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Abd El-Hamid^{ab}; A. A. Ismail^a; Adel M. E. Attia^b

^a Menoufia University, Shebin El-Koom, Egypt ^b Tanta University (Kafr El-Sheikh Branch), Egypt

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SYNTHESIS OF SOME NEW QUINAZOLINE DERIVATIVES ANALOGUES TO MKC-442 AND TNK 561

Abd El-Hamid, A. A. Ismail,^a and Adel M. E. Attia^b
Menoufia University, Shebin El-Koom, Egypt;^a and Tanta
University (Kafr El-Sheikh Branch), Egypt^b

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A series of different acyclo quinazoline nucleosides 6, 7, 8, 10, 12, 13, and 14 have been synthesized. The site of glycosylation was confirmed by ¹H-NMR and ¹³C-NMR spectroscopy.

Keywords: Acyclo quinazoline nucleosides; MKC-442; TNK 561

A number of quinazolin-4-one derivatives have been found to exhibit high activity against a variety of microbes parasitizing animals and plants.^{1–4} Some quinazoline and their condensed derivatives show antiviral, CNS-depressant, anticonvulsant, antimalaric, and anticancer.^{5–8} A major challenge facing medicinal chemistry over the next few years will be the development of drugs with significantly improved resistance profiles for chronic use as anti-HIV combination therapy. An important component of such regimens will be nonnucleoside inhibitors of HIV-1 reverse transcriptase (NNRTI's). NNRTs are a class of structurally diverse aromatic compounds such as HEPT, MKC-442, and thiocarboxanilides.^{9,10} Structural studies have revealed that NNRTIs inhibit HIV-1 RT by binding to an allosteric site, approximately 10 Å from the polymerase active site,^{11–13} causing a distortion of the catalytic aspartate triad.¹⁴ The high selectivity of NNRTIs for HIV-1 RT over HIV-2 RT and cellular polymerases contributes to lower cellular toxicity

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Address correspondence to A. A. Ismail, Chemistry Department, Faculty of Science, Menoufia University, Shebin El-Koom, Egypt. E-mail: abdelhamide2002@yahoo.com

level than nucleoside analogues (NRTIs) such as AZT, ddI or ddC. As a part of our program of research on the synthesis of new glycosides^{15–20} with considerable biological activity, we report in this paper the synthesis of a new class of non-nucleosides analogues to MKC-442 and TNK-561.

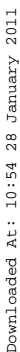
RESULTS AND DISCUSSION

3-Aryl-2-thio-quinazolin-4-ones **3** were prepared in high yields in two steps from the reaction of anthranilic acid **1** with aryl isothiocyanates **2** according to reported procedures.²¹ Compounds **3** or **4** can be coupled with different compounds **5**, **9** and **11** to give a new series of quinazoline acyclonucleosides. For example **3** or **4** reacted with chloromethyl ethyl ether or chloromethyl benzyl ether **5** in the presence of sodium hydride in dry dimethylformamide at room temperature to furnish the corresponding S²-acyclonucleosides **6a–f** or N¹-derivatives **8a–c** in high yields (Scheme 1). Only the S²-nucleoside **6c** and N¹-nucleoside **7** were obtained in the reaction of **3c** with chloromethyl ethyl ether **5** as the major and minor products, respectively. The products **6c** and **7** were easily separated by silica gel column chromatography and fully characterized by elemental and spectral analysis.

The site of glycosylation of compound **3** was confirmed from their ¹³C-NMR spectral. Thus, the observed shifts of C-2 (160.48 ppm) in **6c** and C-2 (176.38 ppm) in **7** clearly show glycosidation on a sulfur atom S² in quinazoline derivative **6c** and on a nitrogen atom N¹ in another derivative **7**, respectively (see Experimental part). Similarly, compounds **3** reacted with bromoethylacetate **9** or isopropylidenedioxy propyl chloride **11** in the presence of NaH and DMF to give the corresponding acyclo quinazoline S-nucleosides **10** and **12**, respectively (Scheme 2).

