This article was downloaded by: [Florida State University] On: 07 October 2014, At: 01:18 Publisher: Taylor & Francis Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information: http://www.tandfonline.com/loi/gpss20

Synthesis of Some New Quinazoline Derivatives Analogues to MKC-442 and TNK 561

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

^a Menoufia University, Shebin El-Koom, Egypt

^b Tanta University (Kafr El-Sheikh Branch), Egypt

Published online: 27 Oct 2010.

To cite this article: Abd El-Hamid , A. A. Ismail & Adel M. E. Attia (2003) Synthesis of Some New Quinazoline Derivatives Analogues to MKC-442 and TNK 561, Phosphorus, Sulfur, and Silicon and the Related Elements, 178:6, 1231-1240, DOI: 10.1080/10426500307910

To link to this article: http://dx.doi.org/10.1080/10426500307910

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at http://www.tandfonline.com/page/terms-and-conditions



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

(Received September 8, 2002; accepted November 10, 2002)

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 us 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 divers aromatic compounds such as HEPT, MKC-442, and thiocarboxanilides,^{9,10} Structural studies have revealed that NNRTIs inihibit HIV-1 RT by binding to an allosteric site, approximately 10Å from the polymerase active site,¹¹⁻¹³ causing a distortion of the catalytic aspartite triad.¹⁴ The high selectivity of NNRTIs for HIV-1 RT over HIV-2 RT and cellular polymerases contributes to lower cellular toxicity

The authors would like to express their thanks to DANIDA establishment Denmark, which supports the project "Development of New Drugs Against Hepatitis" at the Chemistry Department, Faculty of Science, Monoufia University for the laboratory facilities and spectroscopic measurements.

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 13 C-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 acylcic 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 acetoxy protons in its ¹H-NMR (see Experimental part).



SCHEME 1

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

EXPERIMENTAL

NMR spectra were recorded on a Brucker 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 untill TLC shows no starting material left. Evaporated the solvent under vacuum, the residue was dissolved in 30 mL ethylacetate and 20 mL of H_2O . The extracted organic layer was dried over Na_2SO_4 and the solvent evaporated under vacuum, the residue was purified by silica gel column chromatography (cyclohoxane/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-d₋₆), δ 8.11-7.43 (m, 8H, Ar-H), 5.41 (s, 2H, H-1'), 3.57 (m, 2H, OCH₂ CH₃), 1.13 (t, J = 14.04 Hz, OCH₂CH₃); ¹³C-NMR (DMSO-d₋₆), 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. cald 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-d₋₆) δ 8.25-7.43 (m, 8H, Ar-H), 5.87 (s, 2H, H-1'), 3.69 (m, 2H, OC<u>H</u>₂ CH₃), 3.18 (s, 3H, CH₃-tolyl), 1.27 (t, 3H, J = 9.13 Hz, CH₂C<u>H₃); ¹³C-NMR (DMSO-d₋₆) 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 (O<u>C</u>H₂CH₃), 14.77 (CH₃-tolyl), 14.56 (OCH₂<u>C</u>H₃); Anal. cald for C₁₈H₁₈N₂O₂S (326.33) C, 66.25; H, 5.56; N, 8.58. found C, 66.49; H, 5.33; N, 8.66%.</u>

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

Seperated by silica gel column chromatography (cyclohexane/ethyl-acetate 90/10, v/v) as fraction (1); Yield 72%; m.p. 133–134°C as a white powder; ¹H-NMR (DMSO-d_6) 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-d_6) 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 (OCH₂<u>C</u>H₃); Anal cald for C_{18} H₁₈ N₂O₃S (342.33) C, 63.15; H, 5.30; H, 8.18; found C, 62.96; H, 5.55; N, 7.00.

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

Yield 67%; m.p. 100–102°C as a white powder; ¹H-NMR (DMSO-d₋₆) δ 7.96-7.15 (m, 14H, Ar-H), 5.33 (s, 2H, H-1'), 4.35 (s, 2H, OCH₂Ph); ¹³C-NMR (DMSO-d₋₆) δ 160.80 (C-2), 155.77 (C-4), 146.92 137.32, 135.98, 134.84, 129.78, 129.70, 129.30, 128.21, 127.74, 127.55 (Ar-C), 87.89 (C-1'), 70.82 (OCH₂Ph); MS: m/z 374 (M⁺); Anal. cald for C₂₂H₁₈N₂O₂S (374.41) C, 70.57; H, 4.85; N, 7.48 found C, 70.70; H, 4.75; N, 7.76%.

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

Yield 78%; m.p. 120–121°C as a white powder; ¹H-NMR (DMSO-d₋₆) δ 7.89-7.05 (m, 13H, Ar-H), 5.26 (s, 2H, H-1'), 4.29 (s, 2H, OC<u>H₂</u>Ph), 3.13 (s, 3H, CH₃-tolyl); ¹³C-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 (O<u>C</u>H₂Ph), 21.40 (CH₃-tolyl); MS: m/z 388 (M⁺); Anal. cald for C₂₃H₂₀N₂O₂S (388.48) C, 71.10; H, 5.19; N, 7.21; found C, 71.20; H, 5.59; N, 7.25%.

