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AN INTERACTION OF 2-THIAZOLEACETONITRILES WITH *N*-(2-CHLOROACETYL)ANTHRANILIC ACID ESTER

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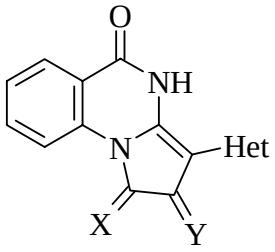
Abstract – The title ester was found to react with 2-benzothiazoleacetonitrile yielding 3-(2-benzothiazolyl)-2,4-dihydropyrrolo[1,2-*a*]quinazoline-1,5-dione. At the same time 4-aryl-2-thiazoleacetonitriles gave 3,4-dihydro-β,4-dioxo-α,δ-*bis*(4-aryl-2-thiazolyl)-2-quinazolinepentanenitriles potassium salts under identical conditions. These results were explained in terms of different solubility of the intermediate compounds. Upon acidification the obtained salts were shown to undergo intramolecular Thorpe addition leading to the 3-amino-2,4-*bis*(4-aryl-2-thiazolyl)-4-[4(3*H*)-oxo-2-quinazolinyl]-2-cyclopenten-1-ones. Above mentioned pyrrolo[1,2-*a*]quinazoline derivative was treated with benzylamines and active methylene nitriles to yield β-(2-benzothiazolyl)-*N*-arylmethyl-3,4-dihydro-4-oxo-2-quinazolinepropanamides and 2-substituted 3-amino-4-(2-benzothiazolyl)-4-[4(3*H*)-oxo-2-quinazolinyl]-2-cyclopenten-1-ones, respectively.

INTRODUCTION

An increasing interest in pyrrolo[1,2-*a*]quinazoline derivatives has descended from the researches of *Peganine* family alkaloids, their structural isomers. So a number of synthetic pathways to pyrrolo[1,2-*a*]quinazolines has been developed[1-4] and, as a result, compounds with analgesic, antihypertensive and CNS depressing activities have been obtained.[5] Our recent investigations have been devoted to preparation[4,6] of the hetaryl substituted pyrrolo[1,2-*a*]quinazoline-2,5-diones (**1**) (Figure 1) and

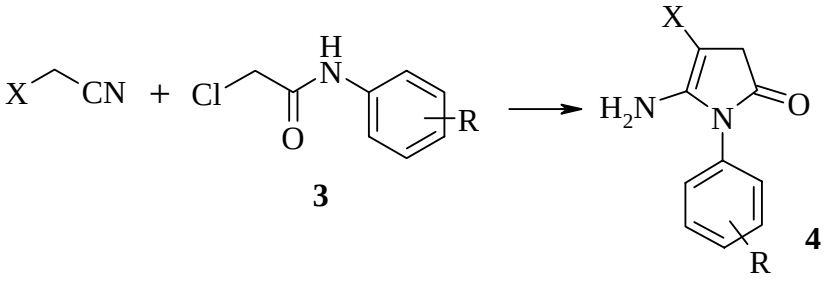
related derivatives. Continuing these researches we were interested in obtaining of the isomeric 1,5-diones (**2**) to compare their properties with those of compounds (**1**).



1,2

Figure 1. **1:** X = H_2, Y = O; **2:** X = O, Y = H_2; Het = 2-benzothiazolyl, 2-benzimidazolyl, 4-aryl-2-thiazolyl etc.

Malonodinitrile and ethyl cyanoacetate were reported to undergo alkylation with chloroacetoanilides (**3**) yielding pyrrolones (**4**) (Scheme 1).[3,7] Recently this reaction has been successfully applied by us to the 2-benzothiazoleacetonitrile.[8] Therefore, use of the anthranilic acid derived chloroacetamide (**3**) (R = 2-CO_2Me) should result in the pyrrolone (**4**) (R = 2-CO_2Me) with suitably arranged amino and ester groups which were assumed to react one with another to give the target derivatives (**2**). Thus this approach was examined, however, somewhat unexpected results were obtained.