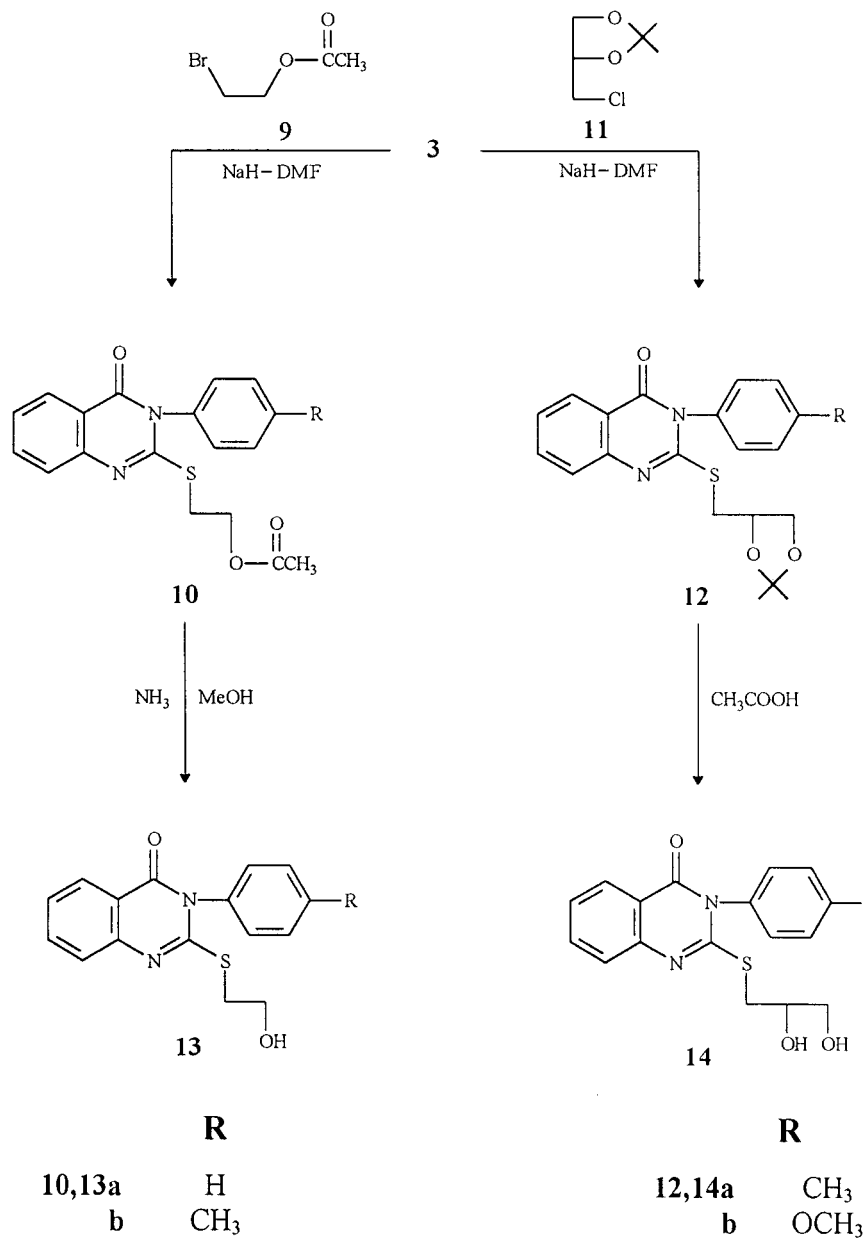
TLC of the acyclonucleosides **10** and **12** showed that single compounds were produced and their structures were further confirmed by elemental analysis and spectral data (see Experimental part).

