argon or nitrogen and monitored by TLC with silica gel 60 F254 precoated aluminium plates (0.25 mm). Visualization was performed with a UV light at 254 and 312 nm. Purification was performed on an Armen Instrument Spot 2 Flash System equipped with a dual UV/Vis spectrophotometer (200–600 nm), a fraction collector (192 tubes), a dual piston pump (1–250 mL/min, p_{max} = 50 bar/725 psi) allowing quaternary gradients, and an additional inlet for purging with air. Samples can be injected in liquid or solid mode. Purification was controlled and monitored on an integrated panel PC with a touch screen controlled by Armen Glider Flash v3.1d software. Biotage SNAP flash chromatography cartridges (KP-Sil, normal phase, 10–340 g) were used for the purification process. Melting points of solid compounds were measured with a WME Köfler hot-stage with a precision of ±2 °C. IR spectra were recorded with a PerkinElmer Spectrum 100 Series FT-IR spectrometer by using a single reflection attenuated total reflectance (ATR) accessory.

^{1}H and ^{13}C NMR spectra were recorded with a Bruker DXP 300 spectrometer at 300 and 75 MHz, respectively. Abbreviations used for peak multiplicities are as follows: s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet. Coupling constants *J* are in Hz and the chemical shifts are given in ppm and calibrated with [D_6]DMSO (residual solvent signals) or $CDCl_3$. Mass spectroscopy was performed by the Mass Spectrometry Laboratory of the University of Rouen. Mass spectra (EI) were recorded with a Waters LCP 1er XR spectrometer.

Microwave experiments were conducted in two different commercial microwave reactors especially designed for synthetic chemistry. 1) RotoSYNTH™ (Milestone S.r.l. Italy) is a multimode cavity with a microwave power delivery system ranging from 0 to 1200 W. Open vessel experiments were carried out in round-bottomed flasks (from 25 mL to 4 L) fitted with a reflux condenser. The temperature was monitored by means of a contactless IR pyrometer (IRT) and fiber-optic contact thermometer (FO). Temperature, pressure and power profiles were controlled and monitored through the EASY-Control software provided by the manufacturer. 2) Anton Paar Monomode 300™ is a monomode cavity with a microwave power delivery system ranging from 0 to 850 W allowing pressurized reactions (0–30 bars) to be carried out in sealed glass vials (4–30 mL) equipped with a snap cap and a silicon septum. The temperature (0–300 °C) was monitored by means of a contactless IR sensor and was calibrated with a Ruby Thermometer. Temperature, pressure, and power profiles were controlled and monitored through a touch-screen control panel.

The crystal structure of **44** was determined by single-crystal X-ray diffraction with a SMART APEX diffractometer (with Mo-$K_{\alpha 1}$ radiation: λ = 0.71073 Å). The cell parameters and the orientation matrix of the crystal were preliminarily determined by using the SMART software.[13] Data integration and global cell refinement were performed with the SAINT software.[14] Intensities were corrected for Lorentzian polarization, decay and absorption effects (SAINT and SADABS software) and reduced to F_o^2. The structures were solved by direct methods (SHELXS-97[15]). Anisotropic displacement parameters were refined for all non-hydrogen atoms by using SHELXL-97[16] available in the WinGX[17] package. All hydrogen atoms were located by Fourier-difference synthesis and fixed geometrically according to their environment with a common isotropic factor.

General Procedure for the Microwave-Mediated One-Pot Synthesis of N^3-Substituted Quinazolin-4(3*H*)-one and Pyrido[2,3-*d*]pyrimidin-4(3*H*)-one Derivatives: A stirred suspension of amino acid (7.24 mmol, 1 equiv.) in *N*,*N*-dimethylformamide dimethyl acetal (DMFDMA; 1.92 mL, 18.1 mmol, 2.5 equiv.) and DMF (7.2 mL) was heated at 100 °C for 15 min under microwave irradiation at atmospheric pressure (RotoSYNTH™, time measured when the mixture reached the programmed temperature after a ramp period of 2 min under a power of 900 W). The solvents were removed in vacuo and propargylamine (464 μL, 7.96 mmol, 1.1 equiv.) was added followed by AcOH (7.2 mL). The mixture was irradiated at

100 °C for 15 min at atmospheric pressure (RotoSYNTH™, time measured when the mixture reached the programmed temperature after a ramp period of 2 min under a power of 900 W). Evaporation of the solvent gave a crude product which was purified by flash chromatography using petroleum ether/dichloromethane (100:0 to 0:100, v/v) as eluent for the quinazolinone series and dichloromethane/ethyl acetate (100:0 to 0:100, v/v) for the pyridopyrimidinone series.

3-(Prop-2-ynyl)quinazolin-4(3*H*)-one (3): Yield 90% (1.2 g); colorless solid, m.p. 116–118 °C (ref.[18] 116 °C). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.46 (s, 1 H, 2-H), 8.17 (dd, J = 8.0, 1.2 Hz, 1 H, 5-H), 7.88–7.82 (m, 1 H, 6-H), 7.70 (d, J = 8.0 Hz, 8-H), 7.60–7.54 (m, 1 H, 7-H), 4.84 (d, J = 2.5 Hz, 2 H, CH$_2$), 3.44 (t, J = 2.5 Hz, 1 H, C-H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 159.5, 147.8, 147.1, 134.6, 127.4, 127.3, 126.1, 121.4, 78.6, 75.7, 35.2 ppm. IR: $\tilde{\nu}_{max}$ = 3217, 1658, 1600, 1470, 1379, 1269, 1169, 767, 696 cm^{-1}.

3-(Prop-2-ynyl)pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (4): Yield 97% (1.3 g); colorless solid, m.p. 162–164 °C (ref.[19] 122–123 °C). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.00 (dd, J = 4.6, 2.0 Hz, 1 H, 7-H), 8.69 (s, 1 H, 2-H), 8.58 (dd, J = 7.9, 2.0 Hz, 1 H, 5-H), 7.62 (dd, J = 7.9, 4.6 Hz, 1 H, 6-H), 4.84 (d, J = 2.5 Hz, 1 H, CH$_2$), 3.48 (t, J = 2.5 Hz, 1 H, CH) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 160.1, 157.7, 156.1, 150.2, 135.9, 123.1, 116.8, 78.2, 76.0, 35.4 ppm. IR: $\tilde{\nu}_{max}$ = 3222, 2972, 2939, 2123, 1675, 1566, 1432, 1362, 1224, 1103, 938, 798, 709 cm^{-1}. HRMS: calcd. for $C_{10}H_8N_3O$ [M + H]$^+$ 186.0667; found 186.0674.

6-Bromo-3-(prop-2-ynyl)quinazolin-4(3*H*)-one (19): Yield 94% (1.7 g); colorless solid, m.p. 134–136 °C. ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 8.51 (s, 1 H, 2-H), 8.24 (d, J = 2.3 Hz, 1 H, 5-H), 8.00 (dd, J = 8.7, 2.3 Hz, 1 H, 7-H), 7.66 (d, J = 8.7 Hz, 1 H, 8-H), 4.82 (d, J = 2.5 Hz, 1 H, CH$_2$), 3.45 (t, J = 2.5 Hz, 1 H, CH) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 158.4, 147.6, 146.7, 137.4, 129.7, 128.1, 122.9, 119.8, 78.2, 75.9, 35.4 ppm. IR: $\tilde{\nu}_{max}$ = 3292, 3178, 2120, 1669, 1597, 1468, 1367, 1317, 1259, 839, 613, 495 cm^{-1}. HRMS: calcd. for $C_{11}H_8{}^{79}BrN_2O$ [M + H]$^+$ 262.9820; found 262.9821.

6-Bromo-3-(prop-2-ynyl)pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (20): A stirred suspension of 2-aminonicotinic acid (**2**; 1.0 g, 7.24 mmol) in DMFDMA (1.92 mL, 18.1 mmol) and DMF (7.2 mL) was heated at 100 °C for 15 min under microwave irradiation at atmospheric pressure (RotoSYNTH™, time measured when the mixture reached the programmed temperature after a ramp period of 2 min under a power of 900 W). Freshly recrystallized NBS[20] (1.353 g, 7.60 mmol, 1.05 equiv.) was added to the cooled solution, which was vigorously stirred for 4 h at room temperature. The solvents were removed in vacuo and propargylamine (464 μL, 7.96 mmol, 1.1 equiv.) was added followed by AcOH (7.2 mL). The mixture was irradiated at 100 °C for 15 min at atmospheric pressure (RotoSYNTH™, time measured when the mixture reached the programmed temperature after a ramp period of 2 min under a power of 900 W). The solvents were removed in vacuo. Purification of the oily residue by flash chromatography using dichloromethane/ethyl acetate (100:0 to 0:100, v/v) as eluent gave the desired compound (1.644 g, 6.23 mmol) in 86% yield as a colorless solid; m.p. 148–150 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.09 (d, J = 2.6 Hz, 1 H, 7-H), 8.72 (s, 1 H, 2-H), 8.70 (d, J = 2.6 Hz, 1 H, 5-H), 4.84 (d, J = 2.5 Hz, 1 H, CH$_2$), 3.49 (t, J = 2.5 Hz, 1 H, CH) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 159.1, 156.7, 156.3, 150.6, 137.4, 118.0, 117.8, 77.9, 76.1, 35.6 ppm. IR: $\tilde{\nu}_{max}$ = 3116, 3067, 2125, 1672, 1596, 1461, 1247, 1231, 1092, 920, 810 cm^{-1}. HRMS: calcd. for $C_{10}H_7{}^{79}BrN_3O$ [M + H]$^+$ 263.9772; found 263.9767.

General Procedure for the Microwave-Assisted Click Chemistry of *N*^{3}-Propargylquinazolin-4(3*H*)-one and Pyrido[2,3-*d*]pyrimidin-4(3*H*)-one Derivatives: In a sealed tube, a stirred suspension of alkyne (0.5 mmol, 1 equiv.), azidotrimethylsilane (0.75 mmol, 99 μL, 1.5 equiv.), and copper iodide (5 mg, 25 μmol, 0.05 equiv.) in a mixture of DMF (972 μL) and MeOH (108 μL) was heated at 130 °C for 40 min under microwave irradiation under ambient pressure (Anton Paar Monomode 300™, time measured when the mixture reached the programmed temperature after a ramp period of 2 min under a power of 850 W). Evaporation of the solvents gave a crude product which was purified by flash chromatography using dichloromethane/ethyl acetate (100:0 to 0:100, v/v) as eluent for product **5** and ethyl acetate/methanol (100:0 to 95:5, v/v) for product **6**.

3-[(1*H*-1,2,3-Triazol-4-yl)methyl]quinazolin-4(3*H*)-one (5): Yield 76% (86 mg); colorless solid, m.p. 196–198 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 15.0 (br. s, 1 H, NH), 8.54 (s, 1 H, 2-H), 8.14 (dd, J = 1.3, 8.0 Hz, 1 H, 5-H), 7.83–7.70 (m, 1 H + 1 H, triazole-H, 6-H), 7.68 (d, J = 7.7 Hz, 1 H, 8-H), 7.57–7.52 (m, 1 H, 7-H), 5.31 (s, 2 H, CH$_2$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 159.9, 147.9 (2 C), 134.5, 127.3 (2 C), 127.2 (2 C), 126.1, 121.6, 40.8 ppm. IR: $\tilde{\nu}_{max}$ = 3139, 3082, 2917, 2860, 2817, 1673, 1613, 1473, 1324, 1154, 771 cm^{-1}. HRMS: calcd. for $C_{11}H_{10}N_50$ [M + H]$^+$ 228.0885; found 228.0888.