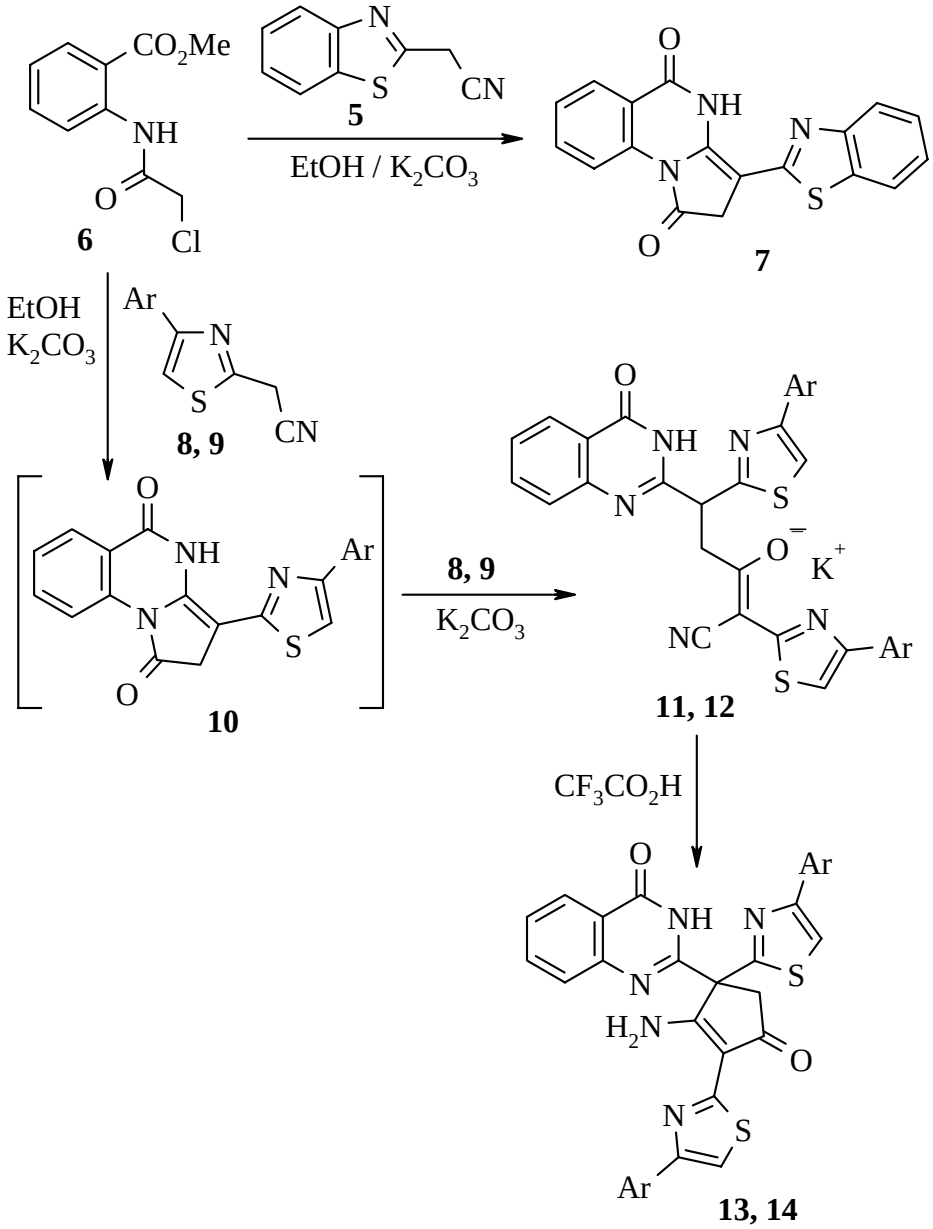
3 **4**

Scheme 1. X = CN, CO_2Et, 2-benzothiazolyl.

RESULTS AND DISCUSSION

According to the described alkylation procedure[8] 2-benzothiazoleacetonitrile (**5**) was treated with *N*-(2-chloroacetyl)anthranilic acid methyl ester (**6**) in anhydrous EtOH in the presence of K_2CO_3 to yield the expected pyrrolo[1,2-*a*]quinazoline-1,5-dione (**7**) (Scheme 2). The structure of compound (**7**) was confirmed by ^{1}H and ^{13}C NMR spectral data. Especially the doublet of 9-H at 8.60 ppm shifted downfield due to deshielding by the magnetically anisotropic carbonyl was remarkable attribute of the tricyclic system formation. Noteworthy, for the isomeric compounds (**1**) the appropriate signal was observed at about 7.7 ppm.[4] The absence of both methoxy and amino groups signals in the ^{1}H NMR spectrum indicated their incorporation into pyrimidine ring while the absence of a cyano absorption both in IR and ^{13}C NMR spectra confirmed pyrrole moiety formation. The singlet of the methylene group protons appeared at 3.56 ppm. In

general, the spectral data of compound (**7**) were in good agreement with those reported for other pyrrolo[1,2-*a*]quinazoline-1,5-dione derivatives.[1]



Scheme 2. **8, 11, 13:** Ar = 4-ClC_6H_4; **9, 12, 14:** Ar = 4-BrC_6H_4

Nevertheless, when the reaction was carried out with 4-aryl-2-thiazoleacetonitriles (**8,9**) under the same conditions corresponding compounds (**10**) were not obtained. Instead the substances consisting of two 4-arylthiazoles and one 4-quinazolinone moieties were isolated. Moreover, their ^{1}H NMR spectra exhibited the ABX system signals at 3.45 (A), 3.72 (B) and 5.09 (X) ppm. The IR spectra showed a strong absorption at 2160 cm^{-1} inherent to cyano group participating a negative charge delocalization. Hence obtained materials were suggested to be the salts and the elemental analysis confirmed the presence of potassium. On the basis of these data the structures of **11,12** were assigned to the compounds depicted in Scheme 2. Their ^{13}C NMR spectra were also in good agreement with the structures of **11,12**.