Finally, removal of the protecting groups from the glycon moieties of **10** and **12** were achieved by treatment of **10** with methanolic ammonia and **12** with acetic acid to afforded the free acyclic nucleosides **13** and **14** receptively as the only isolated product (as tested by TLC analysis) in good yields. The structure of **13a** has been proved by ¹H-NMR and ¹³C-NMR spectrometry in DMSO solution. A strong downfield shift of C-2 signal (160.69 ppm) is an unequivocal indication of the position of alkylation as well as of the disappearance of acetoxo protons in its ¹H-NMR (see Experimental part).



In conclusion, we have achieved a regiospecific synthesis of interesting quinazoline acylconucleosides by the reaction of substituted quinazoline-2-(1*H*)-thiones and their corresponding ketoneses with compounds **5**, **9**, **11**. The obtained quinazoline acyclonucleosides are now under biological evaluation.

NMR spectra were recorded on a Bruker 250 FT NMR spectrometer TMS as internal standard. MS were recorded on a variant mat 311



SCHEME 2

A spectrometer. MS were recorded on a kratos MS-50 spectrometer. Results of elemental analysis were in acceptable range.

General Procedure for Compound 5, 6, 7, 8, 10, and 12

Quinazoline derivatives **3** or **4** (5 mmol) and sodium hydride (6 mmol) in 20 mL dry DMF, stirring at room temperature 1 h. Compound **5**, **9**, or **11** (5.5 mmol) was added and the reaction mixture was stirred 24 h until TLC shows no starting material left. Evaporated the solvent under vacuum, the residue was dissolved in 30 mL ethylacetate and 20 mL of H₂O. The extracted organic layer was dried over Na₂SO₄ and the solvent evaporated under vacuum, the residue was purified by silica gel column chromatography (cyclohexane/ethylacetate, 90/10, v/v).

2-Ethoxymethylthio-3-phenyl-quinazolin-(3H)-4-one (6a)

Yield 80%; m.p. 142–144°C as a white powder; ¹H-NMR (DMSO-d₆), δ 8.11–7.43 (m, 8H, Ar-H), 5.41 (s, 2H, H-1'), 3.57 (m, 2H, OCH₂CH₃), 1.13 (t, *J* = 14.04 Hz, OCH₂CH₃); ¹³C-NMR (DMSO-d₆), δ 135.99, 134.85, 129.68, 129.34, 129.29, 126.49, 126.02, 119.64 (Ar-C), 72.25 (C-1'), 64.59 (OCH₂CH₃), 14.56 (OCH₂CH₃); Anal. calcd for C₁₇H₁₆N₂O₂S (312.31) C, 65.37; H, 5.16; N, 8.97 found C, 65.19; H, 5.00; N, 9.13%.

2-Ethoxymethylthio-3-tolyl-quinazolin-(3H)-4-one (6b)

Yield 75%; m.p. 140–141°C as a white powder; ¹H-NMR (DMSO-d₆) δ 8.25–7.43 (m, 8H, Ar-H), 5.87 (s, 2H, H-1'), 3.69 (m, 2H, OCH₂CH₃), 3.18 (s, 3H, CH₃-tolyl), 1.27 (t, 3H, *J* = 9.13 Hz, CH₂CH₃); ¹³C-NMR (DMSO-d₆) δ 160.78 (C-2), 155.92 (C-4), 146.90, 139.63, 134.44, 131.33, 128.81, 128.14, 126.49, 126.06, 119.63 (Ar-C), 72.34 (C-1'), 64.46 (OCH₂CH₃), 14.77 (CH₃-tolyl), 14.56 (OCH₂CH₃); Anal. calcd for C₁₈H₁₈N₂O₂S (326.33) C, 66.25; H, 5.56; N, 8.58. found C, 66.49; H, 5.33; N, 8.66%.

