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Unexpected Synthesis of Rearranged 3,4-Dihydroquinazolines by a Sequential Ugi 4CC/Aza-Wittig/Carbodiimide-Mediated Cyclization

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Keywords: 3,4-Dihydroquinazolines / Multicomponent reactions / Ugi reaction / Aza-Wittig reaction / Azides / Cyclization

The 2,3,4-trisubstituted 3,4-dihydroquinazolines **4** were unexpectedly obtained from a sequential Ugi four component condensation (4CC)/aza-Wittig/carbodiimide-mediated cyclization.

Introduction

Quinazolines have been found to show widespread biological activities and have been used as antiinflammatory, antiallergic, and antimalarial agents and, especially, as cancer treatment agents.[1–5] Lee et al., for example, recently reported a series of compounds containing the 3,4-dihydroquinazoline backbone that display potent T-type channel blocking activity (Figure 1); in particular, compound KYS06090 shows growth inhibition of human cancer cells similar to that of doxorubicin, together with low cytotoxicity.[6–9]

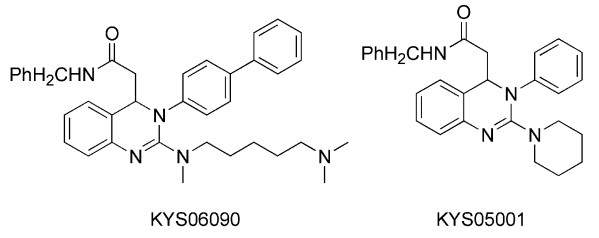


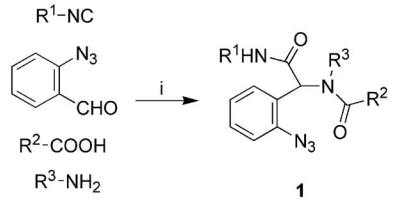
Figure 1. Some 3,4-dihydroquinazolines used as potent cancer-cell inhibitors.

The Ugi reaction is one of the two main isocyanide-based multicomponent reactions (I-MCRs) (the Ugi reaction and the Passerini reaction) and is a powerful, atom-economical reaction between isocyanide, amine, aldehyde (or ketone), and carboxylic acid components that generates a significantly more complex α-acylamino amide adduct.[10–12] Sequences based on classical Ugi isocyanide multicomponent reactions with subsequent postcondensation transformations constitute extremely powerful synthetic tools for the preparation of structurally diverse complex molecules, especially heterocyclic compounds.[13–17]

On the other hand, aza-Wittig reactions are receiving increased attention in view of their utility in the synthesis of nitrogen-containing heterocycles.[18–22] It is therefore clear that the combination of the efficiency of the Ugi condensation with a post-condensation aza-Wittig reaction should facilitate access to a series of biologically useful heterocycles. We have recently been interested in the synthesis of various heterocycles through aza-Wittig reactions, with the aim of evaluating their biological activities.[23–27] In continuation of our previous research, here we report an unexpected synthesis of rearranged 3,4-dihydroquinazolines by a sequential Ugi four component condensation (4CC)/aza-Wittig/carbodiimide-mediated cyclization.

Results and Discussion

Mixtures of 2-azidobenzaldehyde (1 equiv.), an amine (1 equiv.), an isocyanide (1 equiv.), and an acid (1 equiv.) were stirred in methanol at room temperature for 12–36 h until a solid precipitated (Scheme 1). The Ugi reactions proceeded smoothly, and the azide products **1** were obtained after recrystallization in satisfactory yields (Table 1).



Scheme 1. Reaction conditions: (i) MeOH, room temp., 12–36 h, 67–93%.

When the azides **1** were treated with triphenylphosphane in toluene, the iminophosphoranes **2** were easily formed. Subsequent treatment of compounds **2** with isocyanate at room temperature gave the carbodiimides **3**, which were heated at reflux for 6–24 h in toluene. To our surprise, the rearranged 2,3,4-trisubstituted 3,4-dihydroquinazolines **4**, the products of R^2CO group migration from NR^3 to NR^4,

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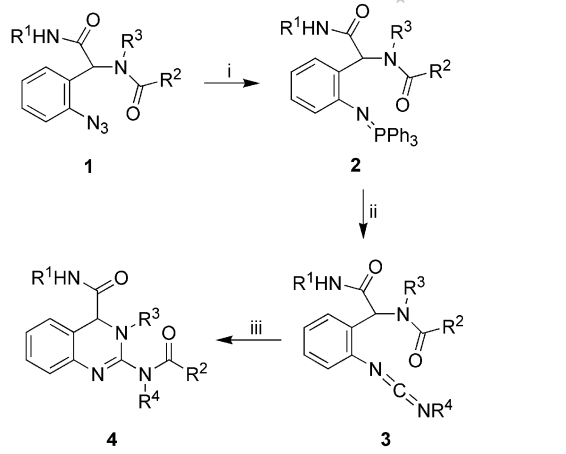
Table 1. Preparation of azides **1** through Ugi 4CC reactions.

Compound	R^1	R^2	R^3	Reaction time [h]	Yield[a] (%)
1a	*t*Bu	Ph	*i*Pr	36	67
1b	*t*Bu	Ph	*n*Pr	12	95
1c	*t*Bu	Ph	*n*Bu	24	87
1d	*t*Bu	Ph	Et	12	76
1e	*t*Bu	Ph	Me	12	89
1f	*t*Bu	4-ClC_6H_4	Et	12	93
1g	*t*Bu	4-ClC_6H_4	Me	12	90
1h	*n*Bu	Ph	*n*Pr	36	91
1i	*n*Bu	Ph	*n*Bu	36	92
1j	*t*Bu	Me	Ph	36	85
1k	*n*Bu	4-ClC_6H_4	4-ClC_6H_4	24	75
1l	*n*Bu	$(CH_2)_2Ph$	Ph	24	70
1m	*n*Bu	Me	*n*Pr	24	79
1n	*n*Bu	Me	*n*Bu	24	63

[a] Isolated yields.



Scheme 2. Reaction conditions: (i) PPh_3, toluene, room temp., 2–4 h; (ii) R^4NCO, toluene, room temp., 2–6 h; (iii) toluene, reflux, 6–24 h, 0–90%.

were obtained from the reaction mixtures when R^3 = alkyl (Scheme 2). The results are listed in Table 2. As can be seen, the yield of the product is related to the R^3 substituent: good yields were achieved when R^3 was a primary alkyl group (**4b**–**4v**), whereas a low yield was obtained when a secondary alkyl group was used (**4a**). The carbodiimides **3** were recovered unchanged if R^3 was an aryl group (**4w**, **4x**). The structures of the 2,3,4-trisubstituted 3,4-dihydroquinazolines **4** were confirmed by their spectral data. Furthermore, a single crystal of **4u** was obtained from a CH_2Cl_2 solution of **4u**. X-ray structure analysis verified the proposed structure, and showed intramolecular hydrogen-bond formation between one amido hydrogen atom (N4-H) and another amido oxygen atom (O1), forming a nine-membered cycle (Figure 2).

It is noteworthy that there are no reports relating to reactions between *N*,*N*-disubstituted amides (containing no N–H moiety) and carbodiimides.[28] However, carbodiimides with adjacent amide groups containing N–H groups generally tend to cyclize directly to form five- or six-membered heterocycles. The cyclization of the carbodiimides **5**, for example, gave the quinazolinones **6** in good yields in toluene at reflux (Scheme 3).[29] Heating of the carbodiimides **3**, however, did not provide the expected benzodiazepines **7** (Scheme 4, below), probably because of the restricted conformation of the amido side chains, which could be entropically unfavorable for the cyclizations.

Table 2. Preparation of 2,3,4-trisubstituted 3,4-dihydroquinazolines **4**.