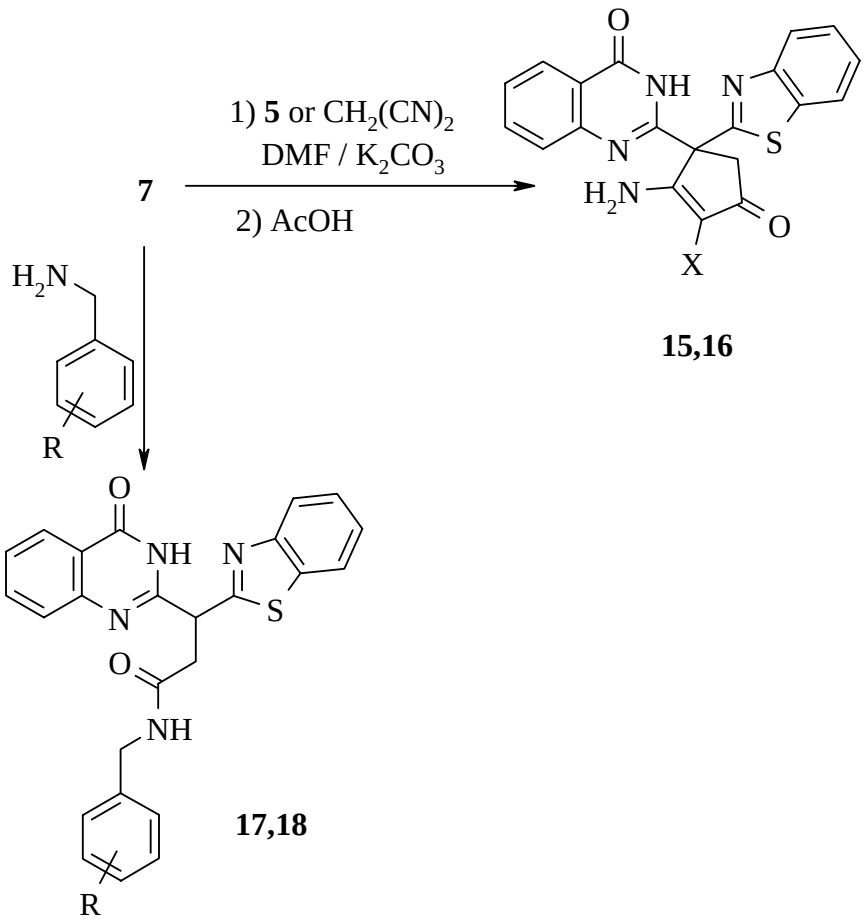
The salts (**11,12**) were conceivably formed *via* Claisen type acylation of the nitriles (**8,9**) by the intermediates like **10**. It should be emphasized that compounds (**11,12**) were the sole isolated products using various reagents ratio. However the best yields (~ 60 %) were achieved with the chloroacetamide **6** : nitrile **8,9** : K_2CO_3 ratio 1:2:2.3.

An attempt to convert the salts (**11,12**) into corresponding acids also gave unexpected result. Thus acidification of the compounds (**11,12)** appeared to induce their transformation into 3-amino-2-cyclopenten-1-ones (**13,14**) *via* intramolecular Thorpe addition of the methyne moiety activated by two heterocycles to the nitrile group. The ring closure was found to proceed quantitatively upon keeping compounds (**11,12**) in trifluoroacetic acid at room temperature. The structure of the cyclopentenones (**13,14**) was confirmed by IR, ^1H, ^{13}C and 2D NMR (COSY, NOESY, HSQC and HMBC experiment) spectral data. Thus the methylene protons were observed in the ^1H NMR spectra as two one-proton doublets at 3.45 and 3.60 ppm with geminal spin-spin coupling (J ~ 17 Hz), i. e. as AB system instead of ABX one of the starting materials (**11,12**). Moreover, the long range C-H correlation (HMBC) experiment performed for compound (**13**) revealed six correlations of the both doublets with the following carbons signals: 4-C at 57.5 ppm, 2-C at 106.0 ppm, 3-C at 155.0 ppm, 2'-C of thiazole and quinazoline substituents at position 4 at 170.0 and 171.9 ppm, respectively, and 1-C at 194.8 ppm. This correlations set proves certainly the structure (**13,14**). The absence of the nitrile absorption in IR and ^{13}C NMR spectra also indicated the ring closure with its participation. Finally, MS spectrum of derivative (**13**) exhibited an appropriate m/z value 627 for $M^{\bullet+}$.

It should be noted that ^{13}C NMR spectra of various 3-dialkylamino-2,4,5-(un)substituted 2-cyclopenten-1-ones were thoroughly investigated[9] in view of their structural relation to prostanoids. In the present case the ^{13}C NMR shifts of the cyclopentenone moiety were found to be in good agreement with those reported[9] for related systems. Also it is noteworthy that the amino group protons of compounds (**13,14**) appeared in the ^1H NMR spectra as two separate one-proton singlets at 8.8-9.3 ppm. Probably, it is due to a strong vinylogous amide-like conjugation with the carbonyl. The similar effect was observed for other cyclic five-member enaminones.[10]

Different behavior of benzothiazole- and thiazoleacetonitriles (**5**) and (**8,9**) in the reaction with compound (**6**) is explained by different solubility of the compound (**7**) and derivatives like **10**. Really, pyrrolo[1,2-*a*]quinazoline (**7**) was precipitated from the boiling reaction mixture thus escaping further transformations, whereas intermediates (**10**) remained in the solution and reacted with another molecule of the starting nitrlie (**8,9**). Consequently, compound (**7**) also should possess acylative properties. Indeed, its reaction with 2-benzothiazoleacetonitrile (**5**) or with malonodinitrile in DMF in the presence of K_2CO_3, the conditions providing complete solubility, resulted after further acidification in cyclopentenones (**15,16**) (Scheme 3). Spectral data of the derivatives (**15,16**) were similar to those of **13,14**. Moreover,