3-[(1*H*-1,2,3-Triazol-4-yl)methyl]pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (6): Yield 70% (80 mg); colorless solid, m.p. 194–196 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 14.90 (br. s, 1 H, NH), 8.98 (dd, J = 4.6, 1.9 Hz, 1 H, 7-H), 8.76 (s, 1 H, 2-H), 8.54 (dd, J = 7.9, 1.9 Hz, 1 H, 5-H), 7.81 (s, 1 H, triazole-H), 7.58 (dd, J = 7.9, 4.6 Hz, 1 H, 6-H), 5.31 (s, 2 H, CH$_2$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 160.5, 157.9, 156.0 (2 C), 151.1, 135.9 (2 C), 122.9, 116.9, 41.1 ppm. IR: $\tilde{\nu}_{max}$ = 1685, 1619, 1562, 1369, 1224, 974, 795 cm^{-1}. HRMS: calcd. for $C_{10}H_9N_6O$ [M + H]$^+$ 229.0838; found 229.0829.

General Procedure for the Synthesis of *para*-Substituted (Azidomethyl)benzenes: A stirred solution of *para*-substituted benzyl chloride (12.42 mmol, 1 equiv.) and sodium azide (888 mg, 13.66 mmol, 1.1 equiv.) in DMF (12 mL) was gradually heated to 60 °C and stirred for 6 h. The cooled reaction mixture was partitioned between diethyl ether and water. The organic layer was washed with water and brine, and dried with magnesium sulfate. Evaporation of the solvent under a flow of nitrogen yielded analytically pure *para*-substituted (azidomethyl)benzene.

1-(Azidomethyl)-4-methylbenzene (7): Yield 93% (1.945 g); colorless oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.22 (s, 4 H, Ph-H), 4.30 (s, 2 H, CH$_2$), 2.38 (s, 3 H, CH$_3$) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 137.2, 131.4, 128.6 (2 C), 127.3 (2 C), 53.2, 19.5 ppm. IR: $\tilde{\nu}_{max}$ = 3025, 2924, 2876, 2090, 1616, 1515, 1343, 1252, 801, 753, 664, 536, 467 cm^{-1}. HRMS: calcd. for $C_8H_9N_3$ [M]$^+$ 147.0796; found 147.0777.

1-(Azidomethyl)-4-methoxybenzene (8): Yield 97% (2.024 g); colorless oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.25 (d, J = 8.5 Hz, 2 H, Ph-H), 6.91 (d, J = 8.5, Hz, 2 H, Ph-H), 4.27 (s, 2 H, CH$_2$), 3.82 (s, 3 H, OCH$_3$) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 160.2, 130.2 (2 C), 127.8, 114.5 (2 C), 55.3, 54.3 ppm. IR: $\tilde{\nu}_{max}$ = 3003, 2936, 2837, 2089, 1610, 1585, 1512, 1303, 1242, 1174, 1031, 811, 550, 514 cm^{-1}. HRMS: calcd. for $C_8H_9N_3O$ [M]$^+$ 163.0736; found 163.0745.

1-(Azidomethyl)-4-chlorobenzene (9): Yield 91% (1.882 g); colorless oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.36 (d, J = 8.5 Hz, 2 H, Ph-H), 7.26 (d, J = 8.5 Hz, 2 H, Ph-H), 4.32 (s, 2 H, CH$_2$) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 134.7, 134.3, 130.0 (2 C), 129.5 (2 C), 54.0 ppm. IR: $\tilde{\nu}_{max}$ = 2935, 2091, 1597, 1492, 1408, 1341, 1246,

1089, 1015, 796, 516 cm^{-1}. HRMS: calcd. for $C_7H_6ClN_3$ $[M]^+$ 167.0250; found 167.0258.

General Procedure for the Microwave-Assisted [3+2] Cycloaddition of N^3-Propargylquinazolin-4(3*H*)-one and Pyrido[2,3-*d*]pyrimidin-4(3*H*)-one Derivatives: Copper sulfate pentahydrate (137 mg, 0.55 mmol, 0.1 equiv.) and sodium ascorbate (218 mg, 1.1 mmol, 0.2 equiv.) were added to a stirred suspension of alkyne (5.5 mmol, 1 equiv.) and the appropriate benzyl azide in *tert*-butanol (11 mL) and water (11 mL) at room temperature. The mixture was heated at 80 °C for 30 min under microwave irradiation at atmospheric pressure (Rotosynth™, time measured when the mixture reached the programmed temperature after a ramp period of 2 min under a power of 900 W). Evaporation of the solvents gave a crude product which was purified by flash chromatography using dichloromethane/ethyl acetate (100:0 to 0:100, v/v) as eluent for the quinazolinone series and ethyl acetate/methanol (100:0 to 95:5, v/v) for the pyridopyrimidinone series.

3-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl]quinazolin-4(3*H*)-one (10): Yield 88% (1.54 g); colorless solid, m.p. 134–136 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.56 (s, 1 H, 2-H), 8.21 (s, 1 H, triazole-H), 8.14 (dd, J = 1.3, 8.0 Hz, 1 H, 5-H), 7.86–7.80 (m, 1 H, 6-H), 7.69 (d, J = 8.0 Hz, 1 H, 8-H), 7.57–7.52 (m, 1 H, 7-H), 7.36–7.30 (m, 5 H, Bn-H), 5.56 (s, 2 H, CH_2), 5.27 (s, 2 H, CH_2) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 159.9, 147.9, 142.7, 135.9, 134.5, 128.8 (2 C), 128.2, 128.0 (2 C), 127.3, 127.2, 126.1, 123.8, 121.6, 52.8, 41.1 ppm. IR: $\tilde{\nu}_{max}$ = 3161, 3142, 3057, 1670, 1611, 1603, 1474, 1382, 1292, 1167, 1051, 931, 768, 727 cm^{-1}. HRMS: calcd. for $C_{18}H_{16}N_5O$ $[M + H]^+$ 318.1355; found 318.1351.

3-{[1-(4-Methylbenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}quinazolin-4(3*H*)-one (11): Yield 78% (1.42 g); colorless solid, m.p. 134–136 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.54 (s, 1 H, 2-H), 8.16–8.12 (m, 1H + 1H, triazole-H, 5-H), 7.89–7.79 (m, 1 H, 6-H), 7.69 (d, J = 7.7 Hz, 1 H, 8-H), 7.59–7.52 (m, 1 H, 7-H), 7.21 (d, J = 8.2 Hz, 2 H, Bn-H), 7.16 (d, J = 8.2 Hz, 2 H, Bn-H), 5.50 (s, 2 H, CH_2), 5.25 (s, 2 H, CH_2), 2.27 (s, 3 H, Bn-CH_3) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 165.1, 153.2, 153.1, 147.9, 142.7, 139.6, 138.1, 134.5 (2 C), 133.3 (2 C), 132.5, 132.4, 131.3, 128.8, 126.8, 57.9, 46.2, 25.9 ppm. IR: $\tilde{\nu}_{max}$ = 3137, 3064, 2917, 1674, 1608, 1472, 1321, 1291, 1154, 1052, 772, 697, 546, 474 cm^{-1}. HRMS: calcd. for $C_{19}H_{18}N_5O$ $[M + H]^+$ 332.1511; found 332.1524.

3-{[1-(4-Methoxybenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}quinazolin-4(3*H*)-one (12): Yield 85% (1.55 g); colorless solid, m.p. 174–176 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.54 (s, 1 H, 2-H), 8.15 (s, 1 H, triazole-H), 8.15–8.12 (m, 1 H, 5-H), 7.86–7.82 (m, 1 H, 6-H), 7.69 (d, J = 8.0 Hz, 8-H), 7.57–7.52 (m, 1 H, 7-H), 7.29 (d, J = 8.8 Hz, 2 H, Bn-H), 6.91 (d, J = 8.8 Hz, 2 H, Bn-H), 5.47 (s, 2 H, CH_2), 5.25 (s, 2 H, CH_2), 3.72 (s, 3 H, Bn-OCH_3) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 159.8, 159.1, 147.9, 142.6, 134.4, 129.7 (2 C), 127.8, 127.2, 127.1, 126.0, 123.4, 121.5, 114.1 (2 C), 55.1, 52.3, 41.0 ppm. IR: $\tilde{\nu}_{max}$ = 3144, 3058, 2999, 2947, 1658, 1610, 1511, 1473, 1361, 1324, 1250, 1173, 1048, 1024, 779, 768 cm^{-1}. HRMS: calcd. for $C_{19}H_{18}N_5O_2$ $[M + H]^+$ 348.1461; found 348.1454.

3-{[1-(4-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}quinazolin-4(3*H*)-one (13): Yield 88% (1.70 g); colorless solid, m.p. 158–160 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.56 (s, 1 H, 2-H), 8.22 (s, 1 H, triazole-H), 8.14 (dd, J = 8.0, 1.4 Hz, 1 H, 5-H), 7.81 (m, 1 H, 6-H), 7.69 (d, J = 8.0 Hz, 8-H), 7.54 (m, 1 H, 7-H), 7.42 (d, J = 8.8 Hz, 2 H, Bn-H), 7.33 (d, J = 8.8 Hz, 2 H, Bn-H), 5.57 (s, 2 H, CH_2), 5.27 (s, 2 H, CH_2) ppm. ^{13}C NMR (75 MHz, [D$_6$]-DMSO): δ = 159.9, 147.9, 142.8, 134.9, 134.4, 132.9, 130.0 (2 C), 128.7 (2 C), 127.3, 127.2, 126.1, 123.9, 121.6, 52.0, 41.0 ppm. IR: $\tilde{\nu}_{max}$ = 3135, 3052, 1669, 1609, 1474, 1382, 1312, 1294, 1226, 1053, 1025, 780, 772, 698 cm^{-1}. HRMS: calcd. for $C_{18}H_{15}ClN_5O$ $[M + H]^+$ 352.0965; found 352.0954.

3-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl]pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (14): Yield 88% (1.54 g); colorless solid, m.p. 192–194 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.99 (dd, J = 4.6, 1.9 Hz, 1 H, 7-H), 8.77 (s, 1 H, 2-H), 8.54 (dd, J = 7.9, 1.9 Hz, 1 H, 5-H), 8.21 (s, 1 H, triazole-H), 7.58 (dd, J = 7.9, 4.6 Hz, 1 H, 6-H), 7.37–7.29 (m, 5 H, Bn-H), 5.56 (s, 2 H, CH_2), 5.28 (s, 2 H, CH_2) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 160.5, 157.8, 155.9, 151.1, 142.4, 135.9, 128.8 (2 C), 128.2, 128.0 (2 C), 123.9, 122.9, 116.9, 52.9, 41.3 ppm. IR: $\tilde{\nu}_{max}$ = 3076, 2934, 1674, 1600, 1469, 1430, 1310, 1216, 1046, 796, 724 cm^{-1}. HRMS: calcd. for $C_{17}H_{15}N_6O$ $[M + H]^+$ 319.1307; found 319.1293.

