Supporting Information

1-Alkyl-4-phenyl-6-alkoxy-1H-quinazolin-2-ones:

A Novel Series of Potent Calcium-Sensing Receptor Antagonists

Leo Widler[*]*, Eva Altmann, René Beerli, Werner Breitenstein, Rochdi Bouhelal, Thomas Buhl, Rainer Gamse, Marc Gerspacher, Christine Halleux, Markus R. John, Hansjoerg Lehmann, Oskar Kalb, Michaela Kneissel, Martin Missbach, Irene R. Müller, Sibylle Reidemeister, Johanne Renaud, Agnes Taillardat, Ruben Tommasi, Sven Weiler, Romain M. Wolf and Klaus Seuwen*

Contents: Chemical synthesis and spectroscopic data:

Compounds **2b**-**2e** and **2h** were prepared analogously to **2a**.

Spectroscopic data:

1-Isopropyl-4-phenyl-6-methoxy-1H-quinazolin-2-one (**2b**). mp 142-144 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72-7.78 (m, 2H), 7.48-7.59 (m, 4H), 7.35 (dd, 1H), 7.24 (d, 2H), 5.23 (broad hept, 1H), 3.76 (s, 3H), 1.70 (d, 6H). MS: 295 $(M+1)^+$.

1-Isopropyl-4-(4-methyl-phenyl)-6-methoxy-1H-quinazolin-2-one (**2c**). mp 133 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, 2H), 7.53 (d, 1H), 7.36-7.30 (m, 3H), 7.28 (d, 1H), 5.21 (broad hept, 1H), 3.77 (s, 3H), 2.45 (s, 3H), 1.69 (d, 6H). MS: 309 $(M+1)^+$.

1-Isopropyl-4-(4-ethyl-phenyl)-6-methoxy-1H-quinazolin-2-one (**2d**). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, 2H), 7.53 (d, 1H), 7.36-7.29 (m, 4H), 5.21 (broad hept, 1H), 3.77 (s, 3H), 2.75 (q, 2H), 1.69 (d, 6H), 1.30 (t, 3H). MS: 323 $(M+1)^+$.

1-Isopropyl-4-(4-cyclopropyl-phenyl)-6-methoxy-1H-quinazolin-2-one (**2e**). mp 55-58 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64-7.69 (m, 2H), 7.52 (d, 1H), 7.28-7.36 (m, 2H), 7.16-7.21 (m, 2H), 3.77 (s, 3H), 1.94-2.00 (m, 1H), 1.69 (d, 6H), 1.04-1-10 (m, 2H), 0.78-0.83 (m, 2H). MS: 335 $(M+1)^+$.

1-Isopropyl-4-(4-isopropoxy-phenyl)-6-methoxy-1H-quinazolin-2-one (**2h**). mp 146-148 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.76 (d, 2H), 7.50-7.57 (m, 1H), 7.31-7.37 (m, 2H), 7.02 (d, 2H), 5.21 (broad hept, 1H), 4.68 (hept, 1H), 3.80 (s, 3H), 1.70 (d, 6H), 1.40 (d, 6H). MS: 353 $(M+1)^+$.

Chemical synthesis and spectroscopic data of **2g**, **2i** and **2j:**

4-Biphenyl-4-yl-1-isopropyl-6-methoxy-1H-quinazolin-2-one (**2g)** was prepared from 4-biphenyl aldehyde in 5% overall yield in an analogous way as **2f**: ^{1}H NMR (300 MHz, DMSO-d_6): 7.90-7.77 (m, 7H) 7.54-7.48 (m, 3H), 7.40 (t, 1H), 7.19 (d, 1H), 5.10 (hept, 1H), 3.73 (s, 3H), 1.56 (d, 6H). MS: 371 $(M+1)^+$.