pyrroloqunazoline (**7**) was shown to interact as acylating agent with benzylamines yielding β-(2-benzothiazolyl)-4-oxo-2-quinazolinepropanamides (**17,18**). Their structure was confirmed by ^{1}H and ^{13}C NMR spectral data. The propanamide moiety protons of the derivatives (**17,18**) appeared in the ^{1}H NMR spectra as ABX system signals at 3.2 (A), 3.5 (B) and 5.1 (X) ppm, thus resembling compounds (**11,12**). For the *N*-CH_2 protons both geminal spin-spin coupling and the coupling with NH were observed. Hence the two one-proton doublet of doublets were present at 4.0-4.2 and 4.2-4.4 ppm, while the NH signal appeared as triplet at 8.6-8.7 ppm. ^{13}C NMR spectral data were also in good agreement with the assigned structure.



Scheme 3. **15:** X = 2-benzothiazolyl, **16:** X = CN; **17:** R = H, **18:** R = 3,4-CH_2O_2

According to the literature, the general method for preparation of 3-amino-2-cyclopenten-1-one derivatives is an amination of cyclic 1,3-diones[11] or 3-chloro-2-cyclopenten-1-ones.[12,13] Furthermore the cyclic 1,2-diones transformation into 2-hydroxy substituted enaminones through halogenation/amination or nitrosation/reduction sequences was also reported.[14] Finally, a few very specific syntheses of 3-amino-2-cyclopenten-1-ones were described.[15,16] Hence the preparation of compounds (**13-16**) is the first example utilizing Thorpe reaction for cyclic enaminones obtaining. Moreover derivatives (**13-16)** are the rare representatives of 4,4-disubstituted aminocyclopentenones. Although the methods of substituents introduction into positions 4 and 5 of 3-amino-2-cyclopenten-1-ones have been developed[17] they do not

allow to bring in two substituents at the same atom.[18] A few known 4,4-disubstituted derivatives were prepared *via* either unusual recyclization of comenic acid ester[15] or amination of difficulty available precursors with a ready substitution pattern.[12] Finally it goes without saying that compounds (**13-16**) are the first cyclic enaminones bearing heterocyclic substituents on the ring.

To resume, the chloroacetamide (**6**) has been found to react with 2-benzothiazoleacetonitrile (**5**) yielding expected pyrrolo[1,2-*a*]quinazoline-1,5-dione (**7**), whereas with thiazoleacetonitriles (**8,9**) the salts (**11,12**) have been obtained. The latter undergo ring closure reaction upon acidification leading to the enaminones (**13,14**). Pyrroloquinazoline (**7)** has been shown to act as acylating agent towards amines and active methylene nitriles. As the result 2-quinazolinepropanamides (**17,18**) and aminocyclopentenones (**15,16**) have been prepared.

EXPERIMENTAL

2-Benzothiazoleacetonitrile (**5**),[19] 4-Aryl-2-thiazoleacetonitriles (**8,9**)[20] and N-(2-chloroacetyl)anthranilic acid methyl ester (**6**)[21] were prepared as reported. All mp values were determined in open capillary tubes in a Thiele apparatus and are uncorrected. IR spectra were obtained on a Pye Unicam SP 3-300 apparatus for KBr tablets. ^{1}H NMR spectra were recorded on a Varian VXR-300 (300 MHz) and Mercury 400 (400 MHz) spectrometers in DMSO-d_6 solutions. Chemical shifts (δ) are given in ppm downfield from internal $SiMe_4$. J values are in Hz. ^{13}C and 2D NMR experiments were performed on a Bruker Avance 500 (500 MHz for ^{1}H and 125 MHz for ^{13}C) spectrometer. Throughout the experimental section in the spectra descriptions H and C atoms of quinazoline, benzothiazole, thiazole and aryl moieties are referred with subscripts Q, Bth, Th and Ar, respectively. MS spectra were determined with a Varian 212 instrument at 70 eV. The purity of all compounds prepared was checked by ^{1}H NMR.

3-(2-Benzothiazolyl)-2,4-dihydropyrrolo[1,2-*a*]quinazoline-1,5-dione (7): Powdered K_2CO_3 (0.48 g, 0.0035 mol) was added to a solution of the nitrile (**5**) (0.52 g, 0.003 mol) and chloroacetamide (**6**) (0.68 g, 0.003 mol) in anhydrous EtOH (7 mL) and the mixture was refluxed for 1.5 h. After cooling the precipitate formed was filtered, thoroughly washed with water to remove inorganic materials, dried and recrystallized from DMF to yield 0.71 g (71 %) of **7**.

mp >300°C. ^{1}H NMR: δ = 3.56 (s, 2H, CH_2), 7.05 (t, J = 7.5, 1H, 5-H_{Bth}), 7.25 (m, 2H, 6-H_{Bth}, 7-H), 7.55 (m, 2H, 7-H_{Bth}, 8-H), 7.78 (d, J = 7.5, 1H, 4-H_{Bth}), 7.94 (d, J = 8.4, 1H, 6-H), 8.60 (d, J = 8.4, 1H, 9-H), 10.15 (s, 1H, NH). ^{13}C NMR: δ = 26.6 (2-C), 71.9 (3-C), 104.7 (9-C), 106.3 (7-C), 108.0 (6-C_{Bth}), 113.2 (5-C_{Bth}), 116.9 (7-C_{Bth}), 118.6 (8-C), 119.0 (4-C_{Bth}), 119.8 (6-C), 120.9 (7a-C_{Bth}), 126.7 (5a-C), 129.1 (9a-C), 129.7 (3a-C_{Bth}), 137.3 (2-C_{Bth}), 156.2 (3a-C), 163.8 (1-C), 168.3 (5-C). Anal Calcd for $C_{18}H_{11}N_3O_2S$: C 64.85, H 3.33, N 12.60, S 9.62. Found C 64.94, H 3.19, N 12.64, S 9.78.

