Synthesis and Intramolecular Cyclization of 2-Methylsulfany-4-oxo-3(4*H*)-quinazolinyl)acetohydrazide

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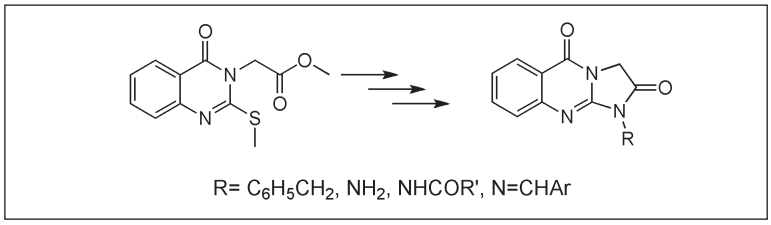

Treatment of ambident sodium salt of 2-methylsulfanyl-4(3*H*)-quinazolinone with methyl bromoacetate resulted in $N_{(3)}$-alkyl ester formation. Reaction of the resulted ester with hydrazine hydrate gave 2-methylsulfanyl-4-oxo-3(4*H*)-quinazolinyl)acetohydrazide, which underwent intramolecular cyclization under heating in dimethylformamide to give 1-aminoimidazo[2,1-*b*]quinazoline-2,5(1*H*,3*H*)-dione. The latter took place in acylation reaction and in condensation with aromatic aldehydes.

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A number of bioactive naturally occuring products contain 4(3*H*)-quinazolinone skeleton [1,2]. 4(3*H*)-Quinazolinone derivatives were found to show hypolipidemic, vasorelaxant, antibacterial or anticonvulsant activity [3-6]. 4(3*H*)-Quinazolinones, particulary those $N_{(3)}$-substituted, have been attracting attention for a few decades and have renewed continuing interest in recent years due to their multitude important activities. Febrifugine as a representative of $N_{(3)}$-substituted 4(3*H*)-quinazolinones is known to be highly active against malaria [7-11]. 4(3*H*)-Quinazolinone $N_{(3)}$-alkanoic acid derivatives exhibit anti-inflammatory, antitumor [12], analgetic [13], antihistaminic [14], fungicidal or plant growth regulator properties [15,16]. The most common synthetic methods to $N_{(3)}$-alkyl 4-oxo-2-mercaptoquinazolines are based on cyclocondensation reactions of anthranilic acid or its derivatives with isothiocyanates [17-19], glycinates [20,21] or thiophosgene [22].

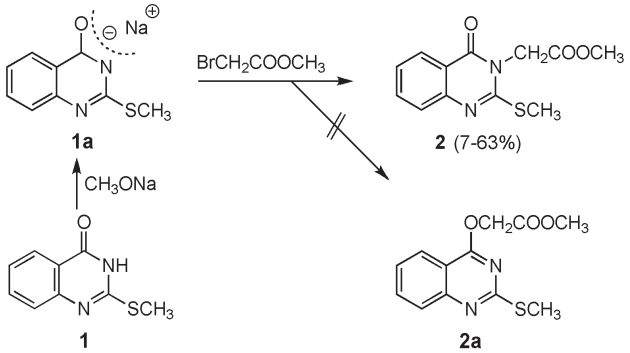
In this paper we report on the synthesis of methyl (2-methylsulfanyl-4-oxo-3(4*H*)-quinazolinyl)acetate (**2**) by the alkylation of 2-methylsulfanyl-4(3*H*)-quinazolinone (**1**) with methyl bromoacetate. Treatment of ester **2** with hydrazine hydrate and further modifications of resulting hydrazide **3** will be discussed.

2-Methylsulfanyl-4(3*H*)-quinazolinone (**1**) was prepared by base-catalysed treatment of 2-thioxo-4(*3H*)-quinazolinone with iodomethane. We used sodium methoxide as a base instead of potassium hydroxide as earlier reported [23,24]. This replacement allowed us to increase yield of desired 2-methylsulfanyl derivative **1** to 91%. (According to the ref. [23,24] 2-methylsulfanyl-4(3*H*)-quinazolinone (**1**) was obtained in 55-56% yield.)