2-Ethoxymethylthio-3-(4-methoxyphenyl)-quinazolin-(3H)-4-one (6c)

Separated by silica gel column chromatography (cyclohexane/ethylacetate 90/10, v/v) as fraction (1); Yield 72%; m.p. 133–134°C as a white powder; ¹H-NMR (DMSO-d₆) δ 8.31–6.95 (m, 8H, Ar-H), 5.70 (s, 2H, H-1'), 3.75 (m, 2H, OCH₂CH₃), 3.60 (s, 3H, OCH₃), 1.25 (t, *J* = 6.13 Hz, 3H, OCH₂CH₃); ¹³C-NMR (DMSO-d₆) δ 160.84, (C-2), 159.40 (C-4), 147.53, 134.51, 130.14, 129.07, 127.44, 127.17, 126.32, 125.91, 125.25, 124.39, 114.41 (Ar-C), 72.96 (C-1'), 64.39 (OCH₂CH₃), 55.38 (OCH₃),

14.02 (OCH_2CH_3); Anal. calcd for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_3\text{S}$ (342.33) C, 63.15; H, 5.30; N, 8.18; found C, 62.96; H, 5.55; N, 7.00.

2-Benzylloxymethylthio-3-phenyl-quinazolin-(3H)-4-one (6d)

Yield 67%; m.p. 100–102°C as a white powder; $^1\text{H-NMR}$ (DMSO-d_6) δ 7.96–7.15 (m, 14H, Ar-H), 5.33 (s, 2H, H-1'), 4.35 (s, 2H, OCH_2Ph); $^{13}\text{C-NMR}$ (DMSO-d_6) δ 160.80 (C-2), 155.77 (C-4), 146.92 (C-3), 137.32, 135.98, 134.84, 129.78, 129.70, 129.30, 128.21, 127.74, 127.55 (Ar-C), 87.89 (C-1'), 70.82 (OCH_2Ph); MS: m/z 374 (M^+); Anal. calcd for $\text{C}_{22}\text{H}_{18}\text{N}_2\text{O}_2\text{S}$ (374.41) C, 70.57; H, 4.85; N, 7.48 found C, 70.70; H, 4.75; N, 7.76%.

2-Benzylloxymethylthio-3-tolyl-quinazolin-(3H)-4-one (6e)

Yield 78%; m.p. 120–121°C as a white powder; $^1\text{H-NMR}$ (DMSO-d_6) δ 7.89–7.05 (m, 13H, Ar-H), 5.26 (s, 2H, H-1'), 4.29 (s, 2H, OCH_2Ph), 3.13 (s, 3H, $\text{CH}_3\text{-tolyl}$); $^{13}\text{C-NMR}$ (DMSO-d_6) δ 161.50 (C-2), 156.67 (C-4), 1473.56, 139.99, 137.97, 135.43, 133.97, 129.62, 128.55, 128.25, 127.11, 126.64 (Ar-C), 72.67 (C-1'), 71.45 (OCH_2Ph), 21.40 ($\text{CH}_3\text{-tolyl}$); MS: m/z 388 (M^+); Anal. calcd for $\text{C}_{23}\text{H}_{20}\text{N}_2\text{O}_2\text{S}$ (388.48) C, 71.10; H, 5.19; N, 7.21; found C, 71.20; H, 5.59; N, 7.25%.

3-Benzylloxymethylthio-3-(4-methoxyphenyl)-quinazolin-(3H)-4-one (6f)

Yield 82%; m.p. 105–107°C as a white powder; $^1\text{H-NMR}$ (DMSO-d_6) δ 8.28–7.45 (m, 13H, Ar-H), 5.48 (s, 2H, H-1'), 4.68 (s, 2H, OCH_2Ph), 3.66 (s, 3H, OCH_3); $^{13}\text{C-NMR}$ (DMSO-d_6) δ 160.49 (C-2), 156.21 (C-4), 147.45 (C-3), 138.99, 134.52, 130.13, 128.35, 127.94, 127.85, 127.16, 126.33, 125.96 (Ar-C); MS: m/z 404 (M^+); Anal. calcd for $\text{C}_{23}\text{H}_{20}\text{N}_2\text{O}_3\text{S}$ (404.48) C, 68.30; H, 4.98; N, 6.93 found C, 68.09; H, 5.18; N, 6.86%.