Salts (11,12). General procedure: Powdered K_2CO_3 (0.63 g, 0.0046 mol) was added to a solution of the nitrile (**8,9**) (0.004 mol) and chloroamide (**6**) (0.46 g, 0.002 mol) in anhydrous EtOH (10 mL) and the mixture was refluxed for 1.5 h. After cooling the precipitated solid was filtered, washed with water, dried and recrystallized from DMF to give compounds (**11,12**).

α,δ-*Bis*[4-(4-chlorophenyl)-2-thiazolyl]-3,4-dihydro-β,4-dioxo-2-quinazolinepentanenitrile potassium salt (11): (0.8 g, 60 %). mp 280°C. ^{1}H NMR: δ = 3.45 (dd, ^{2}J = 18.0, ^{3}J = 4.0, 1H, CH_2), 3.72 (dd, ^{2}J = 18.0, ^{3}J = 8.0, 1H, CH_2), 5.09 (dd, ^{3}J = 8.0, ^{3}J = 4.0, 1H, CH), 7.20 (s, 1H, 5-H_{Th}), 7.35 (d, J =8.7, 2H, H_{Ar}), 7.43 (m, 3H, H_{Ar}, 6-H_Q), 7.65 (d, J = 7.8, 1H, 8-H_Q), 7.75 (t, J = 7.8, 1H, 7-H_Q), 7.89 (d, J = 9.0, 2H, H_{Ar}), 7.94 (d, J =8.7, 2H, H_{Ar}), 7.97 (s, 1H, 5-H_{Th}), 8.11 (d, J = 7.8, 1H, 5-H_Q), 12.72 (s, 1H, NH). ^{13}C NMR: δ = 30.6 (CH_2), 37.4 (>CH-), 76.8 (*C*-CN), 115.7 (CN), 125.5 (3,5-C_{Ar}), 125.6 (3,5-C_{Ar}), 126.1 (6-C_Q), 126.4 (8-C_Q), 127.5 (2,6-C_{Ar}), 128.5 (5-C_Q), 128.7 (2,6-C_{Ar}), 131.1 (1-C_{Ar}), 131.2 (1-C_{Ar}), 134.8 (5-C_{Th}), 135.1 (7-C_Q), 135.3 (4-C_{Ar}), 135.4 (4-C_{Ar}), 137.6 (5-C_{Th}), 139.5 (4a-C_Q), 146.0 (4-C_{Th}), 148.4 (4-C_{Th}), 149.2 (2-C_{Th}), 149.8 (8a-C_Q), 154.8 (2-C_{Th}), 160.8 (2-C_Q), 165.6 (4-C_Q), 178.4 (C-O^-). Anal. Calcd for $C_{31}H_{18}N_5O_2Cl_2KS_2$: C 55.85, H 2.72, N 10.51, Cl 10.64, S 9.62, K 5.87. Found C 55.97, H 2.64, N 10.53, Cl 10.54, S 9.79, K 5.69.

α,δ-*Bis*[4-(4-bromophenyl)-2-thiazolyl]-3,4-dihydro-β,4-dioxo-2-quinazolinepentanenitrile potassium salt (12): (0.88 g, 58 %). mp >300°C. ^{1}H NMR: δ = 3.48 (dd, ^{2}J = 18.0, ^{3}J = 4.0, 1H, CH_2), 3.72 (dd, ^{2}J = 18.0, ^{3}J = 8.0, 1H, CH_2), 5.09 (dd, ^{3}J = 8.0, ^{3}J = 4.0, 1H, CH), 7.35 (s, 1H, 5-H_{Th}), 7.51 (t, J = 8.0, 1H, 6-H_Q), 7.57 (d, J = 8.4, 2H, H_{Ar}), 7.63 (d, J = 8.0, 2H, H_{Ar}), 7.68 (d, J = 8.0, 1H, 8-H_Q), 7.81 (t, J = 8.0, 1H, 7-H_Q), 7.89 (m, 4H, H_{Ar}), 8.13 (m, 2H, 5-H_{Th}, 5-H_Q), 12.80 (s, 1H, NH). ^{13}C NMR: δ = 30.2 (CH_2), 37.2 (>CH-), 77.8 (*C*-CN), 115.7 (CN), 122.1 (4-C_{Ar}), 122.5 (4-C_{Ar}), 126.5 (6-C_Q), 127.4 (2,6-C_{Ar}), 127.9 (8-C_Q), 128.4 (2,6-C_{Ar}), 128.8 (5-C_Q), 130.9 (3,5-C_{Ar}), 131.0 (3,5-C_{Ar}), 132.5 (1-C_{Ar}), 134.4 (5-C_{Th}), 134.7 (5-C_{Th}), 134.8 (1-C_{Ar}), 135.1 (7-C_Q), 140.9 (4a-C_Q), 146.0 (4-C_{Th}), 149.2 (8a-C_Q), 149.6 (4-C_{Th}), 154.8 (2-C_{Th}), 156.8 (2-C_{Th}), 157.3 (2-C_Q), 162.6 (4-C_Q), 176.6 (C-O^-). Anal. Calcd for $C_{31}H_{18}N_5O_2Br_2KS_2$: C 49.28, H 2.40, N 9.27, Br 21.15, S 8.49, K 5.18. Found C 49.21, H 2.46, N 9.42, Br 21.01, S 8.62, K 5.30.