4-(1-Isopropyl-6-methoxy-2-oxo-1,2-dihydro-quinazolin-4-yl)-benzoic acid methyl ester (**2i**): In an analogous way as described for **2f,** the intermediate 4-(1-isopropyl-6-methoxy-2-oxo-1,2,3,4-tetrahydro-quinazolin-4-yl)-benzoic acid methyl ester was obtained from 4-formyl-benzoic acid methyl ester in 23% yield. Thus, a solution of 600 mg (1.69 mmol) of the intermediate dissolved in a mixture of 3 mL CH_2Cl_2, 3mL CH_3CN, and 6 mL water was treated with 543 mg (2.54 mmol) $NaIO_4$ followed by 3 mg $RuCl_3$ and stirred at rt for 72 h. The reaction mixture was diluted with water and extracted with ethyl acetate. Recrystallization from diethyl ether/hexanes afforded 450 mg (75 %) **2i**. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.13 (d, 2H), 8.85-8.81 (m, 3H), 7.49 (dd, 1H), 7.01 (d, 1H), 5.10 (hept, 1H), 3.90 (s, 3H), 3.70 (s, 3H), 1.55 (d, 6H). MS: 353 $(M+1)^+$.

4-(1-Isopropyl-6-methoxy-2-oxo-1,2,3,4-tetrahydro-quinazolin-4-yl)-benzoic acid (**2j**): A solution of 50 mg (0.142 mmol) **2i** in 2 mL THF was treated with 3 mL 0.1 M aq. NaOH solution and stirred for 3 h at rt. The reaction mixture was acidified by adding 1M HCl and extracted with ethyl acetate. After evaporation of the organic phase the residue could be crystallized from Et_2O yielding 21 mg (44%) **2j**. ^{1}H NMR (300 MHz, DMSO-d_6): δ 13.2 (s, broad, 1H, COO<u>H</u>), 8.11 (d, 2H), 7.85 - 7.80 (m, 3H), 7.50 (dd, 1H), 7.03 (d, 1H), 5.10 (hept, 1H), 3.70 (s, 3H), 1.56 (d, 6H). MS: 339 $(M+1)^+$.

Compounds **7b** - **7e** and **7g – 7i** were prepared in analogy to example **7f.**

Spectroscopic data:

6-Ethoxy-1-isopropyl-4-(4-isopropyl-phenyl)-1H-quinazolin-2-one (**7b**) by alkylation with ethyl iodide in 75% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70 (d, 2H), 7.53 (d, 1H), 7.37 (d, 2H), 7.33 (d, 1H), 7.31 (s, 1H), 5.21 (hept, 1H), 3.98 (q, 2H), 3.00 (hept, 1H), 1.69 (d, 6H), 1.40 (t, 3H), 1.31 (d, 6H). MS: 351 $(M+1)^+$.

1-Isopropyl-4-(4-isopropyl-phenyl)-6-propoxy-1H-quinazolin-2-one (**7c**) by alkylation with propyl iodide in 39% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70 (d, 2H), 7.52 (d, 1H), 7.37 (d, 2H), 7.34 (dd, 1H), 7.31 (d, 1H), 5.21 (hept, 1H), 3.87 (t, 2H), 3.00 (hept, 1H), 1.79 (hex, 2H), 1.71 (d, 6H), 1.31 (d, 6H), 1.02 (t, 3H). MS: 365 $(M+1)^+$.

6-Isopropoxy-1-isopropyl-4-(4-isopropyl-phenyl)-1H-quinazolin-2-one (**7d**) by alkylation with isopropyl iodide in 55% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.69 (d, 2H), 7.52 (m, 1H), 7.37 (d, 2H), 7.34 - 7.30 (m, 2H), 5.21 (hept, 1H), 4.45 (hept, 1H), 3.00 (hept, 1H), 1.69 (d, 6H), 1.31 (d, 6H), 1.31 (d, 6H). MS: 365 $(M+1)^+$.