1-Ethoxymethyl-3-(4-methoxyphenyl)-2-thio-1,2,3,4-tetrahydroquinazolin-4-one (7)

Separated by silica gel column chromatography (cyclohexane/ethyl-acetate 90/10, v/v) as fraction (2); Yield 20%; m.p. 138–139°C as a white powder; $^1\text{H-NMR}$ (DMSO-d_6) δ 8.15–7.00 (m, 8H, Ar-H), 5.55 (s, 2H, H-1'), 3.86 (m, 2H, OCH_2CH_3), 3.60 (s, 3H, OCH_3), 1.18 (t, $J = 8.61$ Hz, 3H OCH_2CH_3); $^{13}\text{C-NMR}$ (DMSO-d_6) δ 176.36 (C=O), 158.68 (C-4), 139.56, 135.48, 131.83, 129.96, 128.49, 127.82, 127.35, 124.21, 123.17 (Ar-C), 72.96 (C-1'), 63.49 (OCH_2CH_3), 55.93 (OCH_3), 14.96 (OCH_2CH_3); Anal. calcd for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_3\text{S}$ (342.33) C, 63.15; H, 5.30; N, 8.18 found C, 62.91; H, 4.07; N, 8.40%.

1-Ethoxymethyl-3-phenyl-1,2,3,4-tetrahydroquinazolin-2,4-dione (8a)

Yield 71%; m.p. 138–140°C as a white powder; $^1\text{H-NMR}$ (DMSO- d_6) δ 8.09–7.23 (m, 9H, Ar-H); 5.58 (s, 2H, H-1'), 3.67 (m, 2H, OCH_2CH_3), 1.16 (t, $J = 5.00$ Hz, 3H, OCH_2CH_3); $^{13}\text{C-NMR}$ (DMSO- d_6) δ 161.26 (C-2), 150.82 (C-4), 139.73, 139.62, 136.01, 135.26, 128.82, 128.75, 128.13, 127.81, 123.22, 115.32 (Ar-C), 72.96 (C-1'), 63.54 (OCH_2CH_3), 14.78 (OCH_2CH_3); MS: m/z 296 (M^+); Anal. calcd for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_3$ (296.29) C, 68.91, H, 5.44, N, 9.45, found C, 69.08, H, 5.51, N, 9.33%.

1-Ethoxymethyl-3-tolyl-1,2,3,4-tetrahydroquinazolin-2,4-dione (8b)

Yield 75%; m.p. 143–145°C as a white powder; $^1\text{H-NMR}$ (DMSO- d_6) δ 8.26–7.14 (m, 8H, Ar-H), 5.64 (s, 2H, H-1'), 3.74 (m, 2H, OCH_2CH_3), 2.41 (s, 3H, CH_3 -tolyl), 1.26 (t, $J = 10.04$ Hz, 3H, OCH_2CH_3); $^{13}\text{C-NMR}$ (DMSO- d_6) δ 161.99 (C-2), 151.83 (C-4), 139.77, 135.29, 132.64, 130.06, 128.03, 128.95, 127.92, 123.57, 115.99, 115.03 (Ar-C), 73.83 (C-1'), 64.72 (OCH_2CH_3), 21.86 (CH_3 -tolyl), 14.92 (OCH_2CH_3); Anal. calcd for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_3$ (310.35) C, 69.86; H, 5.85; N, 9.03 found C, 69.88; H, 5.90; N, 9.29%.