Compound	R^1	R^2	R^3	R^4	Reaction time [h]	Yield[a] (%)
4a	*t*Bu	Ph	*i*Pr	4-ClC_6H_4	20	17
4b	*t*Bu	Ph	*n*Pr	4-FC_6H_4	15	69
4c	*t*Bu	Ph	*n*Pr	3-$CH_3C_6H_4$	10	78
4d	*t*Bu	Ph	*n*Pr	4-ClC_6H_4	8	85
4e	*t*Bu	Ph	*n*Pr	Ph	12	76
4f	*t*Bu	Ph	*n*Bu	4-ClC_6H_4	10	88
4g	*t*Bu	Ph	*n*Bu	Ph	14	85
4h	*t*Bu	Ph	*n*Bu	4-FC_6H_4	12	83
4i	*t*Bu	Ph	Et	Ph	8	90
4j	*t*Bu	Ph	Et	4-FC_6H_4	6	87
4k	*t*Bu	Ph	Et	3-$CH_3C_6H_4$	6	89
4l	*t*Bu	Ph	Me	Ph	8	90
4m	*t*Bu	Ph	Me	4-ClC_6H_4	6	83
4n	*t*Bu	4-ClC_6H_4	Et	Ph	6	89
4o	*t*Bu	4-ClC_6H_4	Et	4-ClC_6H_4	6	88
4p	*t*Bu	4-ClC_6H_4	Et	4-FC_6H_4	8	81
4q	*t*Bu	4-ClC_6H_4	Et	*i*Pr	18	79
4r	*t*Bu	4-ClC_6H_4	Me	3-$CH_3C_6H_4$	6	84
4s	*t*Bu	4-ClC_6H_4	Me	Ph	6	89
4t	*n*Bu	Ph	*n*Pr	4-ClC_6H_4	16	67
4u	*n*Bu	Ph	*n*Bu	4-ClC_6H_4	12	61
4v	*n*Bu	Me	*n*Bu	4-ClC_6H_4	8	67
4w	*t*Bu	Me	Ph	3-$CH_3C_6H_4$	24	0
4x	*n*Bu	4-ClC_6H_4	4-ClC_6H_4	3-$CH_3C_6H_4$	24	0

[a] Isolated yields.

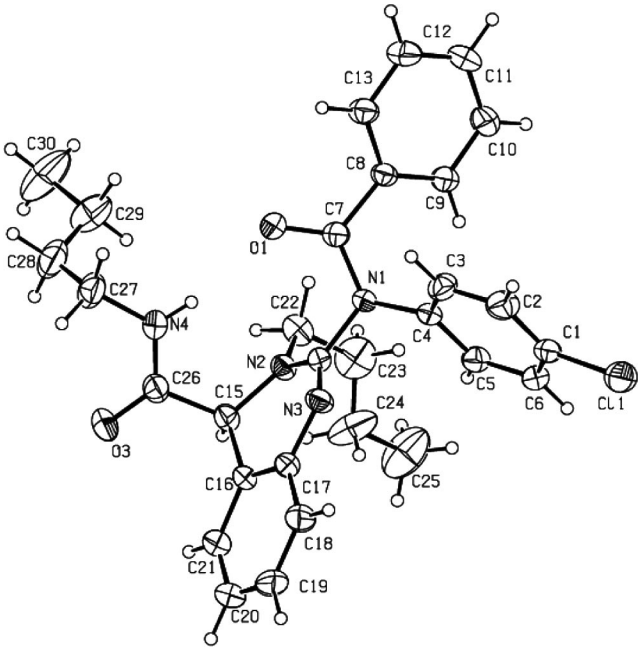
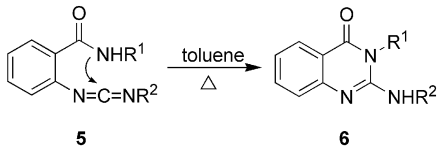
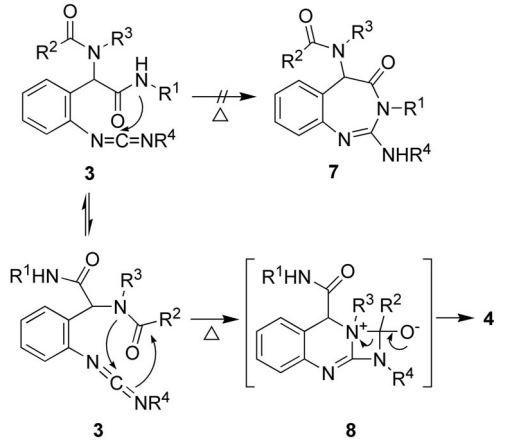


Figure 2. X-ray crystal structure of compound **4u**.



Scheme 3. Literature synthesis of quinazolinones **6** from carbodiimides **5**.

A possible mechanism for the formation of the 3,4-dihydroquinazolines **4** is proposed (Scheme 4). It presumably involves the formation of diazeto[2,1-*b*]quinazoline intermediates **8** through intramolecular cycloaddition between the *N*,*N*-disubstituted amides and the carbodiimide moieties. Further ring-opening would then take place concomitantly with the cleavage of the nitrogen–carbon bond to give the rearranged products **4**. The formation of the intermediates



Scheme 4. Possible mechanism for formation of 3,4-dihydroquinazolines **4**.

8 might be influenced both by the nucleophilicity of the nitrogen atom and by the steric effect of R^3. When R^3 is an electron-releasing and sterically less bulky alkyl group, the intermediate **8** should be easily formed. The reaction would be retarded, however, if R^3 is an aryl group (**4w**, **4x**) or a sterically bulky secondary alkyl group (**4a**).

Conclusions

We report a novel multicomponent synthesis of 3,4-dihydroquinazoline based on the Ugi reaction followed by a Staudinger/aza-Wittig/carbodiimide-mediated reaction. Intramolecular cyclizations of carbodiimides with *N*,*N*-disubstituted amides and subsequent acyl migration have been reported for the first time. Thanks to the easy accessibility of the synthetic approach and the neutral ring closure conditions, this new synthetic approach discussed here offers potential for the synthesis of various 2,3,4-trisubstituted 3,4-dihydroquinazolines, which are of considerable interest as potential biologically active compounds or pharmaceuticals.

Experimental Section

General Procedures: All reactions were performed in round-bottomed flasks. Column chromatography purifications were performed under "flash" conditions with 400–630 mesh silica gel, except where otherwise noted. Analytical thin-layer chromatography (TLC) was carried out with silica gel (60 F_{254}) plates, which were visualized by exposure to ultraviolet light.

Instrumentation: Melting points are uncorrected. Mass spectra were measured with a Finnigan Trace MS spectrometer. IR spectra were recorded with a PE-983 infrared spectrometer as KBr pellets with absorption in cm^{-1}. NMR spectra were recorded in $CDCl_3$ with a Varian Mercury 400 or 600 spectrometer and resonances relative to TMS. Elemental analyses were carried out with a Vario EL III elementary analysis instrument. The X-ray diffraction data were collected with a Bruker SMART AXS CCD diffractometer, Mo-K_α, 2θ = 1.86–27.50°. CCDC-753684 (**4u**) contains 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.

General Procedure for the Preparation of the Azides 1: *o*-Azidobenzaldehyde (0.44 g, 3 mmol), a carboxylic acid (3 mmol), and an isocyanide (3 mmol) were added sequentially at room temperature to a solution of an amine (3 mmol) in methanol (20 mL). The reaction mixture was stirred at ambient temperature for 12–36 h until a solid precipitated, and the solvent was evaporated. The crude reaction mixture was purified by recrystallization from dichloromethane/petroleum ether.

***N*-[(2-Azidophenyl)(*tert*-butylcarbamoyl)methyl]-*N*-isopropylbenzamide (1a):** White crystals (yield 0.79 g, 67%). M.p. 179–180 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.85–0.86 (d, J = 5.4 Hz, 3 H, CH_3), 1.23–1.40 (m, 12 H, 4 CH_3), 4.02 (s, 0.6 H, 0.3 COCH, 0.3 NCH), 5.08 (s, 0.7 H, 0.7 NCH), 5.42 (s, 0.7 H, 0.7 COCH), 7.74 (s, 0.7 H, 0.7 CONH), 7.19–7.59 (m, 9 H, Ar-H), 8.01–8.03 (m, 0.3 H, 0.3 CONH) ppm. IR (KBr): $\tilde{\nu}$ = 3319, 3066, 2975, 2130, 1678, 1613 cm^{-1}. MS: *m*/*z* (%) = 351 (12) $[M - N_3]^+$, 251 (100), 106 (38),

77 (40). $C_{22}H_{27}N_5O_2$ (393.5): calcd. C 67.15, H 6.92, N 17.80; found C 67.10, H 6.99, N 17.98.