Formation of $N_{(3)}$-alkyl or (and) O-alkyl products in the alkylation reactions of 4(3*H*)-quinazolinones is dependent on substituents of the quinazoline ring as well as reaction conditions used. M. Hori and H. Ohtaka [25] studied effects of 2-substituent (alkyl, aminoalkyl, alkyloxy *etc*) on the ratio of N-alkyl/O-alkyl products. For the N-alkylation sodium ethoxide in ethanol [26] was used. Others [12] using potassium carbonate in dimethylformamide prepared mixtures of $N_{(3)}$- and O-alkyl derivatives. Predominant formation of N- versus O-alkyl derivatives was found to depend on the 2-substituent in quinazolinone ring [12,13,26].

Alkylation of the ambident anion **1a** with methyl bromoacetate would occur either at $N_{(3)}$ or at the O-atom (Scheme 1). We did not find any data on alkylation of 2-alkylsulfanyl-4(3*H*)-quinazolinone derivatives. The thorough study of the effects of solvent and base on regioselective $N_{(3)}$-/O-alkylation of 2-alkylsulfanyl-4-pyrimidinones was given in reference [27]. There was found, that in polar protic solvents a mixture of $N_{(3)}$/O-isomers is formed. In nonpolar or less polar aprotic solvents $N_{(3)}$-alkylation took place and O-isomers were obtained in aprotic dipolar solvents. The latter also formed in triethylamine with a catalyst tetrabutylammonium bromide.

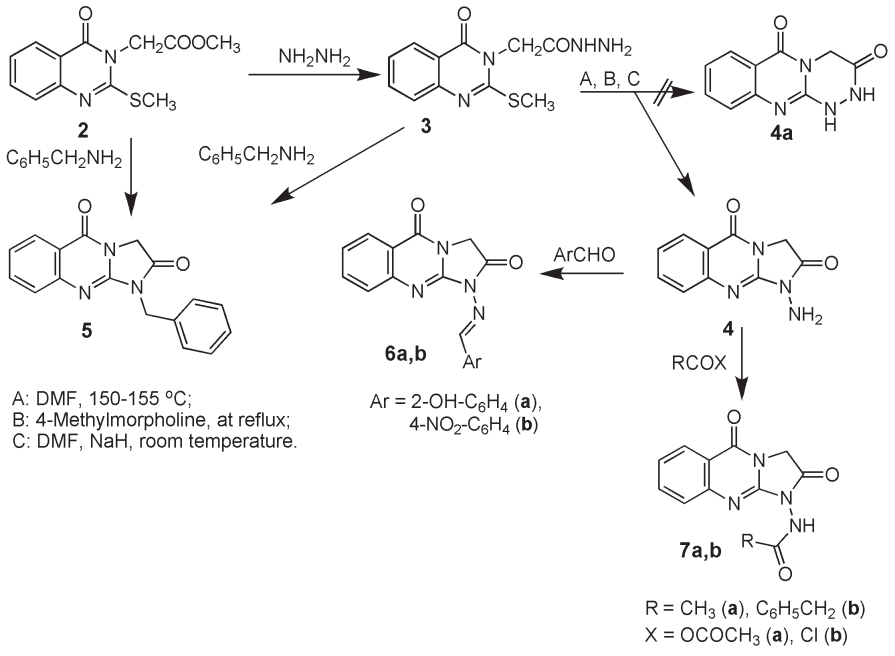
Scheme 1



Based on the above experience we explored the alkylation of **1** with methyl bromoacetate in different solvents and bases to find out the optimal conditions for N-alkyl ester **2** formation. Heating at reflux for different amounts of time (3-18 h) the equimolar amounts of 2-methylsulfanyl-4(3*H*)-quinazolinone (**1**), sodium methoxide and methyl bromoacetate in methanol afforded the ester **2**. The best yield (63%) of compound **2** was obtained under heating of reaction mixture for 18 h. Performing the reaction with dry sodium salt **1a** (prior synthesized) in aprotic nonpolar solvent tetrachloromethane, ester **2** was obtained in 17% yield. Using triethylamine as a base and a solvent along with tetrabutylammonium bromide catalyst, ester **2** was isolated in only 7% yield. Formation of O-isomer **2a** was not detected by tlc and the unreacted 2-methylsulfanyl-4(3*H*)-quinazolinone (**1**) was separated quantitatively in each experiment. The above experiments showed, that the direction of the alkylation reaction of 2-methylsulfanyl-4(3*H*)-quinazolinone **1** in contrast to that of 2-alkylsulfanyl-4(3*H*)-pyrimidinone [27] is not dependent on the reaction conditions used. The applied reaction conditions influence only the yield of the product **2**. The structure of ester **2** was determined from spectral data. The ir spectra of ester **2** gave two absorption peaks arising from C=O stretching at 1744 (ester) and 1673 cm^{-1} (lactam). The ^1H nmr spectra of **2** showed resonances at 4.94 and 2.67 ppm characteristic for N-CH_2 and SCH_3 group protons respectively. Noteworthy, analogous ethyl ester prepared by a different method [21] exhibit characteristic signals of N-CH_2 and SCH_3 group protons at 4.94 and 2.66 ppm. Mp of compound **2** correspond to that previously reported in the literature [20], however it was obtained using another synthetic sequence. These mentioned data support the structure of compound **2**, *i.e.*, $N_{(3)}$ -alkylation.