6-Butoxy-1-isopropyl-4-(4-isopropyl-phenyl)-1H-quinazolin-2-one (**7e**) by alkylation with butyl iodide in 60% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70 (d, 2H), 7.53 (d, 1H), 7.37 (d, 2H), 7.35 – 7.30 (m, 2H), 5.21 (hept, 1H), 3.91 (t, 2H), 3.00 (hept, 1H), 1.75 (quint, 2H), 1.69 (d, 6H), 1.47 (hex, 2H), 1.31 (d, 6H), 0.95 (t, 3H). MS: 379 $(M+1)^+$.

1-Isopropyl-4-(4-isopropyl-phenyl)-6-(2-methyl-allyloxy)-1H-quinazolin-2-one (7g) by alkylation with 3-bromo-2-methylpropene in 70% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.68 (d, 2H), 7.52 (d, 1H), 7.37 – 7.29 (m, 4H), 5.20 (hept, 1H), 5.01 (s, 2H), 4.40 (s, 2H), 2.99 (hept, 1H), 1.78 (s, 3H), 1.69 (d, 6H), 1.30 (d, 6H). MS: 377 $(M+1)^+$.

1-Isopropyl-4-(4-isopropyl-phenyl)-6-propargyloxy-1H-quinazolin-2-one (**7h**) by alkylation with propargylbromide in 90% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72 (d, 2H), 7.55 (d,

1H), 7.45 (d, 1H), 7.40 (dd, 1H), 7.36 (d, 2H), 5.20 (hept, 1H), 4.66 (d, 2H), 3.00 (hept, 1H), 2.56 (t, 1H), 1.69 (d, 6H), 1.31 (d, 6H). MS: 361 $(M+1)^+$.

6-But-2-ynyloxy-1-isopropyl-4-(4-isopropyl-phenyl)-1H-quinazolin-2-one (**7i**) by alkylation with 1-bromo-2-butyne in 35% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72 (d, 2H), 7.54 (d, 1H), 7.45 (d, 1H), 7.38 (dd, 1H), 7.35 (d, 2H), 5.20 (hept, 1H), 4.62 (q, 2H), 3.00 (hept, 1H), 1.87 (t, 3H), 1.70 (d, 6H), 1.31 (d, 6H). MS: 375 $(M+1)^+$.

Chemical synthesis of intermediate **8:**

(2-Amino-5-propargyloxy-phenyl)-(4-isopropyl-phenyl)-methanone (8). A mixture of 98 g (0.586 mol) 5-hydroxy-2-nitro-benzaldehyde, 126 mL (1.27 mol) propargyl bromide (80% in toluene) and 201 mL (1.17 mol) *N*,*N*-diisopropylethylamine (1.17 mol) was stirred in 1200 mL 1,4-dioxane at 80 °C for 20 h. The brown suspension was cooled and the solvent stripped. The residual oil was diluted with ethyl acetate and washed with 1 N aqueous hydrochloric acid, water and brine. The crude oily product was taken up into 200 mL hot ethyl acetate and diluted with 50 mL petroleum ether. The product started to crystallize upon cooling to yield 96.0 g (80%) 2-nitro-5-propargyloxy-benzaldehyde; mp 80-81 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.28 (s, 1H), 8.21 (d, 1H), 7.40 (dd, 1H), 7.33 (d, 1H), 5.04 (d, 2H), 3.70 (t, 1H).

A suspension of 14.3 g (596 mmol) magnesium turnings in 60 mL THF was treated with about 10 g 4-bromo-isopropyl-benzene (neat). Once the Grignard reaction had started the rest of the bromide (91.9 mL (596 mmol) in total) diluted with 750 mL THF was added within 40 min to keep the mixture at gentle reflux. Stirring was continued for another 30 min upon complete addition. After cooling with an ice/water bath this mixture was added within 50 min to 94.0 g (458 mmol) 2-nitro-5-propargyloxy-benzaldehyde in 1100 mL THF cooled to -78 °C. Cooling was removed and the reaction allowed to come to 0 °C. The reaction mixture was poured into one liter of sat. ammonium chloride solution and extracted with diethyl ether. The crude product was purified by filtration through a pad of silica gel to leave 145.0 g (97%) of (4-isopropyl-phenyl)-(2-nitro-5-propargyloxy-phenyl)-methanol as a dark brown oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.09 (d, 1H), 7.45 (d, 1H), 7.26 (d, 2H), 7.19 (d, 2H), 6.98 (dd, 1H), 6.52 (broad, 1H), 4.80 (d, 2H), 2.88 (hept, 1H), 2.71 (broad, 1H), 2.56 (t, 1H), 1.23 (d, 6H). MS: 308 $(M\text{-}OH)^+$.