***N*-[(2-Azidophenyl)(*tert*-butylcarbamoyl)methyl]-*N*-propylbenzamide (1b):** White crystals (yield 1.12 g, 95%). M.p. 159–160 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.62 (t, J = 6.6 Hz, 3 H, CH_3), 0.83–0.90 (m, 0.6 H, 0.6 CH_2), 1.12–1.16 (m, 0.6 H, 0.6 CH_2), 1.27–1.61 (m, 9.8 H, 3 CH_3, 0.8 CH_2), 2.38–2.46 (m, 0.4 H, 0.4 NCH), 3.17–3.24 (m, 1.2 H, 1.2 NCH), 3.41–3.47 (m, 0.4 H, 0.4 NCH), 5.27 (s, 0.6 H, 0.6 COCH), 5.76 (s, 0.4 H, 0.4 COCH), 6.35 (s, 0.6 H, 0.6 CONH), 7.16–7.44 (m, 9 H, Ar-H), 7.71 (s, 0.4 H, 0.4 CONH) ppm. IR (KBr): $\tilde{\nu}$ = 3317, 3064, 2967, 2935, 2877, 2127, 1674, 1607 cm^{-1}. MS: *m*/*z* (%) = 351 (3) [M – N_3]$^+$, 251 (100), 106 (46), 77 (86). $C_{22}H_{27}N_5O_2$ (393.5): calcd. C 67.15, H 6.92, N 17.80; found C 67.01, H 7.14, N 17.93.

***N*-[(2-Azidophenyl)(*tert*-butylcarbamoyl)methyl]-*N*-butylbenzamide (1c):** White crystals (yield 1.06 g, 87%). M.p. 128–130 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.90–1.48 (m, 16 H, 3 CH_3, 1 $CH_3CH_2CH_2$), 3.23 (s, 1.4 H, 0.7 NCH_2), 3.25 (s, 0.3 H, 0.15 NCH_2), 5.27 (s, 0.3 H, 0.15 NCH_2), 5.79 (s, 0.3 H, 0.3 COCH), 6.34 (s, 0.7 H, 0.7 COCH), 7.17–7.56 (m, 9 H, Ar-H), 7.71 (s, 0.7 H, 0.7 CONH), 8.07–8.06 (m, 0.3 H, 0.3 CONH) ppm. IR (KBr): $\tilde{\nu}$ = 3313, 3062, 2961, 2933, 2878, 2129, 1670, 1609 cm^{-1}. MS: *m*/*z* (%) = 365 (3) [M – N_3]$^+$, 265 (100), 106 (35), 77 (60). $C_{23}H_{29}N_5O_2$ (407.5): calcd. C 67.79, H 7.17, N 17.19; found C 67.60, H 7.21, N 17.23.

***N*-[(2-Azidophenyl)(*tert*-butylcarbamoyl)methyl]-*N*-ethylbenzamide (1d):** White crystals (yield 0.86 g, 76%). M.p. 183–184 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.81 (t, J = 6.8 Hz, 3 H, CH_3), 1.38 (s, 9 H, 3 CH_3), 3.42 (s, 1.6 H, 0.8 CH_2), 3.60 (s, 0.4 H, 0.2 CH_2), 5.29 (s, 0.2 H, 0.2 COCH), 5.86 (s, 0.8 H, 0.8 COCH), 6.15 (s, 0.6 H, 0.6 CONH), 7.16–7.45 (m, 9 H, Ar-H), 7.69 (s, 0.25 H, 0.25 CONH), 8.01 (s, 0.15 H, 0.15 CONH) ppm. IR (KBr): $\tilde{\nu}$ = 3358, 3059, 2981, 2937, 2132, 1682, 1618 cm^{-1}. MS: *m*/*z* (%) = 337 (7) [M – N_3]$^+$, 237 (100), 106 (50), 77 (43). $C_{21}H_{25}N_5O_2$ (379.5): calcd. C 66.47, H 6.64, N 18.46; found C 66.41, H 6.88, N 18.39.

***N*-[(2-Azidophenyl)(*tert*-butylcarbamoyl)methyl]-*N*-methylbenzamide (1e):** White crystals (yield 0.97 g, 89%). M.p. 149–150 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.39 (s, 9 H, 3 CH_3), 2.78 (s, 3 H, CH_3), 5.29 (s, 0.3 H, 0.3 COCH), 5.93 (s, 0.7 H, 0.7 COCH), 6.20 (s, 0.3 H, 0.3 CONH), 7.46–7.16 (m, 9 H, Ar-H), 8.10 (d, 0.7 H, 0.7 CONH) ppm. IR (KBr): $\tilde{\nu}$ = 3350, 3056, 2982, 2937, 2137, 1684, 1617 cm^{-1}. MS: *m*/*z* (%) = 337 (14) [M – N_2]$^+$, 223 (100), 106 (59), 77 (41). $C_{20}H_{23}N_5O_2$ (365.4): calcd. C 65.73, H 6.34, N 19.16; found C 65.50, H 6.38, N 19.29.

***N*-[(2-Azidophenyl)(*tert*-butylcarbamoyl)methyl]-4-chloro-*N*-ethylbenzamide (1f):** White crystals (yield 1.15 g, 93%). M.p. 207–209 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.77 (t, J = 6.8 Hz, 3 H, CH_3), 1.37 (s, 9 H, 3 CH_3), 3.28–3.58 (m, 2 H, CH_2), 5.27 (s, 1 H, COCH), 5.86 (s, 1 H, CONH), 7.17–7.62 (m, 8 H, Ar-H) ppm. IR (KBr): $\tilde{\nu}$ = 3353, 3054, 2985, 2939, 2135, 1683, 1613 cm^{-1}. MS: *m*/*z* (%) = 371 (7) [M – N_3]$^+$, 271 (100), 106 (43), 77 (51). $C_{21}H_{24}ClN_5O_2$ (413.9): calcd. C 60.94, H 5.84, N 16.92; found C 60.90, H 5.98, N 16.97.

***N*-[(2-Azidophenyl)(*tert*-butylcarbamoyl)methyl]-4-chloro-*N*-methylbenzamide (1g):** White crystals (yield 1.08 g, 90%). M.p. 211–212 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.38 (s, 9 H, 3 CH_3), 3.75 (s, 3 H, CH_3), 5.26 (s, 0.8 H, 0.8 COCH), 5.64 (s, 0.4 H, 0.2 COCH + 0.2 CONH), 6.13 (s, 0.8 H, 0.8 CONH), 7.17–7.53 (m, 8 H, Ar-H) ppm. IR (KBr): $\tilde{\nu}$ = 3341, 3056, 2978, 2928, 2125, 1689, 1610 cm^{-1}. MS: *m*/*z* (%) = 357 (14) [M – N_3]$^+$, 257 (100), 106 (59), 77 (41). $C_{20}H_{22}ClN_5O_2$ (399.9): calcd. C 60.07, H 5.55, N 17.51; found C 60.21, H 5.69, N 17.26.

***N*-[(2-Azidophenyl)(butylcarbamoyl)methyl]-*N*-propylbenzamide (1h):** White crystals (yield 1.07 g, 91%). M.p. 115–116 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.55–1.64 (m, 12 H, $CH_2CH_2CH_3$ + CH_2CH_3), 3.31–3.46 (m, 4 H, 2 NCH_2), 5.57 (s, 0.2 H, 0.2 COCH), 5.80 (s, 0.8 H, 0.8 COCH), 6.55 (s, 0.8 H, 0.8 CONH), 7.15–7.70 (m, 9 H, Ar-H), 7.99–8.00 (m, 0.2 H, 0.2 CONH) ppm. IR (KBr): $\tilde{\nu}$ = 3350, 3053, 2982, 2941, 2136, 1687, 1619 cm^{-1}. MS: *m*/*z* (%) = 351 (3) [M – N_3]$^+$, 251 (100), 106 (46), 77 (86). $C_{22}H_{27}N_5O_2$ (393.5): calcd. C 67.15, H 6.92, N 17.80; found C 67.07, H 6.96, N 17.94.