The reaction of ester **2** with an excess of hydrazine hydrate at room temperature yielded hydrazide **3** (Scheme 2). In the ir spectra of hydrazide **3** two absorption bands of C=O group appeared at 1687 (amide) and 1668 cm^{-1} (lactam) and the NH bands at 3294 and 3271 cm^{-1}. The ^1H nmr spectra displayed NH_2 and NH group proton signals at 4.35 and 9.42 ppm respectively. The signal of NCH_2 group proton, if compared to that of ester **2**, is shifted upfield by 0.24 ppm. (2-Methylsulfanyl-4-oxo-3(4*H*)-quinazolinyl)-acetohydrazide (**3**) being an active N-nucleophile could react with various electrophiles to yield potential biologically active compounds. On the other hand, compound **3** contains in its molecule (besides the nucleophilic hydrazine moiety) the methylsulfanyl group at the position 2 of quinazolinone ring, which is sensitive to nucleophilic attack. Heterocyclic structures with good leaving groups, such as alkylsulfanyl, adjacent to nucleophilic substituents undergo intramolecular cyclization [22,28]. As an example, there is the formation of 1,2,3,4-tetrahydropyrimido[2,1-*c*]-1,2,4-triazin-3,6-diones from (2-alkylsulfanyl-3,4-dihydro-6-methyl-4-oxo-3-pyrimidinyl)acetohydrazides [28]. According to the cited work [28], we expected 2*H*-[1,2,4]triazino[3,4-*b*]quinazoline-3,6(1*H*,4*H*)-dione (**4a**) formation from the intramolecular cyclization of hydrazide **3**. However hydrazide **3** under heating at 150° temperature in abs. dimethylformamide transformed into 1-aminoimidazo[2,1-*b*]quinazoline-2,5(1*H*,3*H*)-dione (**4**). Heating of hydrazide **3** in benzylamine (as a solvent and a more basic

Scheme 2



catalyst) at 160-165° resulted in the formation of 1-benzylimidazo derivative **5**. The latter compound **5** was also produced under treatment of ester **2** with equimolar amount of benzylamine at 160°. When hydrazide **3** was heated at reflux for 12 h in 4-methylmorpholine (function of a basic catalyst and a solvent) imidazoquinazoline **4** was obtained. Finally, under treatment of hydrazide **3** with sodium hydride in abs. dimethylformamide formation of the same product **4** was confirmed. The structures were supported by spectral data and elemental analysis. In the ^{1}H nmr spectra of compounds **4** and **5** the peak of endocyclic NCH_2 protons was observed at 4.55 and 4.66 ppm respectively. In addition, a broad singlet of NH_2 group protons appeared at 5.26 ppm in **4**, while compound **5** showed a peak at 4.93 ppm of exocyclic NCH_2 group. In both cases the resonances corresponding to the NH and SCH_3 group protons, characteristic for hydrazide **3**, disappeared. The ir spectra of **4** and **5** displayed absorption of C=O group of cyclic five-member and six-member lactones in the region of 1755, 1744 cm^{-1} (C_2=O) and 1696, 1694 cm^{-1} (C_5=O) respectively.

Additionally, the structure of **4** was confirmed performing the following reactions. Imidazoquinazoline-2,5-dione **4** was allowed to react with aromatic aldehydes to give hydrazones **6**. Reactions with aldehydes were performed in acetic acid. Acetylation of **4** with acetic anhydride was performed in acetic acid. Phenylacetamide **7b** was synthesized using pyridine-acetonitrile mixture as a solvent instead of acetic acid. The spectral data of derivatives **6a**,**b** and **7a**,**b** were in accordance with the assigned structures.