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

Yield 82%; m.p 105–107°C as a white powder; ¹H-NMR (DMSO-d₋₆) δ 8.28-7.45 (m, 13H, Ar-H), 5.48 (s, 2H, H-1'), 4.68 (s, 2H, OC<u>H₂</u>Ph), 3.66 (s, 3H, OCH₃); ¹³C-NMR (DMSO-d₋₆) 160.49 (C-2), 156.21 (C-4), 147.45 138.99, 134.52, 130.13, 128.35, 127.94, 127.85, 127.16, 126.33, 125.96 (Ar-C); MS: m/z 404 (M⁺); Anal. cald for C₂₃H₂₀N₂O₃S (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-1,2,3,4tetrahydroquinazolin-4-one (7)

Seperated by silica gel column chromatography (cyclohexaane/ethylacetate 90/10, v/v) as fraction (2); Yield 20%; m.p. 138–139% as a white powder; ¹H-NMR (DMSO-d_6) δ 8.15-7.00 (m, 8H, Ar-H), 5.55 (s, 2H, H-1') 3.86 (m, 2H, OC<u>H</u>₂CH₃), 3.60 (s, 3H, OCH₃), 1.18 (t, J = 8.61 Hz, 3H OCH₂C<u>H₃</u>); ¹³C-NMR (DMSO-d_6) δ 176.36 (C=s), 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 (OCH₂CH₃), 55.93 (OCH₃), 14.96 (OCH₂CH₃); Anal. cald for C₁₈H₁₈N₂O₃S (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; ¹H-NMR (DMSOd₋₆) δ 8.09-7.23 (m, 9H, Ar-H); 5.58 (s, 2H, H-1'), 3.67 (m, 2H, OC<u>H₂</u>CH₃), 1.16 (t, J = 5.00 Hz, 3H, OCH₂C<u>H₃</u>); ¹³C-NMR (DMSOd₋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 (O-<u>C</u>H₂CH₃), 14.78 (OCH₂<u>C</u>H₃); MS: m/z 296 (M⁺); Anal. cald for C₁₇H₁₆N₂O₃ (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; ¹H-NMR (DMSO-d₋₆) δ 8.26-7.14 (m, 8H, Ar-H), 5.64 (s, 2H, H-1'), 3.74 (m, 2H, OCH₂CH₃), 2.41 (s, 3H, CH₃-tolyl), 1.26 (t, J = 10.04 Hz, 3H, OCH₂CH₃); ¹³C-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 (OCH₂CH₃), 21.86 (CH₃-tolyl), 14.92 (OCH₂CH₃); Anal. cald for C₁₈H₁₈N₂O₃ (310.35) C, 69.86; H, 5.85; N, 9.03 found C, 69.88; H, 5.90; N, 9.29%.

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

Yield 74%; m.p. 145–146°C as a white powder; ¹H-NMR (DMSO-d₋₆) δ 8.90-7.17 (m, 13H, Ar-H), 5.67 (s, 2H, H-1'), 4.84 (s, 2H, OC<u>H</u>₂Ph), 2.36 (S, 3H, CH₃-tolyl); ¹³C-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 (O<u>C</u>H₂Ph), 20.69 (CH₃-tolyl); Anal. cald for C₂₃H₂₀N₂O₃ (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; ¹H-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, COC<u>H₃</u>); ¹³C-NMR (DMSO-d₋₆) δ 170.02 (–<u>CO</u>CH₃), 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 (COCH₃); MS: m/z 340 (M⁺). Anal. cald for C₁₈H₁₆N₂O₃S (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; ¹H-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, COC<u>H₃</u>); ¹³C-NMR (DMSO-d₋₆) δ 189.98 (<u>C</u>OCH₃), 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 (CO<u>C</u>H₃); MS: m/z 354 (M⁺); Anal. cald for C₁₉H₁₈N₂O₃S (354.42) C, 64.31; H, 5.12; N, 7.90 found C, 54.01; H, 5.03, N, 7.96%.

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

Yield 66%; m.p. 126–128°C; ¹H-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); ¹³C-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; (A-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. cald for C₂₁H₂₂N₂O₃S (382.38) C, 65.96; 5.80; N, 7.32 found C, 66.07; H, 8.63; N, 7.09%.

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

Yield 63%; m.p. 131–133°C; ¹H-NMR (DMSO-d₋₆), 8.26-7.25 (m, 8H, Ar-H), 4.14 (m, 1H, H-2'), 3.91 (m, 1H, H-1'), 3.65 (s, 3H, OC<u>H₃</u>), 3.36 (m, 1H, H-3'), 1.40 (s, 3H, C<u>H₃</u>-isopropyl), 1.43 (s, 3H, CH₃ isopropyl) ¹³C-NMR (DMSO-d₋₆), 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. cald for $C_{21}H_{22}N_2O_{45}$ (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; ¹H-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′), ¹³C-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. cald for C₁₆H₁₄N₂O₂S (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; ¹H-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, CH₃-tolyl); ¹³C-NMR (DMSO-d_{- δ}) 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 (CH₃-tolyl); MS: m/z 312 (M⁺); Anal. cald for C₁₇H₁₆N₂O₂S (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, untill 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. cald for $C_{18}H_{18}N_2O_3S$ (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. Ral, J. Chem. Eng. Data, 32, 384 (1987).
- [2] R. Lakhan and B. J. Rai, J. Chem. Eng. Data, 31, 501 (1986).
- [3] A. K. Sengsupta 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).