3-{[1-(4-Methylbenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}pyrido[2,3-*d*]-pyrimidin-4(3*H*)-one (15): Yield 77% (1.408 g); colorless solid, m.p. 206–208 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.97 (dd, J = 4.6, 2.0 Hz, 1 H, 7-H), 8.76 (s, 1 H, 2-H), 8.52 (dd, J = 7.9, 2.0 Hz, 1 H, 5-H), 8.17 (s, 1 H, triazole-H), 7.57 (dd, J = 7.9, 4.6 Hz, 1 H, 6-H), 7.21 (d, J = 8.1 Hz, 2 H, Bn-H), 7.15 (d, J = 8.1 Hz, 2 H, Bn-H), 5.50 (s, 2 H, CH_2), 5.27 (s, 2 H, CH_2), 2.26 (s, 3 H, Bn-CH_3) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 160.4, 157.8, 155.9, 151.0, 142.3, 137.5, 135.8, 132.8, 129.2 (2 C), 128.1 (2 C), 123.6, 122.8, 116.8, 52.6, 41.2, 20.6 ppm. IR: $\tilde{\nu}_{max}$ = 3118, 1675, 1604, 1562, 1473, 1431, 1361, 1214, 1096, 1052, 800, 794, 473 cm^{-1}. HRMS: calcd. for $C_{18}H_{17}N_6O$ $[M + H]^+$ 333.1464; found 333.1468.

3-{[1-(4-Methoxybenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}pyrido[2,3-*d*]-pyrimidin-4(3*H*)-one (16): Yield 83% (1.59 g); colorless solid, m.p. 222–224 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.98 (dd, J = 4.6, 1.9 Hz, 1 H, 7-H), 8.76 (s, 1 H, 2-H), 8.53 (dd, J = 7.9, 1.9 Hz, 1 H, 5-H), 8.16 (s, 1 H, triazole-H), 7.58 (dd, J = 7.9, 4.6 Hz, 1 H, 6-H), 7.28 (d, J = 8.6 Hz, 2 H, Bn-H), 6.92 (d, J = 8.6 Hz, 2 H, Bn-H), 5.47 (s, 2 H, CH_2), 5.26 (s, 2 H, CH_2), 3.72 (s, 3 H, Bn-OCH_3) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 160.5, 159.2, 157.9, 156.0, 151.1, 142.4, 135.9, 129.7 (2 C), 127.8, 123.5, 122.9, 116.9, 114.1 (2 C), 55.1, 52.4, 41.2 ppm. IR: $\tilde{\nu}_{max}$ = 3118, 1672, 1605, 1589, 1515, 1360, 1307.1249, 1214, 1191, 1054, 1024, 800, 794, 782 cm^{-1}. HRMS: calcd. for $C_{18}H_{17}N_6O_2$ $[M + H]^+$ 349.1413; found 349.1405.

3-{[1-(4-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (17): Yield 84% (1.64 g); colorless solid, m.p. 224–226 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.98 (dd, J = 4.6, 2.0 Hz, 1 H, 7-H), 8.77 (s, 1 H, 2-H), 8.53 (dd, J = 7.9, 2.0 Hz, 1 H, 5-H), 8.23 (s, 1 H, triazole-H), 7.58 (dd, J = 7.9, 4.6 Hz, 1 H, 6-H), 7.44 (d, J = 8.6 Hz, 2 H, Bn-H), 7.34 (d, J = 8.6 Hz, 2 H, Bn-H), 5.57 (s, 2 H, CH_2), 5.28 (s, 2 H, CH_2) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 160.5, 157.9, 156.0, 151.1, 142.5, 135.9, 134.9, 132.9, 130.0, 128.8, 123.9, 122.9, 116.9, 52.0, 41.2 ppm. IR: $\tilde{\nu}_{max}$ = 3151, 3067, 1673, 1602, 1469, 1435, 1228, 795, 788 cm^{-1}. HRMS: calcd. for $C_{17}H_{14}ClN_6O_2$ $[M + H]^+$ 353.0918; found 353.0913.

3-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-6-bromoquinazolin-4(3*H*)-one (21): Yield 96% (2.09 g); colorless solid, m.p. 176–178 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.59 (s, 1 H, 2-H), 8.20 (s, 1 H, triazole-H), 8.18 (d, J = 2.3 Hz, 1 H, 5-H), 7.95 (dd, J = 8.7, 2.3 Hz, 1 H, 7-H), 7.62 (d, J = 8.7 Hz, 1 H, 8-H), 7.37–7.27 (m, 5 H, Bn-H), 5.56 (s, 2 H, CH_2), 5.26 (s, 2 H, CH_2) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 159.5, 149.1, 147.6, 143.1, 137.9, 136.5, 130.2, 129.3 (2 C), 128.7, 128.6 (2 C), 124.4, 123.7, 120.1, 52.9, 41.3 ppm. IR: $\tilde{\nu}_{max}$ = 3129, 2922, 1667, 1600, 1465, 1318, 1223, 1049, 833, 786, 597 cm^{-1}. HRMS: calcd. for $C_{18}H_{15}{}^{79}BrN_5O$ $[M + H]^+$ 396.0460; found 396.0448.

6-Bromo-3-{[1-(4-methylbenzyl)-1*H*-1,2,3-triazol-4-yl]-methyl}quinazolin-4(3*H*)-one (22): Yield 94% (2.12 g); colorless solid, m.p. 162–164 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.58 (s, 1 H, 2-H), 8.19 (d, J = 2.1 Hz, 1 H, 5-H), 8.15 (s, 1 H, triazole-H), 7.95 (dd, J = 8.7, 2.1 Hz, 1 H, 7-H), 7.62 (d, J = 8.7 Hz, 1 H, 8-H), 7.20 (d, J = 8.2 Hz, 2 H, Bn-H), 7.14 (d, J = 8.0 Hz, 2 H, Bn-H), 5.50 (s, 2 H, CH$_2$), 5.25 (s, 2 H, CH$_2$), 2.25 (s, 3 H, Bn-CH$_3$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 159.5, 149.1, 147.6, 143.0, 138.1, 137.9, 133.4, 130.2, 129.8 (2 C), 128.7, 128.6 (2 C), 124.1, 123.7, 120.1, 52.7, 41.2, 20.5 ppm. IR: $\tilde{\nu}_{max}$ = 3064, 2925, 1662, 1600, 1465, 1317, 1222, 1049, 928, 832, 775, 596 cm^{-1}. HRMS: calcd. for $C_{19}H_{17}{}^{79}BrN_5O$ [M + H]$^+$ 410.0616; found 410.0623.

6-Bromo-3-{[1-(4-methoxybenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-quinazolin-4(3*H*)-one (23): Yield 93% (2.18 g); colorless solid, m.p. 160–162 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.58 (s, 1 H, 2-H), 8.21 (d, J = 2.3 Hz, 1 H, 5-H), 8.13 (s, 1 H, triazole-H), 7.98 (dd, J = 8.7, 2.3 Hz, 1 H, 7-H), 7.64 (d, J = 8.7 Hz, 1 H, 8-H), 7.28 (d, J = 8.7 Hz, 2 H, Bn-H), 6.91 (d, J = 8.7 Hz, 2 H, Bn-H), 5.46 (s, 2 H, CH$_2$), 5.24 (s, 2 H, CH$_2$), 3.72 (s, 3 H, Bn-OCH$_3$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 159.9, 159.5, 149.1, 147.5, 143.0, 137.8, 130.2 (2 C), 130.2, 128.7, 128.3, 124.0, 123.6, 120.1, 114.5 (2 C), 55.2, 52.5, 41.2 ppm. IR: $\tilde{\nu}_{max}$ = 3145, 2999, 2942, 1653, 1609, 1511, 1459, 1358, 1323, 1302, 1248, 1214, 1179, 1029, 957, 876, 834, 776, 651, 597, 552, 490 cm^{-1}. HRMS: calcd. for $C_{19}H_{17}{}^{79}BrN_5O_2$ [M + H]$^+$ 426.0566; found 428.0580.

6-Bromo-3-{[1-(4-chlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-quinazolin-4(3*H*)-one (24): Yield 89% (2.11 g); colorless solid, m.p. 180–182 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.59 (s, 1 H), 8.21 (s, 1 H, triazole-H), 8.19 (d, J = 2.4 Hz, 1 H, 5-H), 7.95 (dd, J = 8.7, 2.4 Hz, 1 H, 7-H), 7.62 (d, J = 8.7 Hz, 1 H, 8-H), 7.41 (d, J = 8.5 Hz, 2 H, Bn-H), 7.32 (d, J = 8.5 Hz, 2 H, Bn-H), 5.57 (s, 2 H, CH$_2$), 5.26 (s, 2 H, CH$_2$) ppm. ^{13}C NMR (75 MHz, [D$_6$]-DMSO): δ = 159.5, 149.2, 147.6, 143.1, 137.9, 135.4, 133.5, 130.5 (2 C), 130.2, 129.3 (2 C), 128.7, 124.4, 123.7, 120.1, 52.1, 41.3 ppm. IR: $\tilde{\nu}_{max}$ = 3137, 2958, 1669, 1601, 1465, 1366, 1318, 1222, 1054, 801, 782 cm^{-1}. HRMS: calcd. for $C_{18}H_{14}{}^{79}BrClN_5O$ [M + H]$^+$ 430,0070; found 430.0091.

3-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-6-bromopyrido[2,3-*d*]-pyrimidin-4(3*H*)-one (25): Yield 93% (2.03 g); colorless solid, m.p. 222–224 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.08 (d, J = 2.6 Hz, 1 H, 7-H), 8.81 (s, 1 H, 2-H), 8.66 (d, J = 2.6 Hz, 1 H, 5-H), 8.21 (s, 1 H, triazole-H), 7.37–7.29 (m, 5 H, Bn-H), 5.56 (s, 2 H, CH$_2$), 5.28 (s, 2 H, CH$_2$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 159.5, 156.6, 156.4, 151.5, 142.1, 137.4, 135.8, 128.7 (2 C), 128.1, 128.0 (2 C), 123.8, 118.1, 117.6, 52.8, 41.4 ppm. IR: $\tilde{\nu}_{max}$ = 3129, 2928, 1680, 1598, 1458, 1293, 1217, 1048, 799, 713 cm^{-1}. HRMS: calcd. for $C_{17}H_{14}{}^{79}BrN_6O$ [M + H]$^+$ 397.0412; found 397.0414.

6-Bromo-3-{[1-(4-methylbenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (26): Yield 90% (2.04 g); colorless solid, m.p. 214–216 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.07 (d, J = 2.6 Hz, 1 H, 7-H), 8.80 (s, 1 H, 2-H), 8.65 (d, J = 2.6 Hz, 1 H, 5-H), 8.17 (s, 1 H, triazole-H), 7.21 (d, J = 8.2 Hz, 2 H, Bn-H), 7.16 (d, J = 8.2 Hz, 2 H, Bn-H), 5.50 (s, 2 H, CH$_2$), 5.26 (s, 2 H, CH$_2$), 2.26 (s, 3 H, Bn-CH$_3$) ppm. ^{13}C NMR (75 MHz, [D$_6$]-DMSO): δ = 159.5, 156.6, 156.4, 151.5, 142.1, 137.5, 137.4, 132.8, 129.4 (2 C), 128.1 (2 C), 123.6, 118.1, 117.6, 52.6, 41.4, 20.7 ppm. IR: $\tilde{\nu}_{max}$ = 3129, 3058, 2926, 1676, 1600, 1459, 1293, 1219, 1049, 1219, 1049, 812, 784 cm^{-1}. HRMS: calcd. for $C_{18}H_{16}{}^{79}BrN_6O$ [M + H]$^+$ 411.0569; found 411.0559.