To an solution of 10.0 g (30.7 mmol) (4-isopropyl-phenyl)-(2-nitro-5-propargyloxy-phenyl)-methanol in 60 mL acetone 17.5 mL (46.6 mmol) 2.66 M Jones reagent[24] was added dropwise. After stirring for 2 h at rt the chromium salts were separated and washed several times with acetone. The combined organic layers were concentrated *in vacuo* and the residue was taken up into water and ethyl acetate. After evaporation of the organic phase the crude product was purified by filtration through a pad of silica gel (dichloromethane/hexanes) to give 7.90 g (79%) of (4-isopropyl-phenyl)-(2-nitro-5-propargyloxy-phenyl)-methanone in the form of a white solid. mp 111-113 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.27 (d, 1H), 7.70 (d, 2H), 7.30 (d, 2H), 7.18 (dd, 1H), 6.97 (d, 1H), 4.81 (d, 2H), 2.96 (hept, 1H), 2.59 (t, 1H), 1.27 (d, 6H).

A suspension of 6.50 g (20.0 mmol) (4-isopropyl-phenyl)-(2-nitro-5-propargyloxy-phenyl)-methanone and 4.46 g (79.9 mmol) iron powder in 150 mL glacial acetic acid was vigorously stirred at 43 °C. After 9 h another 4.5 g of iron powder had to be added to drive the reaction to completion. There was no starting material left after a total reaction time of 16 h. The olive green mixture was cooled to rt and diluted with 100 mL ethyl acetate. It was filtered through Hyflo and the filter cake was washed 5 times with 40 mL ethyl acetate. The filtrate was distributed between water and ethyl acetate and the combined organic layers were washed with water, bicarbonate solution and brine to yield a dark brown oil. Purification by filtration trough a pad of silica gel (dichloromethane/hexanes) afforded 5.0 g (77 %) of yellow **8**. mp 56 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 7.64 (d, 2H), 7.30 (d, 2H), 7.12 (s, 1H), 7.05 (d, 1H), 6.72 (d, 1H), 5.71 (broad, 2H), 4.64 (s, 2H), 2.98 (hept, 1H), 2.48 (s, 1H), 1.30 (d, 6H). MS: 294 $(M+1)^+$.

Compounds **10b -10f and 10h-10j** were prepared in analogy to example **10a** and **10m**. For the preparation of **10g**, **10k** and **10l** sodium cyanoborohydride in methanol plus 1 equiv of acetic acid was used for reductive amination. For the work up of the carboxylic acids **10g** and **10l** the reaction mixture was quenched by the addition of 1 N aqueous HCl and then adjusted to ~pH 4 with 1 N NaOH. Methanol was removed *in vacuo*, the remaining aqueous layer diluted with H_2O and extracted with ethyl acetate.

Spectroscopic data:

4-(4-Isopropyl-phenyl)-1-(4-methyl-benzyl)-6-propargyloxy-1H-quinazolin-2-one (**10b**). mp 92-93 °C. 1H NMR (300 MHz, CDCl3): δ 7.74 (d, 2H), 7.47 (s, 1H), 7.37 (d, 2H), 7.29 (s, 2H), 7.21 (d, 2H), 7.12 (d, 2H), 5.51 (broad s, 2H), 4.63 (broad d, 2H), 3.01 (hept, 1H), 2.55 (broad, 1H), 2.31 (s, 3H), 1.32 (d, 6H). MS: 423 $(M+1)^+$.