3-Amino-2-cyclopenten-1-ones (13,14). General procedure: The salts (**11,12**) (0.002 mol) were dissolved in TFA (5 mL) and the solution was allowed to stand for 3 days at RT. Then it was poured into water, the precipitate formed was filtered, washed consequently with saturated aqueous $NaHCO_3$ and water, dried and recrystallized from dioxane yielding derivatives (**13,14**).

2-{2-Amino-1,3-*bis*[4-(4-chlorophenyl)-2-thiazolyl]-4-oxo-2-cyclopenten-1-yl}-4(3*H*)-quinazolinone (13): (1.25 g, 99 %). mp >300°C. ^{1}H NMR: δ = 3.44 (d, ^{2}J = 17.6, 1H, CH_2), 3.61 (d, ^{2}J = 17.6, 1H, CH_2), 7.49 (m, 4H, H_{Ar}), 7.58 (t, J = 8.0, 1H, 6-H_Q), 7.72 (d, J = 8.0, 1H, 8-H_Q), 7.84 (t, J = 8.0, 1H, 7-H_Q), 7.96 (d, J = 8.6, 2H, H_{Ar}), 8.03 (s, 1H, 5-H_{Th}), 8.08 (d, J = 8.6, 2H, H_{Ar}), 8.17 (d, J = 8.0, 1H, 5-H_Q), 8.30 (s, 1H, 5-H_{Th}), 8.83 (s, 1H, NH_2), 9.24 (s, 1H, NH_2), 12.49 (s, 1H, NH). ^{13}C NMR: δ = 48.9 (CH_2), 57.5 (4-C),

106.0 (2-C), 112.8 (5-C_{Th}), 117.8 (5-C_{Th}), 122.2 (8a-C_Q), 126.6 (5-C_Q), 128.1 (6-C_Q), 128.3 (8-C_Q), 128.5 (2,6-C_{Ar}), 128.6 (2,6-C_{Ar}), 129.5 (3,5-C_{Ar}), 129.6 (3,5-C_{Ar}), 133.2 (1-C_{Ar}), 133.3 (1-C_{Ar}), 133.5 (4-C_{Ar}), 133.6 (4-C_{Ar}), 135.4 (7-C_Q), 148.3 (4a-C_Q), 151.8 (4-C_{Th}), 153.1 (4-C_{Th}), 155.0 (3-C), 160.7 (2-C_{Th}), 162.6 (4-C_Q), 170.0 (2-C_{Th}), 171.9 (2-C_Q), 194.8 (1-CO). Anal. Calcd for $C_{31}H_{19}N_5O_2Cl_2S_2$: C 59.24, H 3.05, N 11.14, Cl 11.28, S 10.20. Found C 59.08, H 2.89, N 11.21, Cl 11.39, S 10.17.

2-{2-Amino-1,3-*bis*[4-(4-bromophenyl)-2-thiazolyl]-4-oxo-2-cyclopenten-1-yl}-4(3*H*)-quinazolinone (14): (1.40 g, 97 %). mp >300°C. ^{1}H NMR: δ = 3.44 (d, ^{2}J = 16.8, 1H, CH_2), 3.58 (d, ^{2}J = 16.8, 1H, CH_2), 7.57 (t, J = 6.0, 1H, 6-H_Q), 7.63 (m, 4H, H_{Ar}), 7.71 (d, J = 6.0, 1H, 8-H_Q), 7.84 (t, J = 6.0, 1H, 7-H_Q), 7.88 (d, J = 6.8, 2H, H_{Ar}), 8.02 (m, 3H, H_{Ar}, 5-H_{Th}), 8.15 (d, J = 6.0, 1H, 5-H_Q), 8.32 (s, 1H 5-H_{Th}), 8.84 (s, 1H, NH_2), 9.22 (s, 1H, NH_2), 12.50 (s, 1H, NH). ^{13}C NMR: δ = 47.4 (CH_2), 52.2 (4-C), 107.1 (2-C), 116.8 (5-C_{Th}), 121.7 (5-C_{Th}), 124.6 (4-C_{Ar}), 124.7 (4-C_{Ar}), 126.4 (8a-C_Q), 126.7 (5-C_Q), 127.0 (6-C_Q), 128.3 (8-C_Q), 129.1 (2,6-C_{Ar}), 129.4 (2,6-C_{Ar}), 130.8 (3,5-C_{Ar}), 130.9 (3,5-C_{Ar}), 133.3 (1-C_{Ar}), 133.5 (1-C_{Ar}), 135.5 (7-C_Q), 146.2 (4a-C_Q), 151.0 (4-C_{Th}), 153.7 (4-C_{Th}), 158.1 (3-C), 161.4 (2-C_{Th}), 161.9 (4-C_Q), 170.0 (2-C_Q), 172.8 (2-C_{Th}), 195.0 (1-CO). Anal. Calcd for $C_{31}H_{19}N_5Br_2O_2S_2$: C 51.90, H 2.67, N 9.76, Br 22.27, S 8.94. Found C 51.99, H 2.51, N 9.87, Br 22.16, S 9.03.