6-Bromo-3-{[1-(4-methoxybenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (27): Yield 84% (1.97 g); colorless solid, m.p. 240–242 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.07 (d, J = 2.6 Hz, 1 H, 7-H), 8.80 (s, 1 H, 2-H), 8.65 (d, J = 2.6 Hz, 1 H, 5-H), 8.15 (s, 1 H, triazole-H), 7.28 (d, J = 8.7 Hz, 2 H, Bn-H), 6.91 (d, J = 8.7 Hz, 2 H, Bn-H), 5.47 (s, 2 H, CH$_2$), 5.26 (s, 2 H, CH$_2$), 3.72 (s, 3 H, Bn-OCH$_3$) ppm. ^{13}C NMR (75 MHz, [D$_6$]-DMSO): δ = 159.5, 159.2, 156.6, 156.5, 151.5, 142.1, 137.4, 129.7 (2 C), 127.8, 123.5, 118.2, 117.7, 114.1 (2 C), 55.1, 52.4, 41.4 ppm. IR: $\tilde{\nu}_{max}$ = 3115, 3059, 2841, 1671, 1601, 1515, 1459, 1249, 1213, 1025, 813, 781 cm^{-1}. HRMS: calcd. for $C_{18}H_{16}{}^{79}BrN_6O_2$ [M + H]$^+$ 427,0518; found 427.0505.

6-Bromo-3-{[1-(4-chlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (28): Yield 71% (1.69 g); colorless solid, m.p. 256–258 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.07 (d, J = 2.5 Hz, 1 H, 7-H), 8.82 (s, 1 H, 2-H), 8.64 (d, J = 2.5 Hz, 1 H, 5-H), 8.23 (s, 1 H, triazole-H), 7.43 (d, J = 8.3 Hz, 2 H, Bn-H), 7.33 (d, J = 8.3 Hz, 2 H, Bn-H), 5.57 (s, 2 H, CH$_2$), 5.28 (s, 2 H, CH$_2$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 159.5, 156.6, 156.4, 151.5, 142.2, 137.4, 134.8, 132.9, 130.0 (2 C), 128.7 (2 C), 123.9, 118.1, 117.6, 52.0, 41.4 ppm. IR: $\tilde{\nu}_{max}$ = 3140, 3057, 2990, 1681, 1599, 1460, 1294, 1219, 1048, 811, 785 cm^{-1}. HRMS: calcd. for $C_{17}H_{13}{}^{79}BrClN_6O$ [M + H]$^+$ 431,0023; found 431.0025.

General Procedure for the Microwave-Mediated Suzuki–Miyaura Cross-Coupling of N^3-Substituted 6-Bromoquinazolin-4(3*H*)-ones and 6-Bromopyrido[2,3-*d*]pyrimidin-4(3*H*)-ones: In a sealed tube, a stirred solution of N^3-substituted 6-bromoquinazolin-4(3*H*)-one or 6-bromopyrido[2,3-*d*]pyrimidin-4(3*H*)-one (200 μmol, 1 equiv.), [1,1′-bis(diphenylphosphanyl)ferrocene]dichloropalladium(II) complexed with dichloromethane (10 wt.-%), sodium carbonate (400 μmol, 42 mg, 2 equiv.), the appropriate phenylboronic acid (1.05 equiv.) in dry DMF (2 mL) was heated at 150 °C for 90 min under microwave irradiation under ambient pressure (Anton Paar Monomode 300™, time measured when the mixture reached the programmed temperature after a ramp period of 2 min under a power of 850 W).

For the pyridopyrimidinone series, ice was added to the cooled solution. The dark precipitate was filtered off and purified by flash chromatography using ethyl acetate/methanol (100:0 to 95:5, v/v) as eluent.

For the quinazolinone series, the cooled solution was partitioned between dichloromethane and water. The organic layer was dried with magnesium sulfate and evaporated in vacuo. The dark residue was purified by flash chromatography using dichloromethane/ethyl acetate (100:0 to 0:100, v/v) as eluent.

3-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-6-phenylquinazolin-4(3*H*)-one (29): Yield 86% (68 mg); colorless solid, m.p. 166–168 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.57 (s, 1 H, 2-H), 8.34 (d, J = 2.0 Hz, 1 H, 5-H), 8.16 (s, 1 H, triazole-H) 8.14 (dd, J = 8.3, 2.0 Hz, 1 H, 7-H), 7.79–7.74 (m, 1 H + 2 H, 8-H, Ph-H), 7.53–7.32 (m, 3 H + 5H, Ph-H, Bn-H), 5.56 (s, 2 H, CH$_2$), 5.29 (s, 2 H, CH$_2$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 159.9, 147.9, 147.2, 142.6, 138.8, 138.7, 135.9, 132.9, 129.1 (2 C), 128.7 (2 C), 128.1, 128.0 (2 C), 126.8 (2 C), 123.7, 123.3, 121.9, 52.8, 41.1 ppm. IR: $\tilde{\nu}_{max}$ = 3121, 3064, 2917, 1674, 1607, 1477, 1364, 1222, 1163, 1072, 844, 796, 764, 711, 693, 569 cm^{-1}. HRMS: calcd. for $C_{24}H_{20}N_5O$ [M + H]$^+$ 394.1668; found 394.1658.

3-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-6-(*p*-tolyl)quinazolin-4(3*H*)-one (30): Yield 88% (72 mg); colorless solid, m.p. 180–182 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.56 (s, 1 H, 2-H), 8.31 (d, J = 2.1 Hz, 1 H, 5-H), 8.20 (s, 1 H, triazole-H), 8.12 (dd, J = 8.6, 2.1 Hz, 1 H, 7-H), 7.75 (d, J = 8.6 Hz, 1 H, 8-H), 7.65 (d, J = 8.2 Hz, 2 H, Ph-H), 7.38–7.30 (m, 5 H + 2 H, Bn-H, Ph-H),

5.56 (s, 2 H, CH_2), 5.28 (s, 2 H, CH_2), 2.36 (s, 3 H, Ph-CH_3) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 159.9, 147.8, 147.0, 142.6, 138.7, 137.5, 135.9, 135.8, 132.7, 129.7 (2 C), 128.7 (2 C), 128.1, 128.0 (2 C), 126.6 (2 C), 123.7, 122.9, 121.9, 52.8, 41.1, 20.7 ppm. IR: $\tilde{\nu}_{max}$ = 3129, 2926, 1680, 1606, 1482, 1335, 1255, 1162, 811, 716 cm^{-1}. HRMS: calcd. for $C_{25}H_{22}N_5O$ [M + H]$^+$ 408.1824; found 408.1826.

3-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-6-(4-methoxyphenyl)-quinazolin-4(3*H*)-one (31): Yield 84% (71 mg); colorless solid, m.p. 186–188 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.54 (s, 1 H, 2-H), 8.28 (d, J = 2.1 Hz, 1 H, 5-H), 8.20 (s, 1 H, triazole-H), 8.11 (dd, J = 8.6, 2.3 Hz, 1 H, 7-H), 7.75–7.69 (m, 1 H + 2 H, 8-H, Ph-H), 7.38–7.30 (m, 5 H, Bn-H), 7.06 (d, J = 8.8 Hz, 2 H, Ph-H), 5.56 (s, 2 H, CH_2), 5.28 (s, 2 H, CH_2), 3.81 (s, 3 H, Ph-OCH_3) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 159.9, 159.3, 147.6, 146.7, 142.7, 138.5, 135.9, 132.5, 131.0, 128.7 (2 C), 128.1 (2 C), 128.0 (2 C), 127.9, 12.7, 122.5, 121.9, 114.6 (2 C), 55.2, 52.8, 41.1 ppm. IR: $\tilde{\nu}_{max}$ = 3129, 2942, 1680, 1605, 1482, 1337, 1259, 1164, 1031, 824, 717 cm^{-1}. HRMS: calcd. for $C_{25}H_{22}N_5O_2$ [M + H]$^+$ 424.1773; found 424.1766.

3-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-6-(4-chlorophenyl)quinazolin-4(3*H*)-one (32): Yield 56% (48 mg); colorless solid, m.p. 166–168 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.58 (s, 1 H, 2-H), 8.32 (d, J = 2.1 Hz, 1 H, 5-H), 8.21 (s, 1 H, triazole-H), 8.12 (dd, J = 8.6, 2.3 Hz, 1 H, 7-H), 7.79–7.75 (m, 1 H + 2 H, 8-H, Ph-H), 7.54 (d, J = 8.6 Hz, 2 H, Ph-H), 7.38–7.30 (m, 5 H, Bn-H), 5.56 (s, 2 H, CH_2), 5.29 (s, 2 H, CH_2) ppm. ^{13}C NMR (75 MHz, [D$_6$]-DMSO): δ = 159.8, 148.1, 147.4, 142.6, 137.5, 137.4, 135.9, 132.9, 132.8, 129.1 (2 C), 128.7 (2 C), 128.6 (2 C), 128.12, 128.06, 128.0 (2 C), 123.7, 123.4, 121.9, 52.8, 41.1 ppm. IR: $\tilde{\nu}_{max}$ = 3078, 1668, 1605, 1477, 1375, 1256, 1096, 821, 717 cm^{-1}. HRMS: calcd. for $C_{24}H_{19}ClN_5O$ [M + H]$^+$ 428.1278; found 428.1273.

3-{[1-(4-Methylbenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6-phenylquinazolin-4(3*H*)-one (33): Yield 79% (64 mg); colorless solid, m.p. 156–158 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.57 (s, 1 H, 2-H), 8.34 (d, J = 2.2 Hz, 1 H, 5-H), 8.16 (s, 1 H, triazole-H) 8.15 (dd, J = 8.2, 2.2 Hz, 1 H, 7-H), 7.81–7.73 (m, 1 H + 2 H, 8-H, Ph-H), 7.52 (t, J = 7.3 Hz, 2 H, Ph-H), 7.42 (t, J = 7.3 Hz, 1 H, Ph-H), 7.22 (d, J = 8.1 Hz, 2 H, Bn-H), 7.16 (d, J = 8.1 Hz, 2 H, Bn-H), 5.50 (s, 2 H, CH_2), 5.28 (s, 2 H, CH_2), 2.26 (s, 3 H, Bn-CH_3) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 160.7, 148.6, 147.9, 143.3, 139.4, 139.3, 138.1, 133.5, 133.4, 129.8 (2 C), 129.7 (2 C), 128.6 (2 C), 128.6, 127.4 (2 C), 124.1, 123.9, 122.4, 52.7, 41.1, 20.6 ppm. IR: $\tilde{\nu}_{max}$ = 3121, 3056, 2917, 1666, 1600, 1478, 1359, 1253, 1047, 927, 837, 791, 759, 714, 568, 479 cm^{-1}. HRMS: calcd. for $C_{25}H_{22}N_5O$ [M + H]$^+$ 408.1824; found 408.1829.

3-{[1-(4-Methylbenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6-(*p*-tolyl)-quinazolin-4(3*H*)-one (34): Yield 81% (68 mg); colorless solid, m.p. 168–170 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.54 (s, 1 H, 2-H), 8.31 (d, J = 2.0 Hz, 1 H, 5-H), 8.15 (s, 1 H, triazole-H), 8.12 (dd, J = 8.6, 2.2 Hz, 1 H, 7-H), 7.75 (d, J = 8.5 Hz, 1 H, 8-H), 7.65 (d, J = 8.1 Hz, 1 H, Ph-H), 7.31 (d, J = 7.9 Hz, 2 H, Ph-H), 7.21 (d, J = 8.0 Hz, 2 H, Bn-H), 7.15 (d, J = 8.0 Hz, 2 H, Bn-H), 5.50 (s, 2 H, CH_2), 5.27 (s, 2 H, CH_2), 2.36 (s, 3 H, Ph-CH_3), 2.26 (s, 3 H, Bn-CH_3) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 160.7, 148.4, 147.7, 143.3, 139.4, 138.1, 138.1, 136.4, 133.5, 133.3, 130.3 (2 C), 129.8 (2 C), 128.6 (2 C), 128.5, 127.2 (2 C), 124.1, 123.4, 122.4, 52.7, 41.1, 20.6 (2 C) ppm. IR: $\tilde{\nu}_{max}$ = 3129, 3015, 2917, 1677, 1606, 1483, 1335, 1262, 1157, 949, 810, 781 cm^{-1}. HRMS: calcd. for $C_{26}H_{24}N_5O$ [M + H]$^+$ 422.1981; found 422.1984.