1-(4-Ethyl-benzyl)-4-(4-isopropyl-phenyl)-6-propargyloxy-1H-quinazolin-2-one (**10c**). mp 75-76 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74 (d, 2H), 7.48 (s, 1H), 7.38 (d, 2H), 7.30 (s, 2H), 7.23 (d, 2H), 7.14 (d, 2H), 5.52 (broad s, 2H), 4.63 (d, 2H), 3.02 (hept, 1H), 2.61 (q, 2H), 2.54 (broad t, 1H), 1.32 (d, 6H), 1.20 (t, 3H). MS: 437 $(M+1)^+$.

1-(4-Isopropyl-benzyl)-4-(4-isopropyl-phenyl)-6-propargyloxy-1H-quinazolin-2-one (**10d**)**.** ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.72 (d, 2H), 7.47-7.54 (m, 4H), 7.36 (m, 1H), 7.18-7.24 (m, 4H), 5.47, broad s, 2H), 4.79 (d, 2H), 3.68 (t, 1H), 3.03 (hept, 1H), 2.84 (hept, 1H), 1.29 (d, 6H), 1.16 (d, 6H). MS: 451 $(M+1)^+$.

4-(4-Isopropyl-phenyl)-1-(4-methoxy-benzyl)-6-propargyloxy-1H-quinazolin-2-one (**10e**)**.** mp 60 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74 (d, 2H), 7.48 (broad s, 1H), 7.38 (d, 2H), 7.24-7.34 (m, 4H), 6.85 (d, 2H), 5.49 (broad, 2H), 4.64 (d, 2H), 3.77 (s, 3H), 3.02 (hept, 1H), 2.55 (t, 1H), 1.32 (d, 6H). MS: 439 $(M+1)^+$.

1-(4-Ethoxy-benzyl)-4-(4-isopropyl-phenyl)-6-propargyloxy-1H-quinazolin-2-one (10f). mp 181-183 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.73 (d, 2H), 7.47 (s, 1H), 7.37 (d, 2H), 7.30 (s, 2H), 7.22-7.28 (m, 2H), 6.83 (d, 2H), 5.47 (broad, 2H), 4.63 (d, 2H), 3.98 (q, 2H), 3.01 (hept, 1H), 2.53 (broad, 1H), 1.38 (t, 3H), 1.31 (d, 6H). MS: 453 $(M+1)^+$.

{4-[4-(4-Isopropyl-phenyl)-2-oxo-6-propargyloxy-2H-quinazolin-1-ylmethyl]-phenoxy}-acetic acid (10g). ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.69 (m, 2H), and 7.44-7.52 (m, 4H), 7.33 (d, 1H), 7.20 (m, 2H), 6.79 (m, 2H), 5.40 (broad s, 2H), 4.77 (d, 2H), 4,33 (broad s, 2H), 3.65 (m, 1H), 3.01 (hept, 1H), 1.27 (d, 6H). MS: 483.7 $(M+1)^+$.

4-(4-Isopropyl-phenyl)-1-(3-methyl-benzyl)-6-propargyloxy-1H-quinazolin-2-one (10h). mp 115-116 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.75 (d, 2H), 7.48 (d, 1H), 7.38 (d, 2H), 7.27-7.34 (m, 2H), 7.20 (t, 1H), 7.03-7.14 (m, 3H), 5.51 (broad s, 2H), 4.64 (d, 2H), 3.02 (hept, 1H), 2.54 (broad, 1H), 2.31 (s, 3H), 1.32 (d, 6H). MS: 423 $(M+1)^+$.

1-(3-Ethyl-benzyl)-4-(4-isopropyl-phenyl)- 6-propargyloxy-1H-quinazolin-2-one (10i). mp 122-125 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.75 (d, 2H), 7.50 (d, 1H), 7.39 (d, 2H), 7.29-7.32 (m, 2H), 7.21 (d, 1H), 7.05-7.14 (m, 3H), 5.52 (broad s, 2H), 4.65 (d, 2H), 3.03 (hept, 1H), 2.60 (q, 2H), 2.56 (t, 1H), 1.32 (d, 6H), 1.22 (t, 3H). MS: 437 $(M+1)^+$.