3-Amino-2-cyclopenten-1-ones (15,16). General procedure: Powdered K_2CO_3 (0.35 g, 0.0025 mol) was added to a solution of pyrroloquinazoline (**7**) (0.67 g, 0.002 mol) and corresponding active methylene nitrile (0.002 mol) in DMF (5 mL) and the mixture was heated at 100°C for 3 h. After cooling it was poured into water and acidified with AcOH till pH 5-6. The solid formed was filtered, dried and recrystallized from dioxane-EtOH (~1:1 v/v) mixture to give compounds (**15,16**).

2-[2-Amino-1,3-di(2-benzothiazolyl)-4-oxo-2-cyclopenten-1-yl]-4(3*H*)-quinazolinone (15): (0.62 g, 61 %). mp 293°C. ^{1}H NMR: δ = 3.50 (d, ^{2}J = 18.0, 1H, CH_2), 3.67 (d, ^{2}J = 18.0, 1H, CH_2), 7.38 (t, J = 7.8, 1H, 6-H_Q), 7.49 (m, 2H. H_{Bth}), 7.59 (m, 2H. H_{Bth}), 7.73 (d, J = 7.8, 1H, 8-H_Q), 7.86 (t, J = 7.8, 1H, 7-H_Q), 7.96 (d, J = 7.8, 1H, H_{Bth}), 8.04 (d, J = 8.1, 1H, H_{Bth}), 8.09 (d, J = 7.8, 1H, H_{Bth}), 8.16 (m, 2H, H_{Bth}, 5-H_Q), 9.20 (s, 1H, NH_2), 9.71 (s, 1H, NH_2), 12.57 (s, 1H, NH). ^{13}C NMR: δ = 50.4 (CH_2), 58.8 (4-C), 109.2 (2-C), 122.8 (7-C_{Bth}), 122.9 (7-C_{Bth}), 125.5 (4-C_{Bth}), 125.8 (4-C_{Bth}), 125.9 (8a-C_Q), 125.5 (6-C_Q), 127.4 (8-C_Q), 127.6 (5-C_{Bth}), 128.2 (5-C_{Bth}), 128.6 (5-C_Q), 129.2 (6-C_{Bth}), 129.5 (6-C_{Bth}), 134.7 (7a-C_{Bth}), 134.9 (7a-C_{Bth}), 135.4 (7-C_Q), 141.5 (4a-C_Q), 151.3 (3a-C_{Bth}), 151.4 (3a-C_{Bth}), 154.5 (3-C), 156.2 (2-C_{Bth}), 161.9 (4-C_Q), 167.6 (2-C_{Bth}), 175.9 (2-C_Q), 194.9 (1-CO). Anal. Calcd for $C_{27}H_{17}N_5O_2S_2$: C 63.89, H 3.38, N 13.80, S 12.63. Found C 64.02, H 3.22, N 13.75, S 12.78.

2-Amino-3-(2-benzothiazolyl)-3-(3,4-dihydro-4-oxo-2-quinazolinyl)-5-oxo-1-cyclopentene-1-carbonitrile (16): (0.46 g, 58 %). mp 300°C. ^{1}H NMR: δ = 3.38 (d, ^{2}J = 18.3, 1H, CH_2), 3.44 (d, ^{2}J = 18.3, 1H, CH_2), 7.57 (m, 3H, 2H_{Bth}, 6-H_Q), 7.71 (d, J = 7.8, 1H, 8-H_Q), 7.86 (t, J = 7.8, 1H, 7-H_Q), 8.05 (d, J = 7.5, 1H, H_{Bth}), 8.17 (m, 2H, H_{Bth}, 5-H_Q), 8.89 (s, 1H, NH_2), 9.47 (s, 1H, NH_2), 12.50 (s, 1H, NH). ^{13}C NMR: δ = 48.9 (CH_2),

54.3 (4-C), 93.9 (2-C), 111.5 (CN), 122.8 (7-C_{Bth}), 125.7 (4-C_{Bth}), 126.0 (6-C_Q), 126.5 (8a-C_Q), 127.2 (8-C_Q), 127.3 (5-C_{Bth}), 128.3 (5-C_Q), 129.5 (6-C_{Bth}), 135.7 (7a-C_{Bth}), 136.5 (7-C_Q), 142.2 (4a-C_Q), 153.7 (3a-C_{Bth}), 158.5 (3-C), 164.9 (4-C_Q), 167.9 (2-C_{Bth}), 172.3 (2-C_Q), 199.7 (1-CO). Anal. Calcd for $C_{21}H_{13}N_5O_2S$: C 63.15, H 3.28, N 17.53, S 8.03. Found C 63.29, H 3.11, N 17.60, S 7.94.

2-Quinazolinepropanamides (17,18). General Procedure: An appropriate amine (0.003 mol) was added to a solution of compound (**7**) (0.67 g, 0.002 mol) in DMF (5 mL) and the mixture was heated at 100°C for 3 h. After cooling it was poured into water and precipitated solid was filtered, dried and recrystallized from dioxane-EtOH (~1:1 v/v) mixture to yield derivatives (**17,18**).