6-(4-Methoxyphenyl)-3-{[1-(4-methylbenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}quinazolin-4(3*H*)-one (35): Yield 74% (65 mg); colorless solid, m.p. 190–192 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.53 (s, 1 H, 2-H), 8.28 (d, J = 1.9 Hz, 1 H, 5-H), 8.15 (s, 1 H, triazole-H), 8.11 (dd, J = 8.5, 1.9 Hz, 1 H, 7-H), 7.76–7.69 (m, 1 H + 2 H, 8-H, Ph-H), 7.21 (d, J = 8.0 Hz, 2 H, Bn-H), 7.16 (d, J = 8.0 Hz, 2 H, Bn-H), 7.07 (d, J = 8.7 Hz, 2 H, Ph-H), 5.50 (s, 2 H, CH_2), 5.27 (s, 2 H, CH_2), 3.81 (s, 3 H, Ph-OCH_3), 2.26 (s, 3 H, Bn-CH_3) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 160.7, 160.1, 148.3, 147.3, 143.3, 139.2, 138.1, 133.5, 133.1, 131.6, 129.8 (2 C), 128.7 (2 C), 128.6 (2 C), 128.5, 124.1, 123.0, 122.4, 115.1 (2 C), 55.3, 52.7, 41.1, 20.6 ppm. IR: $\tilde{\nu}_{max}$ = 3120, 2964, 1675, 1605, 1483, 1369, 1259, 1186, 825 cm^{-1}. HRMS: calcd. for $C_{26}H_{24}N_5O_2$ [M + H]$^+$ 438.1930; found 438.1917.

6-(4-Chlorophenyl)-3-{[1-(4-methylbenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}quinazolin-4(3*H*)-one (36): Yield 72% (64 mg); colorless solid, m.p. 174–176 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.08 (s, 1 H, 2-H), 7.85 (d, J = 1.8 Hz, 1 H, 5-H), 7.71–7.62 (m, 1 H +1 H, triazole-H, 7-H), 7.34–7.27 (m, 1 H + 2 H, 8-H, Ph-H), 7.07 (d, J = 8.4 Hz, 2 H, Ph-H), 6.72 (d, J = 8.0 Hz, 2 H, Bn-H), 6.67 (d, J = 8.0 Hz, 2 H, Bn-H), 5.01 (s, 2 H, CH_2), 4.79 (s, 2 H, CH_2), 1.77 (s, 3 H, Bn-CH_3) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 160.6, 148.8, 148.1, 143.2, 138.2, 138.1, 138.0, 133.5, 133.4, 133.3, 129.8 (2 C), 129.6 (2 C), 129.2 (2 C), 128.6 (2 C), 124.1, 124.0, 122.4, 52.7, 41.1, 20.6 ppm. IR: $\tilde{\nu}_{max}$ = 3129, 2917, 2852, 1662, 1604, 1476, 1368, 1331, 1251, 1156, 1095, 1014, 819, 793, 742, 494, 452 cm^{-1}. HRMS: calcd. for $C_{25}H_{21}ClN_5O$ [M + H]$^+$ 442.1435; found 442.1435.

3-{[1-(4-Methoxybenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6-phenylquinazolin-4(3*H*)-one (37): Yield 77% (65 mg); colorless solid, m.p. 150–152 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.57 (s, 1 H, 2-H), 8.34 (d, J = 2.2 Hz, 1 H, 5-H), 8.18–8.14 (m, 1 H +1 H, 7-H, triazole-H), 7.81–7.74 (m, 1 H + 2 H, 8-H, Ph-H), 7.52 (t, J = 7.4 Hz, 2 H, Ph-H), 7.42 (t, J = 7.3 Hz, 1 H, Ph-H), 7.29 (d, J = 8.7 Hz, 2 H, Bn-H), 6.91 (d, J = 8.7 Hz, 2 H, Bn-H), 5.47 (s, 2 H, CH_2), 5.27 (s, 2 H, CH_2), 3.72 (s, 3 H, Bn-OCH_3) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 160.7, 159.9, 148.6, 147.9, 143.3, 139.4, 139.3, 133.5, 130.3 (2 C), 129.7 (2 C), 128.5, 128.3, 127.4 (2 C), 124.0, 123.9, 122.4, 114.6 (2 C), 55.2, 52.5, 41.1 ppm. IR: $\tilde{\nu}_{max}$ = 3137, 3056, 2925, 2836, 1668, 1601, 1513, 1478, 1251, 1176, 1050, 1024, 934, 835, 793, 759, 693, 568, 546 cm^{-1}. HRMS: calcd. for $C_{25}H_{22}N_5O_2$ [M + H]$^+$ 424.1774; found 424.1771.

3-{[1-(4-Methoxybenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6-(*p*-tolyl)-quinazolin-4(3*H*)-one (38): Yield 73% (64 mg); colorless solid, m.p. 156–158 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.55 (s, 1 H, 2-H), 8.31 (d, J = 2.1 Hz, 1 H, 5-H), 8.17–8.09 (m, 1 H + 1 H, 7-H, triazole-H), 7.76 (d, J = 8.5 Hz, 1 H, 8-H), 7.66 (d, J = 8.4 Hz, 2 H, Ph-H), 7.35–7.23 (m, 4 H, Bn-H), 6.91 (d, J = 8.4 Hz, 2 H, Ph-H), 5.47 (s, 2 H, CH_2), 5.27 (s, 2 H, CH_2), 3.72 (s, 3 H, Bn-OCH_3), 2.36 (s, 3 H, Ph-CH_3) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 160.7, 159.9, 148.5, 147.7, 143.3, 139.4, 138.1, 136.4, 133.3, 130.4 (2 C), 130.3 (2 C), 128.5, 128.4, 127.2 (2 C), 123.9, 123.5, 122.4, 114.6 (2 C), 55.2, 52.5, 41.1, 20.6 ppm. IR: $\tilde{\nu}_{max}$ = 3137, 2925, 2852, 1665, 1603, 1514, 1483, 1372, 1336, 1252, 1177, 1050, 810, 777 cm^{-1}. HRMS: calcd. for $C_{27}H_{26}N_5O_2$ [M + H]$^+$ 438.1930; found 438.1932.

3-{[1-(4-Methoxybenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6-(4-methoxyphenyl)quinazolin-4(3*H*)-one (39): Yield 65% (59 mg); colorless solid, m.p. 150–152 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 8.54 (s, 1 H, 2-H), 8.27 (d, J = 2.2 Hz, 1 H, 5-H), 8.16 (s, 1 H, triazole-H), 8.08 (dd, J = 8.5, 2.2 Hz, 1 H, 7-H), 7.72 (d, J = 8.5 Hz, 1 H, 8-H), 7.68 (d, J = 8.8 Hz, 2 H, Ph-H), 7.29 (d, J = 8.6 Hz, 2 H, Bn-H), 7.05 (d, J = 8.8 Hz, 2 H, Ph-H), 6.90 (d, J = 8.6 Hz, 2 H, Bn-H), 5.47 (s, 2 H, CH_2), 5.27 (s, 2 H, CH_2), 3.80 (s, 3 H, Ph-

OCH_3), 3.71 (s, 3 H, Bn-OCH_3) ppm. ^{13}C NMR (75 MHz, [D_6]-DMSO): δ = 160.7, 160.1, 159.9, 148.3, 147.3, 143.3, 139.1, 133.1, 131.6, 130.3 (2 C), 128.5 (2 C), 128.4, 128.3, 123.9, 123.0, 122.4, 115.1 (2 C), 114.6 (2 C), 55.3, 55.2, 52.5, 41.1 ppm. IR: $\tilde{\nu}_{max}$ = 3129, 2925, 2836, 1674, 1604, 1514, 1481, 1368, 1331, 1247, 1179, 1028, 823, 778, 550, 497 cm^{-1}. HRMS: calcd. for $C_{26}H_{24}N_5O_3$ [M + H]$^+$ 454.1879; found 454.1877.

6-(4-Chlorophenyl)-3-{[1-(4-methoxybenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}quinazolin-4(3*H*)-one (40): Yield 75% (69 mg); colorless solid, m.p. 176–178 °C. ^1H NMR (300 MHz, [D_6]DMSO): δ = 8.57 (s, 1 H, 2-H), 8.31 (d, J = 2.2 Hz, 1 H, 5-H), 8.16 (s, 1 H, triazole-H), 8.11 (dd, J = 8.5, 2.2 Hz, 1 H, 7-H), 7.76 (d, J = 8.6 Hz, 2 H, Ph-H), 7.75 (d, J = 8.5 Hz, 1 H, 8-H), 7.53 (d, J = 8.6 Hz, 2 H, Ph-H), 7.29 (d, J = 8.7 Hz, 2 H, Bn-H), 6.90 (d, J = 8.7 Hz, 2 H, Bn-H), 5.47 (s, 2 H, CH_2), 5.26 (s, 2 H, CH_2), 3.71 (s, 3 H, Bn-OCH_3) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 160.6, 159.9, 148.8, 148.1, 143.2, 138.1, 138.0, 133.5, 133.4, 130.3 (2 C), 129.6 (2 C), 129.2 (2 C), 128.6, 128.3, 123.9, 122.4, 114.6 (2 C), 55.2, 52.5, 41.1 ppm. IR: $\tilde{\nu}_{max}$ = 3148, 3121, 3066, 1668, 1604, 1517, 1477, 1252, 1025, 817, 794 cm^{-1}. HRMS: calcd. for $C_{25}H_{21}ClN_5O_2$ [M + H]$^+$ 458.1384; found 458.1393.

3-{[1-(4-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6-phenylquinazolin-4(3*H*)-one (41): Yield 67% (57 mg); colorless solid, m.p. 178–180 °C. ^1H NMR (300 MHz, [D_6]DMSO): δ = 8.57 (s, 1 H, 2-H), 8.34 (d, J = 2.1 Hz, 1 H, 5-H), 8.22 (s, 1 H, triazole-H), 8.15 (dd, J = 8.5, 2.1 Hz, 1 H, 7-H), 7.81–7.74 (m, 1 H + 2 H, 8-H, Ph-H), 7.51 (t, J = 7.4 Hz, 2 H, Ph-H), 7.43 (m, 1 H + 2 H, Ph-H, Bn-H), 7.34 (d, J = 8.5 Hz, 2 H, Bn-H), 5.57 (s, 2 H, CH_2), 5.29 (s, 2 H, CH_2) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 159.9, 157.9, 147.2, 142.7, 138.8, 138.7, 134.9, 132.9, 132.8, 129.9 (2 C), 129.2 (2 C), 128.7 (2 C), 128.0, 126.8 (2 C), 123.8, 123.3, 121.9, 52.0, 41.1 ppm. IR: $\tilde{\nu}_{max}$ = 3129, 1671, 1607, 1478, 1373, 1337, 1052, 792, 763 cm^{-1}. HRMS: calcd. for $C_{24}H_{19}ClN_5O$ [M + H]$^+$ 428.1278; found 428.1278.