1-(3-Methoxy-benzyl)-4-(4-isopropyl-phenyl)-6-propargyloxy-1H-quinazolin-2-one (10j). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.76 (d, 2H), 7.48 (d, 1H), 7.40 (d, 2H), 7.20-7.32 (m, 3H), 6.88 (d, 1H), 6.84 (s, 1H), 6.79 (d, 1H), 5.51 (broad s, 2H), 4.63 (d, 2H), 3.77 (s, 3H), 3.03 (hept, 1H), 2.55 (broad s, 1H), 1.33 (d, 6H). MS: 439 $(M+1)^+$.

1-(3-Ethoxy-4-methoxy-benzyl)-4-(4-isopropyl-phenyl)-6-propargyloxy-1H-quinazolin-2-one (10k). mp 130 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.71 (d, 2H), 7.47-7.55 (m, 4H), 7.35 (d, 1H), 7.05 (s, 1H), 6.86 (d, 1H), 6.73-6.76 (m, 1H), 5.41 (broad s, 2H), 4.79 (d, 2H), 3.97 (q, 2H), 3.69 (s, 3H), 3.66 (m, 1H), 3.02 (m, 1H), 1.26-1.32 (m, 9H). MS: 483 $(M+1)^+$.

{3-[4-(4-Isopropyl-phenyl)-2-oxo-6-propargyloxy-2H-quinazolin-1-ylmethyl]-phenoxy}-acetic acid (**10l**). ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.71 (m, 2H), and 7.45-7.50 (m, 4H), 7.34 (d, 1H), 7.17 (m, 1H), 6.81 (broad s, 1H), 6.68-6.77 (m, 2H), 5.43 (broad s, 2H), 4.77 (d, 2H), 4,30 (broad s, 2H), 3.65 (m, 1H), 3.01 (hept, 1H), 1.27 (d, 6H). MS: 483.5 $(M+1)^{+}$.

Compounds **16a** – **16d**, **16f**, **16g** and **16i** were prepared analogously to **16e** and **16h.**

Spectroscopic data:

6-(Ethylamino)-1-isopropyl-4-(4-isopropyl-phenyl)-1H-quinazolin-2-one (**16a**). mp 225-227 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 7.69 (d, 2H), 7.45 (d, 1H), 7.35 (d, 2H), 7.06 (dd, 1H), 6.99 (d, 1H), 5.21 (broad hept, 1H), 3.69 (broad s, NH), 3.10 (q, 2H), 2.99 (hept, 1H), 1.68 (d, 6H), 1.30 (d, 6H), 1.24 (t, 3H). MS: 350 $(M+1)^+$

6-Diethylamino-1-isopropyl-4-(4-isopropyl-phenyl)-1H-quinazolin-2-one (**16b**). mp 170-172 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 7.71 (d, 2H), 7.48 (d, 1H), 7.35 (d, 2H), 7.18 (dd, 1H), 7.04 (d, 1H), 5.23 (broad hept, 1H), 3.29 (q, 4H), 2.99 (hept, 1H), 1.68 (d, 6H), 1.30 (d, 6H), 1.12 (t, 6H). MS: 378 $(M+1)^+$

6-(Propylamino)-1-isopropyl-4-(4-isopropyl-phenyl)-1H-quinazolin-2-one (**16c).** mp 231-233 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 7.69 (d, 2H), 7.44 (d, 1H), 7.35 (d, 2H), 7.05 (dd, 1H), 6.97 (d, 1H), 5.20 (broad hept, 1H), 3.66 (broad s, NH), 2.92-3.06 (m, 3H), 1.67 (d, 6H), 1.62 (q, 2H), 1.30 (d, 6H), 0.97 (d, 3H). MS: 364 $(M+1)^+$.