***N*-[(2-Azidophenyl)(butylcarbamoyl)methyl]-*N*-butylbenzamide (1i):** White crystals (yield 1.12 g, 92%). M.p. 100–102 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.60–1.61 (m, 14 H, 2 $CH_2CH_2CH_3$), 3.31–3.56 (m, 4 H, 2 NCH_2), 5.47 (s, 0.3 H, 0.3 CONH), 5.81 (s, 0.5 H, 0.5 COCH), 6.49 (s, 0.5 H, 0.5 COCH), 7.10–7.53 (m, 9 H, Ar-H), 7.70 (s, 0.5 H, 0.5 CONH), 8.03–8.05 (m, 0.2 H, 0.2 CONH) ppm. IR (KBr): $\tilde{\nu}$ = 3352, 3056, 2988, 2947, 2139, 1684, 1623 cm^{-1}. MS: *m*/*z* (%) = 365 (5) [M – N_3]$^+$, 265 (100), 106 (54), 77 (36). $C_{23}H_{29}N_5O_2$ (407.5): calcd. C 67.79, H 7.17, N 17.19; found C 67.55, H 7.29, N 17.22.

***N*-[(2-Azidophenyl)(*tert*-butylcarbamoyl)methyl]-*N*-phenylethylamide (1j):** White crystals (yield 0.93 g, 85%). M.p. 195–196 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 1.36 (s, 9 H, 3 CH_3), 1.88 (s, 3 H, CH_3), 5.55 (s, 1 H, CONH), 6.20 (s, 1 H, COCH), 6.82–7.21 (m, 9 H, Ar-H) ppm. IR (KBr): $\tilde{\nu}$ = 3356, 3051, 2984, 2943, 2131, 1678, 1617 cm^{-1}. MS: *m*/*z* (%) = 323 (7) [M – N_3]$^+$, 223 (100), 106 (50), 77 (19). $C_{20}H_{23}N_5O_2$ (365.4): calcd. C 65.73, H 6.34, N 19.16; found C 65.57, H 6.38, N 19.25.

***N*-[(2-Azidophenyl)(butylcarbamoyl)methyl]-4-chloro-*N*-(4-chlorophenyl)benzamide (1k):** White crystals (yield 1.12 g, 75%). M.p. 197–198 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.88 (t, J = 7.2 Hz, 3 H, CH_3), 1.28–1.36 (m, 2 H, CH_2), 1.46–1.53 (m, 2 H, CH_2), 3.30–3.38 (m, 2 H, CH_2), 5.83 (s, 1 H, CONH), 6.42 (s, 1 H, COCH), 6.95–7.30 (m, 12 H, Ar-H) ppm. IR (KBr): $\tilde{\nu}$ = 3352, 3045, 2981, 2940, 2231, 1669, 1621 cm^{-1}. MS: *m*/*z* (%) = 453 (4) [M – N_3]$^+$, 342 (76), 242 (100), 139 (509), 77 (35). $C_{25}H_{23}C_{12}N_5O_2$ (496.4): calcd. C 60.49, H 4.67, N 14.11; found C 60.63, H 4.52, N 14.23.

***N*-[(2-Azidophenyl)(butylcarbamoyl)methyl]-*N*,3-diphenylpropanamide (1l):** White crystals (yield 0.96 g, 70%). M.p. 180–181 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.90 (t, J = 7.2 Hz, 3 H, CH_3), 1.27–1.33 (m, 2 H, CH_2), 1.43–1.49 (m, 2 H, CH_2), 2.36 (t, J = 7.4 Hz, 2 H, CH_2), 2.93 (t, J = 7.4 Hz, 2 H, CH_2), 3.25–3.35 (m, 2 H, CH_2), 5.85 (s, 1 H, CONH), 6.30 (s, 1 H, COCH), 7.29–6.79 (m, 14 H, Ar-H) ppm. IR (KBr): $\tilde{\nu}$ = 3349, 3053, 2973, 2935, 2191, 1676, 1629 cm^{-1}. MS: *m*/*z* (%) = 413 (10) [M – N_3]$^+$, 280 (45), 180 (100), 77 (69). $C_{27}H_{29}N_5O_2$ (455.6): calcd. C 71.19, H 6.42, N 15.37; found C 71.11, H 6.28, N 15.19.

***N*-[(2-Azidophenyl)(butylcarbamoyl)methyl]-*N*-propylethanamide (1m):** White crystals (yield 0.78 g, 79%). M.p. 100–102 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.68–1.47 (m, 12 H, CH_2CH_3 + $CH_2CH_2CH_3$), 2.17 (s, 2.4 H, 0.8 CH_3), 2.28 (s, 0.6 H, 0.2 CH_3), 3.18–3.30 (m, 4 H, 2 NCH_2), 5.64 (s, 0.2 H, 0.2 COCH), 5.92 (s, 0.8 H, 0.8 COCH), 5.93–6.06 (m, 0.8 H, 0.8 CONH), 6.14–6.15 (m, 0.2 H, 0.2 CONH), 7.14–7.59 (m, 4 H, Ar-H) ppm. IR (KBr): $\tilde{\nu}$ = 3273, 3079, 2959, 2932, 2871, 2126, 1679, 1622 cm^{-1}. MS: *m*/*z* (%) = 289 (3) [M – N_3]$^+$, 246 (63), 146 (100), 77 (38). $C_{17}H_{25}N_5O_2$ (331.4): calcd. C 61.61, H 7.60, N 21.13; found C 61.72, H 7.49, N 21.22.

***N*-[(2-Azidophenyl)(butylcarbamoyl)methyl]-*N*-butylethanamide (1n):** White crystals (yield 0.65 g, 63%). M.p. 121–122 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.64–1.46 (m, 14 H, 2 $CH_2CH_2CH_3$), 2.17

(s, 2.4 H, 0.8 CH_3), 2.28 (s, 0.6 H, 0.2 CH_3), 2.89 (s, 0.2 H, 0.1 NCH_2), 3.24–3.29 (m, 3.6 H, 1.8 NCH_2), 3.50 (s, 0.2 H, 0.1 NCH_2), 5.65 (s, 0.2 H, 0.2 COCH), 5.93 (s, 0.8 H, 0.8 COCH), 6.01 (s, 0.8 H, 0.8 CONH), 6.15 (s, 0.2 H, 0.2 CONH), 7.16–7.60 (m, 4 H, Ar-H) ppm. IR (KBr): $\tilde{\nu}$ = 3271, 3084, 2958, 2932, 2866, 2128, 1679, 1625 cm^{-1}. MS: *m*/*z* (%) = 303 (2) $[M - N_3]^+$, 203 (100), 160 (47), 77 (88). $C_{18}H_{27}N_5O_2$ (331.4): calcd. C 62.58, H 7.88, N 20.27; found C 62.72, H 7.99, N 20.21.

General Procedure for the Preparation of the 2,3,4-Trisubstituted 3,4-Dihydroquinazolines 4: Triphenylphosphane (0.26 g, 1 mmol) was added with stirring to a solution of an azide **1** (1 mmol) in dry toluene (10 mL). After stirring had been continued for 2–4 h, an iminophosphorane **2** had formed, as was monitored by TLC. An isocyanate (1 mmol) was then added dropwise to the mixture. A carbodiimide **3** was formed (two were isolated), and the reaction was found to be complete (monitoring by TLC) at room temperature after 2–6 h. The solution was then heated at reflux for 6–24 h. After the reaction was complete, the solvent was evaporated, and the residue was purified by column chromatography.