1-Benzoyloxymethyl-3-tolyl-1,2,3,4-tetrahydro-quinazolin-2,4-dione (8c)

Yield 74%; m.p. 145–146°C as a white powder; $^1\text{H-NMR}$ (DMSO- d_6) δ 8.90–7.17 (m, 13H, Ar-H), 5.67 (s, 2H, H-1'), 4.84 (s, 2H, OCH_2Ph), 2.36 (s, 3H, CH_3 -tolyl); $^{13}\text{C-NMR}$ (DMSO- d_6) δ 161.27 (C-2), 150.86 (C-4), 139.55, 137.66, 137.49, 135.21, 133.36, 129.26, 128.49, 128.07, 127.49, 123.24 (Ar-C), 73.07 (C-1'), 69.96 (OCH_2Ph), 20.69 (CH_3 -tolyl); Anal. calcd for $\text{C}_{23}\text{H}_{20}\text{N}_2\text{O}_3$ (372.42), C, 74.18; H, 5.41; N, 7.52 found C, 74.05; H, 2.63; N, 7.31%.

2-(Acetoxyethylthio)-3-phenyl-quinazolin-(3H)-4-one (10a)

Yield 77%; m.p. 130–132°C; $^1\text{H-NMR}$ (DMSO- d_6) δ 8.10–8.45 (m, 9H, Ar-H), 4.30 (t, $J = 12.91$ Hz, 2H, H-1'), 3.40 (t, $J = 21.19$ Hz, 2H, H-2'), 1.98 (s, 3H, COCH_3); $^{13}\text{C-NMR}$ (DMSO- d_6) δ 170.02 ($-\text{COCH}_3$), 160.64 (C-2); 158.49 (C-4), 147.05, 135.78, 134.81, 129.77, 129.38, 129.32, 126.46, 125.91, 119.49 (Ar-C); 61.72 (C-1'), 30.00 (C-2), 20.53 (COCH_3); MS: m/z 340 (M^+). Anal. calcd for $\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_3\text{S}$ (340.30) C, 63.51; H, 4.79; N, 8.23 found C, 63.78; H, 5.00; N, 8.10%.

2-(2-Acetoxyethylthio)-3-tolyl-quinazolin-(3H)-4-one (10b)

Yield 86%; m.p. 125–126°C; $^1\text{H-NMR}$ (DMSO- d_6) δ 8.11–7.32 (m, 8H, Ar-H); 4.30 (t, $J = 13.40$ Hz, 2H, H1'), 3.41 (t, $J = 22.87$, 2H, H-2') 2.43 (s, 3H, CH₃-tolyl), 2.00 (s, 3H, COCH₃); $^{13}\text{C-NMR}$ (DMSO- d_6) δ 189.98 (COCH₃), 180.04 (C-2), 156.74 (C-4), 147.01, 139.40, 134.73, 133.10, 129.84, 128.98, 126.42, 125.23, 125.08, 119.44, (Ar-C), 63.53 (C-1'), 61.68 (C-2'), 30.36 (CH₃-tolyl), 20.99 (COCH₃); MS: m/z 354 (M^+); Anal. calcd for C₁₉H₁₈N₂O₃S (354.42) C, 64.31; H, 5.12; N, 7.90 found C, 54.01; H, 5.03, N, 7.96%.

2-(Isopropylidenedioxypopylthio)-3-tolyl-quinazolin-(3H)-4-one (12a)

Yield 66%; m.p. 126–128°C; $^1\text{H-NMR}$ (DMSO- d_6) δ 7.93–7.13 (m, 8H, Ar-H), 4.17 (m, 1H, H-2'), 3.90 (m, 2H, H-1'), 3.19 (m, 3H, H-3), 2.25 (s, 3H, CH₃-tolyl), 1.22 (s, 3H, CH₃-isopropyl), 1.08 (s, 3H, CH₃ isopropyl); $^{13}\text{C-NMR}$ (DMSO- d_6) δ 160.66 (C-2), 157.00 (C-4), 139.38, 134.69, 133.17, 129.86, 128.99, 126.44, 125.78, 119.44; (Ar-C) 108.00 (C-isopropyl) 73.62 (C-2'), 67.00 (C-1'), 34.79 (C-3'), 29.50 (CH₃-tolyl); 26.58, 26.20 (2CH₃-isopropyl); Anal. calcd for C₂₁H₂₂N₂O₃S (382.38) C, 65.96; 5.80; N, 7.32 found C, 66.07; H, 8.63; N, 7.09%.