Compounds were preliminary tested for their anti-inflammatory activity. Several of compounds, *i.e*., **3**, **6a**, **6b** and **7a**, exhibited anti-inflammatory activity (induced in rats by carrageenin or bentonite) for 35-39%.

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. Nuclear magnetic resonance (nmr) spectra were recorded on a Unity Varian INOVA spectrometer at 300 MHz for ^{1}H and 75 MHz for ^{13}C using dimethyl sulfoxide-d_6 as a solvent. Chemical shifts (δ) are reported in ppm relative to TMS as internal standard. The ir spectra were recorded in Nujol mulls on a Spectrum BX FT-IR (Perkin-Elmer, Sweden). The reactions and purity of compounds was controlled by tlc on Silufol UV 254 plates (Kavalier, Czech Rep.) Elemental analyses were performed at the Microanalyses Laboratory of the Department of Organic Chemistry of Vilnius University.

2-Thioxo-2,3-dihydro-4(1*H*)-quinazolinone was synthesized as reported in [29].

2-(Methylsulfanyl)-4(3*H*)-quinazolinone (**1**).

To a stirred mixture of 2-thioxo-2,3-dihydro-4(1*H*)-quinazolinone (1.78 g, 10 mmol) and sodium methoxide (0.23 g, 10 mmol of sodium dissolved in 15 mL of abs. methanol) in abs. methanol (30 mL) at room temperature iodomethane (1.42 g, 0.62 mL, 10 mmol) was added dropwise. Then reaction mixture was heated at reflux for 3 h., cooled to room temperature, filtered and recrystallized from methanol to give 1.75 g (91%) of compound **1**, mp 222-223° (ref. [23] yield 55%, mp 210-211°); ^{1}H nmr: δ 2.63 (s, 3H, SCH_3), 7.50 (m, 1H, Ar-H), 7.61 (d, 1H, Ar-H, J = 8.0 Hz), 7.84 (m, 1H, Ar-H,), 8.50 (d, 1H, Ar-H, J = 8.2 Hz), 14.17 (s, 1H, NH).

Anal. Calcd. for $C_9H_8N_2OS$: C, 56.23; H, 4.19; N, 14.57. Found: C, 56.56; H, 4.25; N, 14.69.

Methyl (2-methylsulfanyl-4-oxo-3(4*H*)-quinazolinyl)acetate (**2**).

Method A.

To a mixture of compound **1** (1.04 g, 5.4 mmol) in methanol (10 mL) and sodium methoxide (0.124 g, 5.4 mmol of sodium dissolved in 10 ml of methanol), methyl bromoacetate (0.84 g, 0.52 mL, 5.5 mmol) was added dropwise. The reaction mixture was heated at reflux for 18 h and cooled to room temperature. The resulting precipitate was collected and stirred with 1% potassium hydroxide solution (20 mL) at room temperature for 20 min. Then the remainder was collected by filtration and recrystallized from isopropyl alcohol to give 0.91 g (63%) of compound **2**, mp 114-115° (ref. [20] mp 117° from ethylacetate-hexane); ir: 1744, 1673 cm^{-1} (CO); ^{1}H nmr: δ 2.67 (s, 3H, SCH_3), 3.74 (s, 3H, OCH_3), 4.94 (s, 2H, CH_2), 7.51 (m, 1H, Ar-H), 7.62 (d, 1H, Ar-H, J = 8.5 Hz), 7.86 (m, 1H, Ar-H), 8.11 (d, 1H, Ar-H, J = 8.0 Hz); ^{13}C nmr: δ 15.40 (SCH_3), 45.51 (NCH_2), 53.35 (OCH_3), 118.98, 126.79, 126.90, 127.21, 135.86, 147.54, 157.65 (C quinazoline), 161.11 (C_4=O), 168.35 (C=O).

Anal. Calcd. for $C_{12}H_{12}N_2O_3S$: C, 54.53; H, 4.58; N, 10.60. Found: C, 54.78; H, 4.51; N, 10.78.

Method B.

A mixture of compound **1** (1.5 g, 7.8 mmol) in methanol (20 ml) and sodium methoxide (0.18 g, 7.8 mmol of sodium dissolved in 6 ml of methanol) was refluxed for 15 min. The solvent was evaporated *in vacuo* and the resultant salt was dried perfectly. Then methyl bromoacetate (1.20 g, 0.75 mL, 7.9 mmol) was added dropwise to stirred salt **1a** in tetrachloromethane (25 mL) The reaction mixture was heated at reflux for 12 h. and worked as above. Yield of **2** 0.36 g (17%), mp 114-115°.