3-{[1-(4-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6-(*p*-tolyl)-quinazolin-4(3*H*)-one (42): Yield 66% (58 mg); colorless solid, m.p. 174–176 °C. ^1H NMR (300 MHz, [D_6]DMSO): δ = 8.55 (s, 1 H, 2-H), 8.31 (d, J = 2.1 Hz, 1 H, 5-H), 8.21 (s, 1 H, triazole-H), 8.12 (dd, J = 8.6, 2.3 Hz, 1 H, 7-H), 7.75 (d, J = 8.6 Hz, 1 H, 8-H), 7.64 (d, J = 8.1 Hz, 2 H, Ph-H), 7.43 (d, J = 8.5 Hz, 2 H, Bn-H), 7.35–7.30 (m, 2 H + 2 H, Bn-H, Ph-H), 5.57 (s, 2 H, CH_2), 5.29 (s, 2 H, CH_2), 2.35 (s, 3 H, Ph-CH_3) ppm. ^{13}C NMR (75 MHz, [D_6]-DMSO): δ = 159.9, 147.8, 147.0, 142.7, 138.7, 137.5, 135.8, 134.9, 132.9, 132.7, 129.9 (2 C), 129.7 (2 C), 128.7, (2 C), 127.9, 126.6 (2 C), 123.8, 122.9, 121.9, 52.0, 41.1, 20.6 ppm. IR: $\tilde{\nu}_{max}$ = 3120, 3068, 2921, 1656, 1605, 1483, 1365, 1233, 818, 777 cm^{-1}. HRMS: calcd. for $C_{25}H_{21}ClN_5O$ [M + H]$^+$ 442.1435; found 442.1433.

3-{[1-(4-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6-(4-methoxyphenyl)quinazolin-4(3*H*)-one (43): Yield 69% (63 mg); colorless solid, m.p. 208–210 °C. ^1H NMR (300 MHz, [D_6]DMSO): δ = 8.54 (s, 1 H, 2-H), 8.29 (d, J = 2.1 Hz, 1 H, 5-H), 8.21 (s, 1 H, triazole-H), 8.12 (dd, J = 8.6, 2.3 Hz, 1 H, 7-H), 7.75 (d, J = 8.6 Hz, 1 H, 8-H), 7.71 (d, J = 8.8 Hz, 2 H, Ph-H), 7.43 (d, J = 8.5 Hz, 2 H, Bn-H), 7.34 (d, J = 8.5 Hz, 2 H, Bn-H), 7.07 (d, J = 8.8 Hz, 2 H, Ph-H), 5.57 (s, 2 H, CH_2), 5.28 (s, 2 H, CH_2), 3.81 (s, 3 H, Ph-OCH_3) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 159.9, 159.3, 147.6, 146.7, 142.7, 138.5, 134.9, 132.9, 132.5, 131.0, 129.9 (2 C), 128.7 (2 C), 128.0 (2 C), 127.9, 123.8, 122.5, 121.9, 114.6 (2 C), 55.2, 52.0, 41.1 ppm. IR: $\tilde{\nu}_{max}$ = 3124, 3085, 3011, 2838, 1671, 1605, 1483, 1368, 1259, 1029, 826, 777 cm^{-1}. HRMS: calcd. for $C_{25}H_{21}ClN_5O_2$ [M + H]$^+$ 458.1384; found 458.1363.

3-{[1-(4-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6-(4-chlorophenyl)quinazolin-4(3*H*)-one (44): Yield 67% (62 mg); colorless solid, m.p. 188–190 °C. ^1H NMR (300 MHz, [D_6]DMSO): δ = 8.58 (s, 1 H, 2-H), 8.33 (d, J = 2.1 Hz, 1 H, 5-H), 8.22 (s, 1 H, triazole-H), 8.14 (dd, J = 8.6, 2.3 Hz, 1 H, 7-H), 7.80–7.76 (m, 3 H, 8-H, Ph-H), 7.42 (d, J = 8.5 Hz, 2 H, Bn-H), 7.33 (d, J = 8.5 Hz, 2 H, Bn-H), 5.57 (s, 2 H, CH_2), 5.29 (s, 2 H, CH_2) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 159.8, 148.1, 147.4, 142.6, 137.5, 137.4, 134.9, 132.92, 132.86, 132.80, 130.0 (2 C), 129.1 (2 C), 128.7 (2 C), 128.6 (2 C), 128.1, 123.8, 123.4, 121.9, 52.0, 41.1 ppm. IR: $\tilde{\nu}_{max}$ = 3120, 3068, 1672, 1607, 1477, 1366, 1102, 818 cm^{-1}. HRMS: calcd. for $C_{24}H_{18}Cl_2N_5O$ [M + H]$^+$ 462.0888; found 462.0886.

Crystal Structure Data for 44: $C_{24}H_{17}Cl_2N_5O$, M = 462.33, monoclinic, $P2_1/n$ (Nr 14), a = 17.9326(17), b = 5.3129(5), c = 23.655(2) Å, β = 104.194(2)°, V = 2184.9(4) Å^3, Z = 4, $d_{calcd.}$ = 1.405. The final cycle of full-matrix least-squares refinement on F_o^2 was based on 4480 observed reflections and 289 variable parameters and converged with unweighted and weighted agreement factors of $R1$ = 0.0829 and $wR2$ = 0.1805 for 3106 reflections with $I > 2\sigma I$, and $R1$ = 0.1166 and $wR2$ = 0.1982 for all data.

CCDC-948758 (for **44**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

3-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-6-phenylpyrido[2,3-*d*]pyrimidin-4(3*H*)-one (45): Yield 68% (79 mg); colorless solid, m.p. 188–190 °C. ^1H NMR (300 MHz, [D_6]DMSO): δ = 9.32 (d, J = 2.6 Hz, 1 H, 7-H), 8.80 (s, 1 H, 2-H), 8.68 (d, J = 2.6 Hz, 1 H, 5-H), 8.23 (s, 1 H, triazole-H), 7.88–7.85 (m, 2 H, Ph-H), 7.58–7.47 (m, 3 H, Ph-H), 7.37–7.29 (m, 5 H, Ph), 5.56 (s, 2 H, Bn-H), 5.28 (s, 2 H, CH_2) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 160.6, 157.1, 154.3, 151.0, 142.4, 135.9, 135.8, 132.5, 129.4 (2 C), 128.8 (2 C), 128.7, 128.2, 128.1 (2 C), 127.2 (2 C), 123.8, 116.7, 52.9, 41.3 ppm. IR: $\tilde{\nu}_{max}$ = 3032, 2934, 2838, 1663, 1595, 1469, 1256, 1225, 1048, 814 cm^{-1}. HRMS: calcd. for $C_{23}H_{19}N_6O$ [M + H]$^+$ 395.1620; found 395.1623.

3-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-6-(*p*-tolyl)pyrido[2,3-*d*]-pyrimidin-4(3*H*)-one (46): Yield 64% (52 mg); colorless solid, m.p. 196–198 °C. ^1H NMR (300 MHz, [D_6]DMSO): δ = 9.31 (d, J = 2.6 Hz, 1 H, 7-H), 8.78 (s, 1 H, 2-H), 8.66 (d, J = 2.6 Hz, 1 H, 5-H), 8.23 (s, 1 H, triazole-H), 7.76 (d, J = 8.2 Hz, 2 H, Ph-H), 7.37–7.29 (m, 5 H + 2 H, Bn-H, Ph-H), 5.57 (s, 2 H, CH_2), 5.30 (s, 2 H, CH_2), 2.38 (s, 3 H, Ph-CH_3) ppm. ^{13}C NMR (75 MHz, [D_6]-DMSO): δ = 160.5, 156.8, 154.0, 150.8, 142.4, 138.2, 135.9, 134.2, 132.8, 132.0, 129.9 (2 C), 128.7 (2 C), 128.1, 128.0 (2 C), 126.9 (2 C), 123.8, 116.6, 52.8 41.3, 20.7 ppm. IR: $\tilde{\nu}_{max}$ = 3048, 2941, 2834, 1665, 1599, 1469, 1256, 1225, 1050, 828, 815 cm^{-1}. HRMS: calcd. for $C_{24}H_{21}N_6O$ [M + H]$^+$ 409.1777; found 409.1789.

3-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-6-(4-methoxyphenyl)-pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (47): Yield 66% (56 mg); colorless solid, m.p. 180–182 °C. ^1H NMR (300 MHz, [D_6]DMSO): δ = 9.28 (d, J = 2.6 Hz, 1 H, 7-H), 8.77 (s, 1 H, 2-H), 8.62 (d, J = 2.6 Hz, 1 H, 5-H), 8.23 (s, 1 H, triazole-H), 7.80 (d, J = 8.8 Hz, 2 H, Ph-H), 7.37–7.30 (m, 5 H, Bn-H), 7.08 (d, J = 8.8 Hz, 2 H, Ph-H), 5.57 (s, 2 H, CH_2), 5.30 (s, 2 H, CH_2), 3.82 (s, 3 H, Ph-OCH_3) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 160.5, 159.7, 156.5, 153.8, 150.5, 147.9, 142.4, 135.9, 134.0, 131.4, 128.7 (2 C), 128.3, 128.1 (2 C), 128.0 (2 C), 127.9, 123.8, 116.6, 114.7, 55.3, 52.8, 41.3 ppm. IR: $\tilde{\nu}_{max}$ = 3048, 2940, 2832, 1666, 1599, 1470, 1257, 1225, 1050, 829, 809 cm^{-1}. HRMS: calcd. for $C_{24}H_{21}N_6O_2$ [M + H]$^+$ 425.1726; found 425.1722.

3-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-6-(4-chlorophenyl)-pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (48): Yield 61% (52 mg); colorless solid, m.p. 212–214 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.32 (d, J = 2.4 Hz, 1 H, 7-H), 8.80 (s, 1 H, 2-H), 8.69 (d, J = 2.5 Hz, 1 H, 5-H), 8.23 (s, 1 H, triazole-H), 7.90 (d, J = 8.5 Hz, 2 H, Ph-H), 7.59 (d, J = 8.4 Hz, 2 H, Ph-H), 7.41–7.26 (m, 5 H, Bn-H), 5.57 (s, 2 H, CH$_2$), 5.31 (s, 2 H, CH$_2$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 160.4, 157.1, 154.1, 151.1, 142.3, 135.8, 134.6, 133.6, 133.0, 132.7, 129.2 (2 C), 128.9 (2 C), 128.7 (2 C), 128.1, 128.0 (2 C), 123.8, 116.6, 52.8, 41.3 ppm. IR: $\tilde{\nu}_{max}$ = 3063, 1672, 1600, 1468, 1227, 1043, 815, 717 cm^{-1}. HRMS: calcd. for $C_{23}H_{18}ClN_6O$ [M + H]$^+$ 429.1231; found 429.1233.

3-{[1-(4-Methylbenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6-phenyl-pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (49): Yield 56% (46 mg); colorless solid, m.p. 222–224 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.32 (s, 1 H, 7-H), 8.78 (s, 1 H, 2-H), 8.68 (d, J = 1.5 Hz, 1 H, 5-H), 8.18 (s, 1 H, triazole-H), 7.85 (d, J = 7.7 Hz, 2 H, Ph-H), 7.57–7.44 (m, 3 H, Ph-H), 7.22 (d, J = 7.5 Hz, 2 H, Bn-H), 7.16 (d, J = 7.8 Hz, 2 H, Bn-H), 5.50 (s, 2 H, CH$_2$), 5.29 (s, 2 H, CH$_2$), 2.26 (s, 3 H, Bn-CH$_3$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 161.3, 157.7, 154.9, 151.6, 143.0, 138.1, 136.3, 134.9, 133.4, 133.1, 129.9 (2 C), 129.8 (2 C), 129.2, 128.7 (2 C), 127.6 (2 C), 124.2, 117.2, 52.8, 41.3, 20.6 ppm. IR: $\tilde{\nu}_{max}$ = 3064, 3039, 2917, 2960, 1668, 1597, 1467, 1327, 1226, 1050, 941, 813, 762, 689, 584, 521, 469 cm^{-1}. HRMS: calcd. for $C_{24}H_{21}N_6O$ [M + H]$^+$ 409.1777; found 409.1790.