2-(Isopropylidenedioxypopylthio)-3-(4-methoxyphenyl)-quinazolin-(3H)-4-one (12b)

Yield 63%; m.p. 131–133°C; $^1\text{H-NMR}$ (DMSO- d_6) δ 8.26–7.25 (m, 8H, Ar-H), 4.14 (m, 1H, H-2'), 3.91 (m, 1H, H-1'), 3.65 (s, 3H, OCH₃), 3.36 (m, 1H, H-3'), 1.40 (s, 3H, CH₃-isopropyl), 1.43 (s, 3H, CH₃ isopropyl) $^{13}\text{C-NMR}$ (DMSO- d_6) δ 160.51 (C-2), 147.52 (C-4), 134.56, 130.21, 130.12, 127.20, 126.14, 125.85, 119.76, 114.89, 114.85, (Ar-C), 109.59 (C-isopropyl); 74.32 (C-2'), 68.57 (C-1'), 55.33 (OCH₃), 35.33 (C-3'), 26.83, 26.87, (2CH₃-isopropyl); Anal. calcd for C₂₁H₂₂N₂O₄ (398.37) C, 63.22; H, 5.57; N, 7.03 found C, 63.40; H, 5.39; N, 7.29%.

General Procedure for Compound 13a,b

Saturated ammonia in methanol (20 mL) was added with stirring to a solutions of **10a** or **10b** in methanol (10 mL) at 0°C. The reaction mixture was stirred at room temperature 24 h (monitored by TLC analysis). The solvent was evaporated under vacuum and the residue purified by silica gel column chromatography (cyclohexane/ethylacetate, 50/50, v/v).

2-(2-Hydroxyethylthio)-3-phenyl-quinazolin-(3H)-4-one (13a)

Yield 68%; m.p. 136–137°C; $^1\text{H-NMR}$ (DMSO-d_6) δ 8.09–7.09 (m, 9H, Ar-H), 4.89 (br, 1H, OH), 3.66 (t, $J = 12.05$ Hz, 2H, H-1'), 3.27 (t, $J = 12.68$ Hz, 2H, H-2'), $^{13}\text{C-NMR}$ (DMSO-d_6) δ 160.89 (C-2), 157.38 (C-4), 147.19, 135.97, 134.79, 129.67, 129.35, 129.00, 126.47, 122.40, 119.44, 115.15 (Ar-C), 59.12 (C-1'), 34.81 (C-2); MS: m/z 298 (M^+); Anal. calcd for $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}_2\text{S}$ (298.36) C, 64.41; H, 4.73; N, 9.39 found C, 64.34; H, 4.82; N, 9.35%.

2-(2-Hydroxyethylthio)-3-tolyl-quinazolin-(3H)-4-one (13b)

Yield 64%; m.p. 142–144°C; $^1\text{H-NMR}$ (DMSO-d_6) δ 8.09–7.30 (m, 8H, Ar-H), 4.99 (m, 1H, OH), 3.66 (t, $J = 11.82$ Hz, 2H, H-1'), 3.24 (t, $J = 12.71$ Hz, 2H, H-2'), 2.38 (s, 3H, CH_3 -tolyl); $^{13}\text{C-NMR}$ (DMSO-d_6) δ 161.34 (C-2), 158.27 (C-4), 147.80, 139.95, 135.36, 133.95, 130.47, 129.67, 127.09, 126.52, 126.33, 120.04 (Ar-C), 59.43 (C-1'), 35.42 (C-2'), 21.39 (CH_3 -tolyl); MS: m/z 312 (M^+); Anal. calcd for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_2\text{S}$ (312.78) C, 65.36; H, 5.16; N, 8.97 found C, 65.64; H, 5.28; N, 8.75%.