Method C.

Methyl bromoacetate (1.84 g, 1.14 mL, 1.2 mmol) was added dropwise to a stirred solution of compound **1** (1.92 g, 10 mmol), tetrabutylammonium bromide (0.32 g, 1 mmol) and triethylamine (25 mL). The reaction mixture was maintained at 70-75° temperature for 8 h and allowed to cool to room temperature. Then the reaction mixture was diluted with water (30 mL) and extracted with trichloromethane (3x20 mL). The solvent was evaporated and the residue was treated at room temperature with 1% potassium hydroxide solution (20 mL) for 20 min. The remainder was filtered and recrystallized from isopropyl alcohol to give **2**, 0.18 g (7%) mp 114-115°.

(2-Methylsulfanyl-4-oxo-3(4*H*)-quinazolinyl)acetohydrazide (**3**).

To a stirred suspension of ester **2** (1.32 g, 5 mmol) in methanol (15 ml) 85% hydrazine hydrate (1.0 g, 1 mL, 20 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 20 h. Then the solid was collected by filtration, washed properly with water and methanol and dried to yield **3** as a white solid, 1.27 g (96%), mp 258-259° (decomp.); ir: 3294, 3271 (NH), 1687, 1668 cm^{-1} (CO); ^{1}H nmr: δ 2.63 (s, 3H, SCH_3), 4.35 (s broad, 2H, NH_2), 4.70 (s, 2H, CH_2), 7.48 (m, 1H,

Ar-H), 7.60 (d, 1H, Ar-H, J = 8.0 Hz), 7.83 (m, 1H, Ar-H), 8.08 (d, 1H, Ar-H, J = 7.4 Hz), 9.42 (s broad, 1H, NH); ^{13}C nmr: δ 15.36 (SCH_3), 45.31 (NCH_2), 119.40, 126.59, 126.68, 127.18, 135.50, 147.65, 158.21 (C quinazoline), 161.32 (C_4=O), 165.86 (C=O).

Anal. Calcd. for $C_{11}H_{12}N_4O_2S$: C, 49.99; H, 4.58; N, 21.20. Found: C, 50.35; H, 4.60; N, 21.09.

1-Aminoimidazo[2,1-*b*]quinazoline-2,5(1*H*,3*H*)-dione (**4**).

Method A.

A suspension of hydrazide **3** (1.32 g, 5 mmol) in dimethylformamide (15 mL) was heated at 150-155 °C temperature for 3 h. The excess of solvent was removed *in vacuo*. The solid was collected by filtration, washed with methanol, dried and recrystallized from water. Yield 0.94 g (87%), mp 334-336°; ir: 3335 (NH), 1755, 1696 cm^{-1} (CO); ^{1}H nmr: δ 4.55 (s, 2H, CH_2), 5.26 (s, 2H, NH_2), 7.43 (m, 1H, Ar-H), 7.61 (d, 1H, Ar-H, J = 8.2 Hz), 7.79 (m, 1H, Ar-H), 8.11 (d, 1H, Ar-H, J = 9.5 Hz); ^{13}C nmr: δ 46.45 (NCH_2), 120.16, 125.51, 126.74, 126.82, 135.42, 149.16, 151.57 (C quinazoline), 158.84 (C_5=O), 168.37 (C_2=O).

Anal. Calcd. for $C_{10}H_8N_4O_2$: C, 55.55; H, 3.73; N, 25.91. Found: C, 55.22; H, 3.78; N, 25.89.

Method B.

A mixture of hydrazide **3** (1.32 g, 5 mmol) in 4-methylmorpholine (10 mL) was heated at reflux for 12 h. The solvent was removed *in vacuo*, the solid was washed with methanol and recrystallized from water to give 0.7 g (65%) of compound **4**, mp 334-336°.

Method C.

Sodium hydride (60%, 0.3 g, 12.5 mmol) was added over a period of 20 min to a stirred suspension of hydrazide **3** (1.32 g, 5 mmol) in dimethylformamide (7 mL) at room temperature. The reaction mixture was stirred under argon at room temperature for 5 h., cooled to 0° and diluted with ice-water (20 mL). The white solid was collected by filtration, washed with water and recrystallized from water to give 0.98 g (91%) of compound **4**, mp 334-336°.

1-Benzylimidazo[2,1-*b*]quinazoline-2,5(1*H*,3*H*)-dione (**5**).