***N*-*tert*-Butyl-2-[*N*-(4-chlorophenyl)benzamido]-3-isopropyl-3,4-dihydroquinazoline-4-carboxamide (4a):** White crystals (yield 0.085 g, 17%). M.p. 243–244 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 1.29–1.38 (m, 15 H, 5 CH_3), 4.57–4.62 (m, 1 H, NCH), 5.09 (s, 1 H, COCH), 6.88–7.48 (m, 13 H, Ar-H), 8.63 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 19.8, 19.9, 22.0, 28.5, 50.6, 51.7, 58.6, 122.5, 123.9, 125.9, 126.8, 128.4, 128.5, 128.6, 129.3, 131.7, 132.6, 133.6, 140.6, 141.0, 149.8, 170.1, 171.3 ppm. IR (KBr): $\tilde{\nu}$ = 3329, 3036, 2975, 1657, 1613 cm^{-1}. MS: *m*/*z* (%) = 402 (100) $[M - 100]^+$, 254 (58), 77 (89). $C_{29}H_{31}ClN_4O_2$ (503.0): calcd. C 69.24, H 6.21, N 11.14; found C 69.01, H 6.37, N 11.19.

***N*-*tert*-Butyl-2-[*N*-(4-fluorophenyl)benzamido]-3-propyl-3,4-dihydroquinazoline-4-carboxamide (4b):** White crystals (yield 0.34 g, 69%). M.p. 222–224 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.91 (t, *J* = 6.6 Hz, 3 H, CH_3), 1.40 (s, 9 H, 3 CH_3), 1.61–1.67 (m, 1 H, CH), 1.82 (s, 1 H, CH), 3.28 (s, 1 H, NCH), 3.59–3.63 (m, 1 H, NCH), 5.08 (s, 1 H, COCH), 6.92–7.48 (m, 13 H, Ar-H), 8.51 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 11.2, 21.5, 28.5, 51.7, 52.0, 64.1, 115.9, 116.1, 121.7, 124.2, 125.6, 126.7, 128.3, 128.6, 128.7, 129.2, 131.6, 133.4, 137.5, 140.8, 149.7, 159.7, 162.2, 169.2, 171.4 ppm. IR (KBr): $\tilde{\nu}$ = 3310, 3054, 2979, 2928, 2872, 1659, 1620 cm^{-1}. MS: *m*/*z* (%) = 386 (100) $[M - 100]^+$, 198 (21), 105 (8). $C_{29}H_{31}FN_4O_2$ (486.6): calcd. C 71.58, H 6.42, N 11.51; found C 71.42, H 6.57, N 11.65.

***N*-*tert*-Butyl-3-propyl-2-[*N*-(*m*-tolyl)benzamido]-3,4-dihydroquinazoline-4-carboxamide (4c):** White crystals (yield 0.38 g, 78%). M.p. 255–256 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.90 (t, *J* = 7.0 Hz, 3 H), 1.40 (s, 9 H, 3 CH_3), 1.78–1.61 (m, 2 H, CH_2), 2.22 (s, 2.65 H, 2.65 Ar-CH), 2.35 (s, 0.35 H, 0.35 Ar-CH), 3.31–3.27 (m, 1 H, NCH), 3.61–3.57 (m, 1 H, NCH), 5.08 (s, 1 H, COCH), 7.50–6.86 (m, 13 H, Ar-H), 8.57 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 11.2, 21.2, 21.5, 28.6, 51.8, 52.1, 64.4, 121.9, 124.1, 124.4, 125.6, 126.7, 127.5, 127.7, 128.2, 128.6, 128.8, 129.0, 129.3, 131.4, 134.0, 139.1, 141.1, 141.4, 149.9, 169.4, 171.4 ppm. IR (KBr): $\tilde{\nu}$ = 3302, 3043, 2977, 2960, 2927, 2872, 1657, 1620 cm^{-1}. MS: *m*/*z* (%) = 382 (100) $[M - 100]^+$, 198 (21), 105 (8). $C_{30}H_{34}N_4O_2$ (482.6): calcd. C 74.66, H 7.10, N 11.61; found C 74.88, H 7.14, N 11.43.

***N*-*tert*-Butyl-2-[*N*-(4-chlorophenyl)benzamido]-3-propyl-3,4-dihydroquinazoline-4-carboxamide (4d):** White crystals (yield 0.43 g, 85%). M.p. 233–235 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.89 (t, *J* = 7.0 Hz, 3 H, CH_3), 1.25 (s, 1 H, 1/3 CH_3), 1.39 (s, 8 H, 8/3 CH_3), 1.61–1.69 (m, 2 H, CH_2), 3.24–3.30 (m, 1 H, NCH), 3.54–3.60 (m, 1 H, NCH), 5.07 (s, 1 H, COCH), 6.92–7.49 (m, 13 H, Ar-H), 8.47 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 11.2, 21.6, 28.6, 29.6, 51.8, 52.2, 64.3, 121.8, 124.3, 125.8, 126.8, 128.1, 128.5, 128.7, 129.3, 131.8, 132.6, 133.4, 140.2, 140.8, 149.7, 169.2, 171.3 ppm. IR (KBr): $\tilde{\nu}$ = 3314, 3056, 2963, 2928, 1659, 1620 cm^{-1}. MS: *m*/*z* (%) = 402 (9) $[M - 100]^+$, 254 (20), 214 (67), 105 (100). $C_{29}H_{31}ClN_4O_2$ (503.0): calcd. C 69.24, H 6.21, N 11.14; found C 69.07, H 6.04, N 11.18.

***N*-*tert*-Butyl-2-(*N*-phenylbenzamido)-3-propyl-3,4-dihydroquinazoline-4-carboxamide (4e):** White crystals (yield 0.36 g, 76%). M.p. 205–206 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.90 (t, *J* = 7.0 Hz, 3 H, CH_3), 1.26 (s, 1 H, 1/3 CH_3), 1.40 (s, 8 H, 8/3 CH_3), 1.61–1.75 (m, 2 H, CH_2), 3.28–3.30 (m, 1 H, NCH), 3.62 (s, 1 H, NCH), 5.08 (s, 1 H, COCH), 6.93–7.50 (m, 14 H, Ar-H), 8.55 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 11.2, 21.5, 28.6, 51.8, 52.1, 64.3, 121.9, 124.3, 125.6, 126.8, 126.9, 126.9, 128.3, 128.7, 129.1, 129.4, 131.6, 133.8, 141.0, 141.6, 149.9, 169.4, 171.4 ppm. IR (KBr): $\tilde{\nu}$ = 3305, 3054, 2977, 2927, 2871, 1659, 1619 cm^{-1}. MS: *m*/*z* (%) = 470 (9) $[M]^+$, 369 (87), 264 (14), 220 (44), 180 (81), 105 (100), 77 (88), 57 (66). $C_{29}H_{32}N_4O_2$ (468.6): calcd. C 74.33, H 6.88, N 11.96; found C 74.54, H 6.83, N 11.72.

3-Butyl-*N*-(*tert*-butyl)-2-[*N*-(4-chlorophenyl)benzamido]-3,4-dihydroquinazoline-4-carboxamide (4f): White crystals (yield 0.45 g, 88%). M.p. 187–188 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.89–0.96 (m, 3 H, CH_3), 1.20–1.42 (m, 11 H, 3 CH_3 + 1 CH_2), 1.53–1.64 (m, 1 H, CH), 1.76–1.89 (m, 1 H, CH), 3.25–3.31 (m, 1 H, NCH), 3.61–3.66 (m, 1 H, NCH), 5.08 (s, 1 H, COCH), 6.91–7.50 (m, 13 H, Ar-H), 8.51 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.8, 20.0, 28.6, 30.4, 50.3, 51.8, 64.1, 121.7, 124.2, 125.8, 126.8, 128.1, 128.5, 128.7, 129.3, 131.9, 132.5, 133.3, 140.2, 140.7, 149.7, 169.2, 171.3 ppm. IR (KBr): $\tilde{\nu}$ = 3309, 3055, 2965, 2931, 2873, 1661, 1619 cm^{-1}. MS: *m*/*z* (%) = 517 (18) $[M]^+$, 416 (100), 312 (16), 214 (81), 105 (75), 77 (18), 57 (17). $C_{30}H_{33}ClN_4O_2$ (517.1): calcd. C 69.69, H 6.43, N 10.84; found C 69.54, H 6.32, N 10.99.