General Procedure for Compounds 14a,b

Compounds **12a** or **12b** (1 mmol) was dissolved in 10 mL 90% CH_3COOH and the reaction mixture was stirred at room temperature 24 h, until the TLC shows no starting material left. The solvent was evaporated under vacuum and the residue purified by silica gel column chromatography (cyclohexane/ethylacetate, 50/50, v/v).

2-(2,3-Dihydroxypropylthio)-3-tolyl-quinazolin-(3H)-4-one (14a)

Yield 80%; m.p. 108–109°C; Anal. calcd for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_3\text{S}$ (342.31) C, 63.16; H, 5.30; N, 8.18 found C, 63.43; H, 5.51; N, 8.39%.

2-(2,3-Dihydroxypropylthio)-3-(4-methoxyphenyl)-quinazolin-(3H)-4-one (15b)²²**REFERENCES**

- [1] R. Lakhan and B. J. Rai, *J. Chem. Eng. Data*, **32**, 384 (1987).
- [2] R. Lakhan and B. J. Rai, *J. Chem. Eng. Data*, **31**, 501 (1986).
- [3] A. K. Sengupta and T. Bhattacharya, *J. Indian Chem. Soc.*, **60**, 373 (1983).
- [4] M. R. Chaurasia and S. K. Sharma, *Agric. Biol. Chem.*, **44**, 663 (1980).
- [5] M. R. Chaurasia and S. K. Sharma, *Heterocycles*, **14**, 176 (1980).

- [6] A. K. Sen Gupta and A. K. Pandey, *Pestic Sci.*, **28**, 41 (1989).
- [7] K. C. Joshi, V. K. Singh, D. S. Metha, R. C. Sharma, and L. Gupta. *J Pharm. Sci.*, **64**, 1428 (1975).
- [8] J. Reisch and A. R. Ram. Rao, *Monat. Für Chemie*, **124**, 12, 7 (1993).
- [9] M. Baba, H. Tanaka, E. Delercq, et al., *Biochem. Biophys. Res. Commun.*, **165**, 1375 (1989).
- [10] J. P. Bader, J. B. McMahon, R. J. Schultz, et al., *Proc. Natl. Acad. Sci. U.S.A.*, **88**, 6740 (1991).
- [11] L. A Kohlstaedt, J. Wang, J. M. Friedman, P. A. Rice, and T. A. Steltz, *Science*, **256**, 1783 (1992).
- [12] J. Ren, R. Esnouf, E. Garman, et al., *Nature Struct. Biol.*, **2**, 293 (1995).
- [13] J. Ding, K. Das, C. Tantillo, et al., *Proc. Natl. Acad. Sci. U.S.A.*, **88**, 11241 (1991).
- [14] R. Esnouf, J. Ren, C. Ross, et al., *Nature Struct. Biol.*, **2**, 303 (1995).
- [15] A. H. Ismail, *Pharmazie*, **56**, (2001).
- [16] A. H. Ismail, *Synthetic Communications*, **32**, 1791 (2002).
- [17] A. H. Ismail, A. H. Abdel Aleem, H. A. Adel-Bary, and S. El-Assaly, *Nucleosides Nucleotides & Nucleic Acid*, **21**, 469 (2002).
- [18] I. M. Abdou, A. M. Attia, L. Strerowski, and S. E. Patterson, *Tetrahedron lett.*, **41**, 4757 (2000).
- [19] A. M. Attia, *Nucleosides, Nucleotides & Nucleic Acid*, **21**, 207 (2002).
- [20] A. M. Attia, *Tetrahedron*, **58**, 1399, (2002).
- [21] H. P. Papudofaulos and C. P. Torres, *J. Heterocycl. Chem.*, **19**, 269 (1982).
- [22] R. Thesis, K. Kottke, A. Beschout, et al., *Pharmazie*, 273 (1996).