β-(2-Benzothiazolyl)-3,4-dihydro-4-oxo-*N*-benzyl-2-quinazolinepropanamide (17): (0.48 g, 54 %). mp 235°C. ^{1}H NMR: δ = 3.25 (dd, ^{2}J = 15.3, ^{3}J = 6.0, 1H, $COCH_2$), 3.51 (dd, ^{2}J = 15.3, ^{3}J = 9.0, 1H, $COCH_2$), 4.19 (dd, ^{2}J = 15.9, ^{3}J = 5.1, 1H, NCH_2), 4.32 (dd, ^{2}J = 15.9, ^{3}J = 5.1, 1H, NCH_2), 5.10 (dd, ^{3}J = 9.0, ^{3}J = 6.0, 1H, CH), 7.07 (s, 5H, Ph), 7.43 (t, J = 7.5, 1H, 6-H_Q), 7.52 (m, 2H, H_{Bth}), 7.65 (d, J = 7.5, 1H, 8-H_Q), 7.84 (t, J = 7.5, 1H, 7-H_Q), 7.97 (d, J = 7.8, 1H, H_{Bth}), 8.07 (d, J = 7.8, 1H, H_{Bth}), 8.13 (d, J = 7.5, 1H, 5-H_Q), 8.70 (t, J = 5.1, 1H, NH), 12.73 (s, 1H, NH). ^{13}C NMR: δ = 38.3 (*CH_2*CO), 42.4 (NCH_2), 45.9 (>CH-), 121.2 (1-C_{Ph}), 122.8 (7-C_{Bth}), 123.2 (4-C_{Bth}), 125.8 (6-C_Q), 126.4 (6-C_{Bth}), 126.8 (4-C_{Ph}), 127.0 (5-C_{Bth}), 127.1 (2,6-C_{Ph}), 127.3 (8-C_Q), 127.7 (5-C_Q), 128.6 (3,5-C_{Ph}), 135.1 (7-C_Q), 135.4 (7a-C_{Bth}), 139.8 (4a-C_Q), 149.0 (8a-C_Q), 152.7 (3a-C_{Bth}), 156.3 (2-C_{Bth}), 162.1 (CONH), 169.9 (4-C_Q), 170.0 (2-C_Q). Anal. Calcd for $C_{25}H_{20}N_4O_2S$: C 68.16, H 4.58, N 12.72, S 7.28. Found C 68.02, H 4.71, N 12.88, S 7.19.

***N*-(1,3-Benzodioxol-5-ylmethyl)-β-(2-benzothiazolyl)-3,4-dihydro-4-oxo-2-quinazolinepropanamide (18):** (0.54 g, 56 %). mp 159°C. ^{1}H NMR: δ = 3.21 (dd, ^{2}J = 15.6, ^{3}J = 6.0, 1H, $COCH_2$), 3.44 (dd, ^{2}J = 15.6, ^{3}J = 8.4, 1H, $COCH_2$), 4.09 (dd, ^{2}J = 15.2, ^{3}J = 6.8, 1H, NCH_2), 4.18 (dd, ^{2}J = 15.2, ^{3}J = 6.8, 1H, NCH_2), 5.07 (dd, ^{3}J = 8.4, ^{3}J = 6.0, 1H, CH), 5.92 (s, 2H, OCH_2O), 6.56 (m, 2H, 5,6-H_{C6H3}), 6.71 (s, 1H, 2-H_{C6H3}), 7.42 (t, J = 7.6, 1H, 6-H_Q), 7.52 (m, 2H, H_{Bth}), 7.61 (d, J = 7.6, 1H, 8-H_Q), 7.81 (t, J = 7.6, 1H, 7-H_Q), 7.95 (d, J = 8.0, 1H, H_{Bth}), 8.05 (d, J = 8.0, 1H, H_{Bth}), 8.10 (d, J = 7.6, 1H, 5-H_Q), 8.60 (t, J = 6.8, 1H, NH), 12.69 (s, 1H, NH). ^{13}C NMR: δ = 36.1 (*CH_2*CO), 39.8 (NCH_2), 48.5 (>CH-), 100.8 (OCH_2O), 119.7 (5-C_{C6H3}), 121.8 (2-C_{C6H3}), 123.2 (1-C_{C6H3}), 122.8 (7-C_{Bth}), 124.8 (6-C_{C6H3}), 125.7 (4-C_{Bth}), 126.5 (6-C_Q), 126.6 (5-C_Q), 128.9 (5-C_{Bth}), 129.5 (6-C_{Bth}), 131.4 (8-C_Q), 135.5 (7-C_Q), 135.6 (7a-C_{Bth}), 142.7 (4a-C_Q), 145.7 (4-C_{C6H3}), 147.7 (8a-C_Q), 147.9 (3-C_{C6H3}), 152.7 (3a-C_{Bth}), 159.4 (2-C_{Bth}), 165.4 (4-C_Q), 166.9 (CONH), 176.2 (2-C_Q). Anal. Calcd for $C_{26}H_{20}N_4O_4S$: C 64.45, H 4.16, N 11.56, S 6.62. Found C 64.31, H 3.99, N 11.62, S 6.59.

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