3-Butyl-*N*-(*tert*-butyl)-2-(*N*-phenylbenzamido)-3,4-dihydroquinazoline-4-carboxamide (4g): White crystals (yield 0.41 g, 85%). M.p. 210–211 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.91 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.80–1.92 (m, 13 H, 3 CH_3 + 1 CH_2CH_2), 3.27–3.34 (m, 1 H, NCH), 3.64–3.71 (m, 1 H, NCH), 5.09 (s, 1 H, COCH), 6.92–7.50 (m, 14 H, Ar-H), 8.56 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.7, 20.0, 28.6, 30.3, 51.7, 50.2, 64.2, 114.2, 121.8, 124.3, 125.6, 126.7, 126.9, 128.2, 128.6, 129.1, 129.3, 131.5, 133.7, 141.0, 141.5, 149.9, 169.3, 171.3 ppm. IR (KBr): $\tilde{\nu}$ = 3312, 3058, 2962, 2931, 2874, 1665, 1620 cm^{-1}. MS: *m*/*z* (%) = 382 (44) $[M - 100]^+$, 221 (18), 180 (90), 105 (100), 77 (56). $C_{30}H_{34}N_4O_2$ (482.6): calcd. C 74.66, H 7.10, N 11.61; found C 74.43, H 7.24, N 11.66.

3-Butyl-*N*-(*tert*-butyl)-2-[*N*-(4-fluorophenyl)benzamido]-3,4-dihydroquinazoline-4-carboxamide (4h): White crystals (yield 0.42 g, 83%). M.p. 231–232 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.92 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.28–1.39 (m, 11 H, 3 CH_3 + 1 CH_2), 1.54–1.68 (m, 1 H, CH), 1.72–1.80 (m, 1 H, CH), 3.26–3.34 (m, 1 H, NCH), 3.62–3.70 (m, 1 H, NCH), 5.08 (s, 1 H, COCH), 6.91–7.48 (m, 13 H, Ar-H), 8.53 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.7, 20.0, 28.5, 30.4, 50.2, 51.7, 64.1, 115.9, 116.2, 121.7, 124.2, 125.7, 126.7, 128.3, 128.6, 128.7, 129.2, 131.6, 133.4, 137.6, 140.8, 149.7, 159.7, 162.2, 169.2, 171.4 ppm. IR (KBr): $\tilde{\nu}$ = 3309, 3062, 2964 2933, 2873 1661, 1620 cm^{-1}. MS: *m*/*z* (%) = 400 (100) $[M - 100]^+$, 238 (34), 198 (75), 105 (61), 77 (42), 57 (41). $C_{30}H_{33}FN_4O_2$ (500.6): calcd. C 71.98, H 6.64, N 11.19; found C 71.82, H 6.67, N 11.34.

***N*-(*tert*-Butyl)-3-ethyl-2-(*N*-phenylbenzamido)-3,4-dihydroquinazoline-4-carboxamide (4i):** White crystals (yield 0.41 g, 90%). M.p. 211–213 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.29 (t, J = 6.8 Hz, 3 H, CH_3), 1.40 (s, 9 H, 3 CH_3), 3.45–3.51 (m, 1 H, NCH), 3.73–3.78 (m, 1 H, NCH), 5.09 (s, 1 H, COCH), 6.92–7.50 (m, 14 H, Ar-H), 8.54 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.6, 28.6, 45.1, 51.7, 63.8, 121.8, 124.3, 125.6, 126.7, 126.9, 127.0, 128.2, 128.6, 129.1, 129.3, 131.5, 133.7, 141.0, 141.4, 149.7, 169.4, 171.2 ppm. IR (KBr): $\tilde{\nu}$ = 3323, 3063, 2972, 2931, 1657, 1612 cm^{-1}. MS: *m*/*z* (%) = 354 (3) [M – 100]$^+$, 180 (20), 105 (79), 77 (94), 57 (100). $C_{28}H_{30}N_4O_2$ (454.6): calcd. C 73.98, H 6.65, N 12.33; found C 73.93, H 6.78, N 12.56.

***N*-(*tert*-Butyl)-3-ethyl-2-[*N*-(4-fluorophenyl)benzamido]-3,4-dihydroquinazoline-4-carboxamide (4j):** White crystals (yield 0.41 g, 87%). M.p. 190–192 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.30 (t, J = 7.0 Hz, 3 H, CH_3), 1.40 (s, 9 H, 3 CH_3), 3.45–3.51 (m, 1 H, NCH), 3.72–3.77 (m, 1 H, NCH), 5.09 (s, 1 H, COCH), 6.93–7.48 (m, 13 H, Ar-H), 8.51 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.7, 28.5, 45.1, 51.7, 63.7, 116.0, 116.2, 121.7, 124.2, 125.7, 126.7, 128.3, 128.7, 128.8, 128.8, 129.3, 131.6, 133.4, 140.8, 149.6, 159.8, 162.3, 169.3, 171.3 ppm. IR (KBr): $\tilde{\nu}$ = 3323, 3062, 2972, 2932, 1660, 1613 cm^{-1}. MS: *m*/*z* (%) = 473 (6) [M]$^+$, 372 (75), 268 (8), 198 (87), 105 (100), 77 (47). $C_{28}H_{29}FN_4O_2$ (472.6): calcd. C 71.17, H 6.19, N 11.86; found C 71.02, H 6.34, N 11.89.

***N*-(*tert*-Butyl)-3-ethyl-2-[*N*-(*m*-tolyl)benzamido]-3,4-dihydroquinazoline-4-carboxamide (4k):** White crystals (yield 0.42 g, 89%). M.p. 221–223 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.29 (t, J = 6.8 Hz, 3 H, CH_3), 1.40 (s, 9 H, 3 CH_3), 2.35 (s, 3 H, Ar-CH_3), 3.46–3.51 (m, 1 H, NCH), 3.72–3.77 (m, 1 H, NCH), 5.09 (s, 1 H, COCH), 6.86–7.50 (m, 13 H, Ar-H), 8.56 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.6, 21.2, 28.6, 45.1, 51.7, 63.8, 121.9, 124.2, 124.4, 125.5, 126.7, 127.5, 127.8, 128.1, 128.6, 128.8, 129.3, 131.4, 133.8, 139.1, 141.0, 141.3, 149.8, 169.5, 171.2 ppm. IR (KBr): $\tilde{\nu}$ = 3300, 3040, 2972, 2928, 1658, 1619 cm^{-1}. MS: *m*/*z* (%) = 470 (7) [M]$^+$, 369 (98), 234 (12), 194 (98), 105 (100), 77 (46), 57 (44). $C_{29}H_{32}N_4O_2$ (468.6): calcd. C 74.33, H 6.88, N 11.96; found C 74.30, H 6.61, N 12.09.

***N*-(*tert*-Butyl)-3-methyl-2-(*N*-phenylbenzamido)-3,4-dihydroquinazoline-4-carboxamide (4l):** White crystals (yield 0.40 g, 90%). M.p. 192–193 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.40 (s, 9 H, 3 CH_3), 3.27 (s, 3 H, CH_3), 5.02 (s, 1 H, COCH), 6.91–7.48 (m, 14 H, Ar-H), 8.43 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 28.6, 37.9, 51.7, 67.5, 121.4, 121.4, 124.4, 125.6, 126.9, 127.1, 128.1, 128.6, 129.1, 129.3, 131.5, 133.5, 140.8, 141.3, 149.9, 168.6, 170.8 ppm. IR (KBr): $\tilde{\nu}$ = 3338, 3067, 3032, 2968, 2922, 1676, 1643, 1619 cm^{-1}. MS: *m*/*z* (%) = 440 (1) [M]$^+$, 340 (100), 234 (15), 180 (96), 118 (21), 105 (59), 77 (20). $C_{27}H_{28}N_4O_2$ (440.5): calcd. C 73.61, H 6.41, N 12.72; found C 73.38, H 6.65, N 12.87.