3-{[1-(4-Methylbenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6-(*p*-tolyl)-pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (50): Yield 63% (53 mg); colorless solid, m.p. 198–200 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.30 (d, J = 2.7 Hz, 1 H, 7-H), 8.77 (s, 1 H, 2-H), 8.64 (d, J = 2.7 Hz, 1 H, 5-H), 8.18 (s, 1 H, triazole-H), 7.75 (d, J = 8.1 Hz, 2 H, Ph-H), 7.35 (d, J = 8.1 Hz, 2 H, Ph-H), 7.21 (d, J = 8.3 Hz, 2 H, Bn-H), 7.16 (d, J = 8.3 Hz, 2 H, Bn-H), 5.50 (s, 2 H, CH$_2$), 5.29 (s, 2 H, CH$_2$), 2.37 (s, 3 H, Ph-CH$_3$), 2.26 (s, 3 H, Bn-CH$_3$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 161.3, 157.5, 154.7, 151.4, 143.0, 138.8, 138.1, 134.8, 133.4, 133.3, 132.5, 130.5 (2 C), 129.8 (2 C), 128.6 (2 C), 127.4 (2 C), 124.2, 117.1, 52.8, 41.3, 20.6, 20.5 ppm. IR: $\tilde{\nu}_{max}$ = 3088, 3056, 1677, 1600, 1474, 1364, 1209, 1051, 961, 811, 475 cm^{-1}. HRMS: calcd. for $C_{25}H_{23}N_6O$ [M + H]$^+$ 423.1933; found 423.1922.

6-(4-Methoxyphenyl)-3-{[1-(4-methylbenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (51): Yield 61% (53 mg); colorless solid, m.p. 198–200 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.28 (d, J = 2.5 Hz, 1 H, 7-H), 8.75 (s, 1 H, 2-H), 8.61 (d, J = 2.5 Hz, 1 H, 5-H), 8.18 (s, 1 H, triazole-H), 7.80 (d, J = 8.7 Hz, 2 H, Ph-H), 7.21 (d, J = 8.0 Hz, 2 H, Bn-H), 7.16 (d, J = 8.0 Hz, 2 H, Bn-H), 7.09 (d, J = 8.7 Hz, 2 H, Ph-H), 5.50 (s, 2 H, CH$_2$), 5.29 (s, 2 H, CH$_2$), 3.82 (s, 3 H, Ph-OCH$_3$), 2.26 (s, 3 H, Bn-CH$_3$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 159.2, 158.4, 155.1, 152.4, 149.1, 140.9, 136.0, 132.5, 131.3, 129.9, 127.7 (2 C), 126.8 (2 C), 126.6 (2 C), 126.4 (2 C), 122.1, 115.0, 113.1, 53.3, 50.6, 39.2, 18.5 ppm. IR: $\tilde{\nu}_{max}$ = 3057, 2927, 1678, 1603, 1468, 1254, 1226, 1179, 1052, 809 cm^{-1}. HRMS: calcd. for $C_{25}H_{23}N_6O_2$ [M + H]$^+$ 439.1882; found 439.1898.

6-(4-Chlorophenyl)-3-{[1-(4-methylbenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (52): Yield 64% (57 mg); colorless solid, m.p. 214–216 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.32 (d, J = 2.7 Hz, 1 H, 7-H), 8.79 (s, 1 H, 2-H), 8.69 (d, J = 2.7 Hz, 1 H, 5-H), 8.18 (s, 1 H, triazole-H), 7.90 (d, J = 8.6 Hz, 2 H, Ph-H), 7.59 (d, J = 8.6 Hz, 2 H, Ph-H), 7.22 (d, J = 8.2 Hz, 2 H, Bn-H), 7.16 (d, J = 8.2 Hz, 2 H, Bn-H), 5.50 (s, 2 H, CH$_2$), 5.29 (s, 2 H, CH$_2$), 2.26 (s, 3 H, Bn-CH$_3$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 159.1, 155.8, 152.7, 149.7, 140.9, 136.1, 133.1, 132.1, 131.5, 131.3, 131.2, 127.7 (2 C), 127.6 (2 C), 127.4 (2 C), 126.6 (2 C), 122.1, 115.0, 50.7, 39.2, 18.4 ppm. IR: $\tilde{\nu}_{max}$ = 3064, 2917, 1669, 1597, 1466, 1421, 1226, 1097, 1109, 928, 813, 746, 522, 475, 458 cm^{-1}. HRMS: calcd. for $C_{24}H_{20}ClN_6O$ [M + H]$^+$ 443.1387; found 443.1375.

3-{[1-(4-Methoxybenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6-phenyl-pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (53): Yield 72% (61 mg); colorless solid, m.p. 192–194 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.32 (d, J = 2.3 Hz, 1 H, 7-H), 8.79 (s, 1 H, 2-H), 8.67 (d, J = 2.3 Hz, 1 H, 5-H), 8.18 (s, 1 H, triazole-H), 7.85 (d, J = 7.4 Hz, 2 H, Ph-H), 7.59–7.42 (m, 3 H, Ph-H), 7.29 (d, J = 8.4 Hz, 2 H, Bn-H), 6.91 (d, J = 8.4 Hz, 2 H, Bn-H), 5.48 (s, 2 H, CH$_2$), 5.29 (s, 2 H, CH$_2$), 3.72 (s, 3 H, Bn-OCH$_3$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 161.3, 159.9, 157.8, 155.0, 151.7, 143.0, 136.3, 134.9, 133.1, 130.3 (2 C), 129.9 (2 C), 129.2, 128.3, 127.7 (2 C), 124.0, 117.2, 114.6 (2 C), 55.2, 52.5, 41.3 ppm. IR: $\tilde{\nu}_{max}$ = 3120, 3068, 2842, 1671, 1598, 1515, 1472, 1249, 1023, 1054, 814, 766 cm^{-1}. HRMS: calcd. for $C_{24}H_{21}N_6O_2$ [M + H]$^+$ 425.1726; found 425.1728.

3-{[1-(4-Methoxybenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6-(*p*-tolyl)-pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (54): Yield 62% (54 mg); colorless solid, m.p. 210–212 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.29 (d, J = 2.7 Hz, 1 H, 7-H), 8.76 (s, 1 H, 2-H), 8.64 (d, J = 2.7 Hz, 1 H, 5-H), 8.16 (s, 1 H, triazole-H), 7.75 (d, J = 8.2 Hz, 2 H, Ph-H), 7.35 (d, J = 7.9 Hz, 2 H, Ph-H), 7.29 (d, J = 8.7 Hz, 2 H, Bn-H), 6.91 (d, J = 8.7 Hz, 2 H, Bn-H), 5.47 (s, 2 H, CH$_2$), 5.29 (s, 2 H, CH$_2$), 3.72 (s, 3 H, Bn-OCH$_3$), 2.37 (s, 3 H, Ph-CH$_3$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 161.3, 159.9, 157.5, 154.7, 151.4, 144.0, 138.8, 134.8, 133.4, 132.6, 130.5 (2 C), 130.3 (2 C), 128.3, 127.4 (2 C), 123.9, 117.1, 114.6 (2 C), 55.2, 52.5, 41.3, 20.6 ppm. IR: $\tilde{\nu}_{max}$ = 3115, 2983, 1672, 1597, 1249, 1024, 812, 782 cm^{-1}. HRMS: calcd. for $C_{25}H_{23}N_6O_2$ [M + H]$^+$ 439.1882; found 439.1860.

3-{[1-(4-Methoxybenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6-(4-methoxyphenyl)pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (55): Yield 71% (65 mg); colorless solid, m.p. 200–202 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.28 (d, J = 2.6 Hz, 1 H, 7-H), 8.75 (s, 1 H, 2-H), 8.61 (d, J = 2.6 Hz, 1 H, 5-H), 8.17 (s, 1 H, triazole-H), 7.81 (d, J = 8.6 Hz, 2 H, Ph-H), 7.29 (d, J = 8.5 Hz, 2 H, Bn-H), 7.09 (d, J = 8.6 Hz, 2 H, Ph-H), 6.91 (d, J = 8.5 Hz, 2 H, Bn-H), 5.47 (s, 2 H, CH$_2$), 5.28 (s, 2 H, CH$_2$), 3.82 (s, 3 H, Ph-OCH$_3$), 3.72 (s, 3 H, Bn-OCH$_3$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 161.3, 160.6, 159.9, 157.2, 154.6, 151.3, 143.0, 134.7, 132.1, 130.3 (2 C), 128.9 (2 C), 128.5, 128.3, 124.0, 117.2, 115.3 (2 C), 114.6 (2 C), 55.4, 55.2, 52.5, 41.3 ppm. IR: $\tilde{\nu}_{max}$ = 3120, 2936, 1668, 1597, 1474, 1249, 1191, 813, 782 cm^{-1}. HRMS: calcd. for $C_{25}H_{23}N_6O_3$ [M + H]$^+$ 455.1832; found 455.1827.

6-(4-Chlorophenyl)-3-{[1-(4-methoxybenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (56): Yield 69% (63 mg); colorless solid, m.p. 222–224 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.32 (d, J = 2.6 Hz, 1 H, 7-H), 8.80 (s, 1 H, 2-H), 8.70 (d, J = 2.6 Hz, 1 H, 5-H), 8.16 (s, 1 H, triazole-H), 7.91 (d, J = 6.6 Hz, 2 H, Ph-H), 7.60 (d, J = 6.6 Hz, 2 H, Ph-H), 7.29 (d, J = 8.5 Hz, 2 H, Bn-H), 6.92 (d, J = 8.5 Hz, 2 H, Bn-H), 5.48 (s, 2 H, CH$_2$), 5.29 (s, 2 H, CH$_2$), 3.73 (s, 3 H, Bn-OCH$_3$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 160.5, 159.2, 157.2, 154.2, 151.2, 142.3, 134.6, 133.6, 133.1, 132.7, 129.7 (2 C), 129.3 (2 C), 129.0 (2 C), 127.8, 123.5, 116.7, 114.1 (2 C), 55.2, 52.4, 41.3 ppm. IR: $\tilde{\nu}_{max}$ = 3120, 1672, 1602, 1469, 1249, 1053, 814, 782 cm^{-1}. HRMS: calcd. for $C_{24}H_{20}ClN_6O_2$ [M + H]$^+$ 459.1336; found 459.1336.