6-Dipropylamino-1-isopropyl-4-(4-isopropyl-phenyl)-1H-quinazolin-2-one (**16d).** mp 182-184 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 7.68 (d, 2H), 7.46 (d, 1H), 7.33 (d, 2H), 7.12 (dd, 1H), 6.91 (d, 1H), 5.24 (broad hept, 1H), 3.16 (t, 4H), 2.98 (hept, 1H), 1.67 (d, 6H), 1.54 (q, 4H), 1.28 (d, 6H), 0.85 (t, 6H). MS: 406 $(M+1)^+$.

6-(Allyl-methyl-amino)-1-isopropyl-4-(4-isopropyl-phenyl)-1H-quinazolin-2-one (**16f**). Obtained by methylation of **16e**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.71 (d, 2H), 7.49 (d, 1H), 7.34 (d, 2H), 7.20 (dd, 1H), 7.09 (d, 1H), 5.71-5.86 (m, 1H), 5.22 (hept, 1H), 5.05-5.19 (m, 2H), 3.87 (d, 2H), 2.99 (hept, 1H), 2.92 (s, 3H), 1.68 (d, 6H), 1.30 (d, 6H). MS: 376 $(M+1)^+$

6-(Propargylamino)-1-isopropyl-4-(4-isopropyl-phenyl)-1H-quinazolin-2-one (**16g).** mp 227-229 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72 (d, 2H), 7.49 (d, 1H), 7.35 (d, 2H), 7.12-7.18

(m, 2H), 5.21 (broad hept, 1H), 3.87-4.00 (m, 3H), 3.00 (hept, 1H), 2.24 (broad s, 1H), 1.68 (d, 6H), 1.31 (d, 6H). MS: 360 $(M+1)^+$

6-(Benzylylamino)-1-isopropyl-4-(4-isopropyl-phenyl)-1H-quinazolin-2-one (**16i**). ^{1}H NMR (300 MHz, $CDCl_3$): 7.51 (d, 2H), 7.44 (d, 1H), 7.20-7.38 (m, 7H), 7.11 (dd, 1H), 6.93 (d, 1H), 5.20 (broad hept, 1H), 4.29 (broad s, 2H + NH), 2.97 (hept, 1H), 1.67 (d, 6H), 1.29 (d, 6H). MS: 412 $(M+1)^+$.

Derivatives **21a** and **21c** were prepared analogously to **21b**.

Spectroscopic data:

***N*-{3-[4-(4-Isopropyl-pheny)-2-oxo-6-propargyloxy-2H-quinazolin-1-ylmethyl]-phenyl}-2-[4-methyl-piperazin-1-yl]-acetamide** (**21a**)**.** mp 159-161 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.07 (broad, NH), 7.76 (d, 2H), 7.59 (s, 1H), 7.56-7.47 (m, 2H), 7.39 (d, 2H), 7.28-7.35 (m, 3H), 7.05 (d, 1H), 5.54 (broad s, 2H), 4.64 (d, 2H), 3.12 (s, 2H), 3.02 (hept, 1H), 2.69-2.59 (broad, 4H), 2.57-2.47 (broad, 4H), 2.54 (t, 1H), 2.54 (t, 1H), 1.32 (d, 6H).

2-[4-(3-Dimethylamino-propyl) piperazin-1-yl]- *N*-{3-[4-(4-isopropyl-pheny)-2-oxo-6-propargyloxy-2H-quinazolin-1-ylmethyl]-phenyl}-acetamide (**21c**). mp 170-172 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.08 (broad, NH), 7.75 (d, 2H), 7.60 (s, 1H), 7.55-7.48 (m, 2H), 7.39 (d, 2H), 7.34-7.27 (m, 3H), 7.05 (d, 1H), 5.54 (broad s, 2H), 4.65 (d, 2H), 3.12 (s, 2H), 3.02 (hept, 1H), 2.70-2.60 (broad, 4H), 2.59-2.48 (broad, 4H), 2.55 (t, 1H), 2.41 (t, 2H), 2.32 (t, 2H), 2.24 (s, 6H), 1.68 (quint, 2H + water), 1.32 (d, 6H). MS: 635 $(M+1)^+$.