***N*-(*tert*-Butyl)-2-[*N*-(4-chlorophenyl)benzamido]-3-methyl-3,4-dihydroquinazoline-4-carboxamide (4m):** White crystals (yield 0.39 g, 83%). M.p. 203–204 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.40 (s, 9 H, 3 CH_3), 3.25 (s, 3 H, CH_3), 5.01 (s, 1 H, COCH), 6.91–7.48 (m, 13 H, Ar-H), 8.35 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 28.6, 38.0, 51.8, 67.5, 121.3, 124.4, 125.8, 126.5, 128.2, 128.4, 128.8, 129.3, 129.4, 131.8, 132.8, 133.2, 140.0, 140.7, 149.8, 168.5, 170.8 ppm. IR (KBr): $\tilde{\nu}$ = 3332, 3067, 3032, 2970, 2926, 1678, 1651, 1621 cm^{-1}. MS: *m*/*z* (%) = 474 (2) [M]$^+$, 374 (100), 268 (11), 214 (94), 140 (7), 105 (78), 77 (20). $C_{27}H_{27}ClN_4O_2$ (475.0): calcd. C 68.27, H 5.73, N 11.80; found C 68.13, H 5.87, N 11.84.

***N*-(*tert*-Butyl)-2-(4-chloro-*N*-phenylbenzamido)-3-ethyl-3,4-dihydroquinazoline-4-carboxamide (4n):** White crystals (yield 0.43 g, 89%). M.p. 264–265 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.26 (t, J = 6.8 Hz, 3 H, CH_3), 1.39 (s, 9 H, 3 CH_3), 3.43–3.49 (m, 1 H, NCH), 3.69–3.74 (m, 1 H, NCH), 5.08 (s, 1 H, COCH), 6.93–7.44 (m, 13 H, Ar-H), 8.46 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.6, 28.6, 45.1, 51.8, 63.8, 121.7, 124.4, 125.7, 126.7, 127.0, 127.2, 128.5, 128.7, 129.3, 130.8, 132.0, 137.8, 140.8, 141.1, 149.5, 169.4, 170.1 ppm. IR (KBr): $\tilde{\nu}$ = 3327, 2973, 2931, 1665, 1609 cm^{-1}. MS: *m*/*z* (%) = 488 (4) [M]$^+$, 388 (100), 360 (21), 283 (79), 105 (25), 77 (61). $C_{28}H_{29}ClN_4O_2$ (489.0): calcd. C 68.77, H 5.98, N 11.46; found C 68.72, H 6.13, N 11.59.

***N*-(*tert*-Butyl)-2-[4-chloro-*N*-(4-chlorophenyl)benzamido]-3-ethyl-3,4-dihydroquinazoline-4-carboxamide (4o):** White crystals (yield 0.46 g, 88%). M.p. 254–255 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.27 (t, J = 6.4 Hz, 3 H, CH_3), 1.39 (s, 9 H, 3 CH_3), 3.44–3.47 (m, 1 H, NCH), 3.65–3.70 (m, 1 H, NCH), 5.08 (s, 1 H, COCH), 6.92–7.44 (m, 12 H, Ar-H), 8.38 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.7, 28.6, 45.2, 51.8, 63.8, 121.7, 124.3, 125.9, 126.8, 128.2, 128.7, 129.5, 130.8, 131.6, 133.0, 138.1, 139.8, 140.7, 149.3, 169.3, 170.0 ppm. IR (KBr): $\tilde{\nu}$ = 3318, 3036, 2974, 1662, 1615 cm^{-1}. MS: *m*/*z* (%) = 522 (2) [M]$^+$, 422 (100), 254 (20), 153 (67), 111 (40). $C_{28}H_{28}Cl_2N_4O_2$ (523.5): calcd. C 64.25, H 5.39, N 10.70; found C 64.18, H 5.43, N 10.94.

***N*-(*tert*-Butyl)-2-[4-chloro-*N*-(4-fluorophenyl)benzamido]-3-ethyl-3,4-dihydroquinazoline-4-carboxamide (4p):** White crystals (yield 0.41 g, 81%). M.p. 254–255 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.28 (t, J = 6.8 Hz, 3 H, CH_3), 1.39 (s, 9 H, 3 CH_3), 3.43–3.48 (m, 1 H, NCH), 3.68–3.73 (m, 1 H, NCH), 5.08 (s, 1 H, COCH), 6.92–7.43 (m, 12 H, Ar-H), 8.41 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.6, 28.5, 45.0, 51.7, 63.7, 116.2, 116.4, 121.6, 124.2, 125.8, 126.7, 128.6, 128.7, 128.8, 130.7, 131.7, 137.1, 137.8, 140.6, 149.3, 159.9, 162.4, 169.2, 170.1 ppm. IR (KBr): $\tilde{\nu}$ = 3333, 2977, 1667, 1612 cm^{-1}. MS: *m*/*z* (%) = 506 (1) [M]$^+$, 406 (100), 377 (26), 248 (45), 140 (21), 77 (72). $C_{28}H_{28}ClFN_4O_2$ (507.0): calcd. C 66.33, H 5.57, N 11.05; found C 66.48, H 5.42, N 11.21.

***N*-(*tert*-Butyl)-2-(4-chloro-*N*-isopropylbenzamido)-3-ethyl-3,4-dihydroquinazoline-4-carboxamide (4q):** White crystals (yield 0.36 g, 79%). M.p. 232–234 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.16–1.54 (m, 18 H, 6 CH_3), 3.40–3.43 (m, 1 H, NCH), 3.48–3.52 (m, 1 H, NCH), 4.20–4.22 (m, 1 H, CH), 5.02 (s, 1 H, COCH), 7.12–7.49 (m, 8 H, Ar-H), 8.38 (s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.0, 19.5, 23.8, 28.4, 44.3, 51.5, 52.9, 63.2, 122.1, 124.2, 125.5, 126.6, 127.9, 128.6, 129.0, 133.6, 136.5, 140.4, 147.0, 169.3, 172.2 ppm. IR (KBr): $\tilde{\nu}$ = 3305, 3051, 2972, 2932, 2878, 1668, 1647, 1613 cm^{-1}. MS: *m*/*z* (%) = 454 (3) [M]$^+$, 354 (100), 283 (15), 255 (32), 153 (54). $C_{25}H_{31}ClN_4O_2$ (455.0): calcd. C 65.99, H 6.87, N 12.31; found C 65.74, H 6.85, N 12.26.

***N*-(*tert*-Butyl)-2-[4-chloro-*N*-(*m*-tolyl)benzamido]-3-methyl-3,4-dihydroquinazoline-4-carboxamide (4r):** White crystals (yield 0.41 g, 84%). M.p. 233–234 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.39 (s, 9 H, 3CH_3), 2.26 (s, 3 H, CH_3), 3.24 (s, 3 H, NCH), 5.02 (s, 1 H, COCH), 6.86–7.43 (m, 12 H, Ar-H), 8.36 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 21.2, 28.6, 37.8, 51.7, 67.5, 121.3, 124.2, 124.5, 125.6, 126.4, 127.2, 128.2, 128.4, 128.6, 129.1, 130.7, 132.0, 137.7, 139.4, 140.7, 140.9, 149.7, 168.6, 169.7 ppm. IR (KBr): $\tilde{\nu}$ = 3318, 3044, 2976, 1666, 1615 cm^{-1}. MS: *m*/*z* (%) = 488 (2) [M]$^+$, 388 (91), 234 (11), 228 (100), 139 (38), 111 (13), 57 (13). $C_{28}H_{29}ClN_4O_2$ (489.0): calcd. C 68.77, H 5.98, N 11.46; found C 68.82, H 5.94, N 11.32.