3-{[1-(4-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6-phenyl-pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (57): Yield 72% (62 mg); colorless

solid, m.p. 206–208 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.32 (d, J = 2.6 Hz, 1 H, 7-H), 8.79 (s, 1 H, 2-H), 8.69 (d, J = 2.6 Hz, 1 H, 5-H), 8.24 (s, 1 H, triazole-H), 7.86 (d, J = 7.0 Hz, 2 H, Ph-H), 7.57–7.49 (m, 3 H, Ph-H), 7.46 (d, J = 8.4 Hz, 2 H, Bn-H), 7.34 (d, J = 8.4 Hz, 2 H, Bn-H), 5.58 (s, 2 H, CH$_2$), 5.31 (s, 2 H, CH$_2$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 161.3, 157.7, 154.9, 151.7, 143.1, 136.3, 135.5, 134.9, 133.5, 133.1, 130.6 (2 C), 129.9 (2 C), 129.3 (2 C), 129.2, 127.7 (2 C), 124.4, 117.2, 41.3 ppm. IR: $\tilde{\nu}_{max}$ = 3287, 3057, 1678, 1646, 1598, 1501, 1451, 1313, 1222, 1048, 817, 693 cm^{-1}. HRMS: calcd. for $C_{23}H_{18}ClN_6O$ [M + H]$^+$ 429.1231; found 429.1232.

3-{[1-(4-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6-(*p*-tolyl)-pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (58): Yield 67% (59 mg); colorless solid, m.p. 186–188 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.30 (d, J = 2.7 Hz, 1 H, 7-H), 8.78 (s, 1 H, 2-H), 8.65 (d, J = 2.7 Hz, 1 H, 5-H), 8.23 (s, 1 H, triazole-H), 7.75 (d, J = 8.0 Hz, 2 H, Ph-H), 7.43 (d, J = 8.4 Hz, 2 H, Bn-H), 7.35 (d, J = 8.0 Hz, 2 H, Ph-H), 7.33 (d, J = 8.4 Hz, 2 H, Bn-H), 5.57 (s, 2 H, CH$_2$), 5.30 (s, 2 H, CH$_2$), 2.37 (s, 3 H, Ph-CH$_3$) ppm. ^{13}C NMR (75 MHz, [D$_6$]-DMSO): δ = 161.3, 157.5, 154.8, 151.5, 143.1, 138.8, 135.5, 134.9, 133.5, 133.4, 132.6, 130.6 (2 C), 130.5 (2 C), 129.3 (2 C), 127.5 (2 C), 124.4, 117.2, 52.1, 41.3, 20.6 ppm. IR: $\tilde{\nu}_{max}$ = 3265, 1680, 1603, 1469, 1313, 1230, 1052, 814, 751 cm^{-1}. HRMS: calcd. for $C_{24}H_{20}ClN_6O$ [M + H]$^+$ 443.1387; found 443.1366.

3-{[1-(4-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6-(4-methoxyphenyl)pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (59): Yield 66% (61 mg); colorless solid, m.p. 222–224 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.27 (d, J = 2.3 Hz, 1 H, 7-H), 8.76 (s, 1 H, 2-H), 8.59 (d, J = 2.3 Hz, 1 H, 5-H), 8.24 (s, 1 H, triazole-H), 7.78 (d, J = 8.8 Hz, 2 H, Ph-H), 7.42 (d, J = 8.5 Hz, 2 H, Bn-H), 7.33 (d, J = 8.5 Hz, 2 H, Bn-H), 7.07 (d, J = 8.8 Hz, 2 H, Ph-H), 5.58 (s, 2 H, CH$_2$), 5.30 (s, 2 H, CH$_2$), 3.81 (s, 3 H, Ph-OCH$_3$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 161.3, 160.5, 157.2, 154.6, 151.2, 143.1, 135.5, 134.6, 133.5, 132.0, 130.6 (2 C), 129.3 (2 C), 128.9 (2 C), 128.5, 124.4, 117.1, 115.2 (2 C), 55.4, 52.1, 41.3 ppm. IR: $\tilde{\nu}_{max}$ = 3051, 2834, 1668, 1603, 1469, 1226, 1180, 1052, 1011, 807 cm^{-1}. HRMS: calcd. for $C_{24}H_{20}ClN_6O_2$ [M + H]$^+$ 459.1336; found 459.1349.

3-{[1-(4-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6-(4-chlorophenyl)pyrido[2,3-*d*]pyrimidin-4(3*H*)-one (60): Yield 55% (51 mg); colorless solid, m.p. 232–234 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.32 (d, J = 2.7 Hz, 1 H, 7-H), 8.80 (s, 1 H, 2-H), 8.70 (d, J = 2.7 Hz, 1 H, 5-H), 8.23 (s, 1 H, triazole-H), 7.90 (d, J = 8.6 Hz, 2 H, Ph-H), 7.59 (d, J = 8.6 Hz, 2 H, Ph-H), 7.43 (d, J = 8.5 Hz, 2 H, Bn-H), 7.34 (d, J = 8.5 Hz, 2 H, Bn-H), 5.57 (s, 2 H, CH$_2$), 5.31 (s, 2 H, CH$_2$) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 160.5, 157.2, 154.1, 151.1, 142.4, 134.9, 134.6, 133.6, 133.1, 132.9, 132.7, 130.0 (2 C), 129.2 (2 C), 129.0 (2 C), 128.8 (2 C), 123.9, 116.7, 52.0, 41.3 ppm. IR: $\tilde{\nu}_{max}$ = 1679, 1605, 1466, 1406, 1229, 1095, 1052, 943, 823 cm^{-1}. HRMS: calcd. for $C_{23}H_{17}Cl_2N_6O$ [M + H]$^+$ 463.0841; found 463.0860.

Supporting Information (see footnote on the first page of this article): General experimental methods, general experimental procedures and characterization data, ^{1}H and ^{13}C NMR spectra of compounds, ORTEP diagram of compound **44** and crystallographic data.

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[1] For our recent work, see: a) Y. Loidreau, P. Marchand, C. Dubouilh-Benard, M.-R. Nourrisson, M. Duflos, N. Loaëc, L. Meijer, T. Besson, *Eur. J. Med. Chem.* **2013**, *59*, 283–295; b) Y. Loidreau, P. Marchand, C. Dubouilh-Benard, M.-R. Nourrisson, M. Duflos, N. Loaëc, L. Meijer, T. Besson, *Eur. J. Med. Chem.* **2012**, *58*, 171–183.

[2] D. Hédou, R. Guillon, C. Lecointe, C. Logé, E. Chosson, T. Besson, *Tetrahedron* **2013**, *69*, 3182–3191; A. Testard, L. Picot, O. Lozach, M. Blairvac, L. Meijer, L. Murillo, J.-M. Piot, V. Thiéry, T. Besson, *J. Enzyme Inhib. Med. Chem.* **2005**, *20*, 557–568; F.-R. Alexandre, A. Berecibar, R. Wrigglesworth, T. Besson, *Tetrahedron Lett.* **2003**, *44*, 4455–4458; T. Besson, J. Guillard, C. W. Rees, *Tetrahedron Lett.* **2000**, *41*, 1027–1030.

[3] a) C. Logé, A. Testard, V. Thiéry, O. Lozach, M. Blairvacq, J.-M. Robert, L. Meijer, T. Besson, *Eur. J. Med. Chem.* **2008**, *43*, 1469–1477; b) A. Testard, C. Logé, B. Léger, J.-M. Robert, O. Lozach, M. Blairvacq, L. Meijer, V. Thiéry, T. Besson, *Bioorg. Med. Chem. Lett.* **2006**, *16*, 3419–3423.

[4] E. Deau, D. Hédou, E. Chosson, V. Levacher, T. Besson, *Tetrahedron Lett.* **2013**, *54*, 3518–3521.

[5] For reviews on triazoles as bioactive agents, see: a) N. Siddiqui, W. Ahsan, M. S. Alam, R. Ali, S. Jain, B. Azad, J. Akhtar, *Int. J. Pharm. Sci. Rev. Res.* **2011**, *8*, 161–169; b) S. G. Agalave, S. R. Maujan, V. S. Pore, *Chem. Asian J.* **2011**, *6*, 2696–2718.

[6] For the latest advances in microwave-assisted organic synthesis (MAOS), see: A. de la Hoz, A. Loupy (Eds.), *Microwaves in Organic Synthesis* 3rd ed., Wiley-VCH, Weinheim, Germany, **2013**, vol. 1 and 2.

[7] H. Vorbrüggen, *Synlett* **2008**, *11*, 1603–1617.

[8] J. G. Topliss, *J. Med. Chem.* **1972**, *15*, 1006–1011. In this paper, proposals were presented for the stepwise selection for the synthesis of analogues of an active compound. The diagrams are based on a fundamental assumption of the Hansch method that a particular substituent may modify the activity relative to the parent compound by virtue of the resulting changes in hydrophobic, electronic and steric effects. In our study, the use of the Topliss scheme allowed us to choose certain reagents to verify the validity of our methodology and at the same time to start to build a list of molecules with potential biological interest.

[9] T. Jin, S. Kamijo, Y. Yamamoto, *Eur. J. Org. Chem.* **2004**, 3789–3791.

[10] For selected examples, see: a) J. Andersen, S. Bolvig, X. Liang, *Synlett* **2005**, *19*, 2941–2947; b) A. K. Feldman, B. Colasson, V. V. Fokin, *Org. Lett.* **2004**, *6*, 3897–3899; c) K. A. Durugkar, R. G. Gonnade, C. V. Ramana, *Tetrahedron* **2009**, *65*, 3974–3979; d) T. Miao, L. Wang, *Synthesis* **2008**, *3*, 363–368.

[11] Although some substituted benzyl azides are commercially available, most are provided, in: small quantities in solutions of TBME or DCM, hence, they were freshly prepared, in: pure form according to known methods, see: J. McNulty, K. Keskar, R. Vemula, *Chem. Eur. J.* **2011**, *17*, 14727–14730; for a comprehensive review on the chemistry and synthesis of organic azides, see: S. Bräse, C. Gil, K. Knepper, V. Zimmermann, *Angew. Chem.* **2005**, *117*, 5320; *Angew. Chem. Int. Ed.* **2005**, *44*, 5188–5240.

[12] The lost dissipation factor (tanδ) expresses the capacity of a molecule or a material to transform electromagnetic energy into thermal energy. A very high susceptibility to microwaves is characterized by a high value (>0.5) of tanδ. tanδ (acetic acid): δ = 0.174 at 2.45 GHz. For more details, see: C. Gabriel, S. Gabriel, E. H. Grant, B. S. J. Halstead, D. M. P. Mingos, *Chem. Soc. Rev.* **1998**, *27*, 213–224.

[13] *SMART for WNT/2000*, v. 5.622, *Smart software reference manual*, Bruker Advanced X-Ray Solutions, Inc., Madison, WI, **2001**.
[14] *SAINT+*, v. 6.02, *Saint software reference manual*, Bruker Advanced X-Ray Solutions, Inc., Madison, WI, **1999**.
[15] SHELXS-97: G. M. Sheldrick, *Acta Crystallogr., Sect. A* **1990**, *46*, 467–473.
[16] G. M. Sheldrick, *SHELXL-97*, release 97–2, *A Program for Crystal Structure Refinement*, University of Göttingen, Germany, **1997**.
[17] L. J. Farrugia, *WinGX*, v. 1.70.01, *An Integrated System of Windows Programs for the Solution, Refinement and Analysis of Single Crystal X-ray Diffraction Data*, University of Glasgow, Glasgow, **2005**.
[18] D. Ranganathan, R. Rathi, K. S. Kesavan, P. Waheguru, *Tetrahedron* **1986**, *42*, 4873–4878.
[19] C. Usifoh, P. Igbinaduwa, *Acta Pol. Pharm.* **2007**, *3*, 281–284.
[20] When unrecrystallized NBS was used, unknown byproducts were observed in the crude mixture. Freshly recrystallized NBS was obtained according to known procedures. For more details, see: W. L. F. Armarego, C. L. L. Chai, *Purification of Laboratory Chemicals*, 6th ed., Elsevier, Oxford, UK, **2009**, p. 105.

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