***N*-(*tert*-Butyl)-2-(4-chloro-*N*-phenylbenzamido)-3-methyl-3,4-dihydroquinazoline-4-carboxamide (4s):** White crystals (yield 0.42 g,

89%). M.p. 237–238 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.40 (s, 9 H, 3 CH_3), 3.24 (s, 3 H, NCH), 5.01 (s, 1 H, COCH), 7.47–6.91 (m, 13 H, Ar-H), 8.35 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 28.6, 37.9, 51.7, 67.4, 121.3, 124.5, 125.7, 126.4, 126.9, 127.4, 128.5, 128.7, 129.4, 130.8, 131.8, 137.8, 140.6, 140.9, 149.7, 168.5, 169.7 ppm. IR (KBr): $\tilde{\nu}$ = 3317, 3037, 2973, 1667, 1615 cm^{-1}. MS: *m/z* (%) = 474 (3) $[M]^+$, 374 (100), 277 (82), 234 (34), 214 (88), 141 (20), 111 (22), 77 (17), 57 (26). $C_{27}H_{27}ClN_4O_2$ (475.0): calcd. C 68.27, H 5.73, N 11.80; found C 68.40, H 5.70, N 11.64.

***N*-Butyl-2-[*N*-(4-chlorophenyl)benzamido]-3-propyl-3,4-dihydroquinazoline-4-carboxamide (4t):** White crystals (yield 0.34 g, 67%). M.p. 123–124 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.88–0.91 (m, 6 H, 2 CH_3), 1.31–1.35 (m, 2 H, CH_2), 1.58–1.60 (m, 3 H, CH + CH_2), 1.94 (s, 1 H, CH), 3.26 (t, *J* = 6.9 Hz, 2 H, NCH_2), 3.32–3.36 (m, 1 H, NCH), 3.60–3.65 (m, 1 H, NCH), 5.17 (s, 1 H, COCH), 6.95–7.50 (m, 13 H, Ar-H), 8.93 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 11.1, 13.6, 20.0, 21.5, 31.1, 39.5, 51.8, 63.5, 121.6, 124.3, 125.8, 126.8, 128.0, 128.4, 128.8, 129.3, 131.9, 132.6, 133.2, 140.0, 140.8, 149.5, 169.6, 171.7 ppm. IR (KBr): $\tilde{\nu}$ = 3297, 3071, 2960, 2931, 2870, 1668, 1651, 1618 cm^{-1}. MS: *m/z* (%) = 503 (1) $[M]^+$, 402 (100), 254 (58), 77 (89). $C_{29}H_{31}ClN_4O_2$ (503.0): calcd. C 69.24, H 6.21, N 11.14; found C 69.46, H 6.14, N 11.01.

***N*,3-Dibutyl-2-[*N*-(4-chlorophenyl)benzamido]-3,4-dihydroquinazoline-4-carboxamide (4u):** White crystals (yield 0.32 g, 61%). M.p. 166–167 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.88–0.92 (m, 6 H, 2 CH_3), 1.21–1.36 (m, 4 H, 2 CH_2), 1.54–1.62 (m, 3 H, $CHCH_2$), 1.77–1.78 (m, 1 H, CH), 3.24–3.28 (m, 2 H, NCH_2), 3.29–3.36 (m, 1 H, NCH), 3.65–3.70 (m, 1 H, NCH), 5.17 (s, 1 H, COCH), 6.94–7.50 (m, 13 H, Ar-H), 8.93 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.7, 19.9, 20.0, 30.3, 31.1, 39.5, 50.0, 63.4, 121.6, 124.3, 125.8, 126.8, 128.0, 128.4, 128.8, 129.3, 131.9, 132.6, 133.2, 140.0, 140.8, 149.6, 169.7, 171.7 ppm. IR (KBr): $\tilde{\nu}$ = 3330, 3068, 2957, 2930, 2870, 1675, 1649, 1614 cm^{-1}. MS: *m/z* (%) = 516 (2) $[M]^+$, 416 (100), 254 (43), 77 (92). $C_{30}H_{33}ClN_4O_2$ (517.1): calcd. C 69.69, H 6.43, N 10.84; found C 69.73, H 6.40, N 10.71.

***N*,3-Dibutyl-2-[*N*-(4-chlorophenyl)acetamido]-3,4-dihydroquinazoline-4-carboxamide (4v):** White crystals (yield 0.30 g, 67%). M.p. 108–109 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.83–0.94 (m, 6 H, 2 CH_3), 1.28–1.81 (m, 8 H, 4 CH_2), 2.07 (s, 3 H, CH_3), 3.14–3.23 (m, 2 H, NCH_2), 3.28–3.32 (m, 1 H, NCH), 3.61–3.66 (m, 1 H, NCH), 5.10 (s, 1 H, COCH), 6.99–7.47 (m, 8 H, Ar-H), 8.92 (s, 1 H, CONH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.7, 13.8, 20.0, 20.1, 23.0, 30.3, 31.2, 39.5, 49.7, 63.1, 121.6, 124.2, 125.9, 126.9, 128.8, 129.4, 129.7, 134.7, 138.3, 140.8, 148.3, 169.5, 172.8 ppm. IR (KBr): $\tilde{\nu}$ = 3290, 3075, 2959, 2932, 2871, 1699, 1650, 1613 cm^{-1}. MS: *m/z* (%) = 454 (4) $[M]^+$, 354 (100), 298 (76), 254 (32), 126 (57), 77 (88). $C_{25}H_{31}ClN_4O_2$ (455.0): calcd. C 65.99, H 6.87, N 12.31; found C 65.71, H 6.93, N 12.50.

Isolation of the Carbodiimides 3: Triphenylphosphane (0.26 g, 1 mmol) was added with stirring to a solution of an azide **1** (1 mmol) in dry toluene. After stirring had been continued for 2–4 h, isocyanate (1 mmol) was added dropwise to the mixture. After further stirring for 2–6 h, the solution was concentrated under reduced pressure, and the residue was recrystallized from dichloromethane/petroleum ether to give a carbodiimide **3**.

Carbodiimide 3w: White crystals (yield 0.39 g, 87%). M.p. 167–168 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 1.38 (s, 9 H, 3CH_3), 1.88 (s, 3 H, $COCH_3$), 2.36 (s, 3 H, CH_3), 5.58 (s, 1 H, CONH), 6.36 (s, 1 H, COCH), 6.84–7.27 (m, 13 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 21.3, 23.3, 28.6, 51.6, 60.4, 124.6, 121.2, 124.8, 125.2, 126.6, 127.8, 128.7, 128.8, 129.3, 129.5, 129.9, 130.0, 131.0, 138.2, 139.6, 140.4, 169.1, 171.0 ppm. IR (KBr): $\tilde{\nu}$ = 3300, 3071, 2970, 2927, 2138, 1683, 1646 cm^{-1}. MS: *m/z* (%) = 454 (10) $[M]^+$, 293 (100), 331 (26), 206 (66), 180 (91), 158 (69), 130 (99), 91 (69), 77 (30). $C_{28}H_{30}N_4O_2$ (454.6): calcd. C 73.98, H 6.65, N 12.33; found C 74.03, H 6.62, N 12.30.

Carbodiimide 3x: White crystals (yield 0.49 g, 84%). M.p. 103–105 °C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.90 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.30–1.49 (m, 2 H, CH_2), 1.48–1.51 (m, 2 H, CH_2), 2.16 (s, 3 H, CH_3), 3.32–3.37 (m, 2 H, CH_2), 5.88 (s, 1 H, CONH), 6.53 (s, 1 H, COCH), 6.80–7.69 (m, 16 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.7, 20.0, 28.6, 31.4, 39.6, 62.0, 124.9, 125.3, 125.5, 125.6, 127.7, 128.3, 128.7, 129.0, 129.6, 129.7, 129.8, 130.0, 131.2, 131.3, 133.7, 134.5, 135.3, 136.3, 137.1, 137.7, 138.0, 169.3, 170.0 ppm. IR (KBr): $\tilde{\nu}$ = 3336, 3062, 2956, 2934, 2870, 2130, 1672, 1632 cm^{-1}. MS: *m/z* (%) = 584 (10) $[M]^+$, 484 (100), 353 (38), 242 (62), 180 (91), 153 (24), 111 (74), 77 (30). $C_{33}H_{30}Cl_2N_4O_2$ (585.5): calcd. C 67.69, H 5.16, N 9.57; found C 67.73, H 5.22, N 9.60.

Supporting Information (see footnote on the first page of this article): Copies of ^{1}H and ^{13}C NMR spectra of **1a**–**n**, **3w**, **3x** and **4a**–**v**.

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