Method A.

A mixture of ester **2** (1.32 g, 5 mmol) and benzylamine (0.54 g, 0.55 mL, 5 mmol) was heated at 160-165° temperature for 3 h. After cooling the mixture was washed with methanol, collected by filtration and recrystallized from isopropyl alcohol to give 1.09 g (75%) of compound **5** as a white solid, mp 184-185°; ir: 1744, 1694 cm^{-1} (CO); ^{1}H nmr: δ 4.66 (s, 2H, CH_2), 4,93 (s, 2H, CH_2-C_6H_5), 7.39 (m, 6H, Ar-H), 7.58 (d, 1H, Ar-H, J = 8.7 Hz), 7.79 (m, 1H, Ar-H), 8.13 (d, 1H, Ar-H, J = 7.9 Hz); ^{13}C nmr: δ 43.0 (NCH_2), 47.89 (CH_2-Ph), 120.25, 125.67, 126.84, 128.25, 129.19, 135.41, 136.33, 148.90, 151.20 (C quinazoline, phenyl), 158.89 (C_5=O), 169.54 (C_2=O).

Anal. Calcd. for $C_{17}H_{13}N_3O_2$: C, 70.09; H, 4.50; N, 14.42. Found: C, 70.36; H, 4.65; N, 14.29.

Method B.

Suspension of hydrazide **3** (1.06 g, 4 mmol) and benzylamine (15 mL) was heated at 160-165° for 3 h. The reaction mixture was than allowed to cool to room temperature, filtered and the filtrate was distilled under reduced pressure to dryness. The residue was crystallized from isopropyl alcohol to give **5** as a white solid, yield 0.95 g (65%), mp 184-185°.

General Procedure for the Synthesis of 1-[(Arylmethylidene)-amino]imidazo[2,1-*b*]quinazoline-2,5(1*H*,3*H*)-diones (**6a**, **6b**).

A mixture of compound **4** (0.55 g, 2.55 mmol) and aromatic aldehyde (2.55 mmol) in acetic acid (15 mL) was heated at reflux for 3 h. An excess of solvent was removed in *vacuo*, the resulting precipitate was collected by filtration, washed with methanol and recrystallized to give compounds **6a**, **6b**.

1-{[(2-Hydroxyphenyl)methylidene]amino}imidazo[2,1-*b*]quinazoline-2,5(1*H*,3*H*)-dione (**6a**).

This compound was obtained as a white solid, 0.5 g (61%), mp 249-251° (acetic acid, decomp.); ir: 3161 (OH), 1757, 1690 cm^{-1} (CO); ^{1}H nmr: δ 4.66 (s, 2H, CH_2), 7.01 (m, 2H, Ar-H), 7.46 (m, 2H, Ar-H), 7.66 (d, 1H, Ar-H, J = 8.6 Hz), 7.81 (m, 2H, Ar-H), 8.15 (d, 1H, Ar-H J = 7.9 Hz), 9.69 (s, 1H, CH), 10.75 (s broad, 1H, OH); ^{13}C nmr: δ 46.96 (NCH_2), 112.59, 117.38, 119.31, 120.27, 120.35, 126.05, 126.77, 127.15, 128.57, 134.47, 135.56, 148.80, 149.22, 159.33 (C quinazoline, phenyl, N=CH), 158.86 (C_5=O), 166.30 (C_2=O).

Anal. Calcd. for $C_{17}H_{12}N_4O_3$: C, 63.75; H, 3.78; N, 17.49. Found: C, 63.44; H, 4.05; N, 17.39.

1-{[(4-Nitrophenyl)methylidene]amino}imidazo[2,1-*b*]quinazoline-2,5(1*H*, 3*H*)-dione (**6b**).

This compound was obtained as a yellow solid, 0.63 g (71%) mp 282-284° (acetic acid); ir: 1756, 1693 (CO), 1516, 1344 cm^{-1} (NO_2); ^{1}H nmr: δ 4.69 (s, 2H, CH_2), 7.49 (m, 1H, Ar-H), 7.73 (d, 1H, Ar-H, J = 8.9 Hz), 7.95 (m, 1H, Ar-H), 8.15 (d, 1H, Ar-H, J = 9.1 Hz), 8.23 (d, 2H, Ar-H J = 9.0 Hz), 8.40 (d, 2H, Ar-H, J = 8.9 Hz), 9.86 (s, 1H, CH); ^{13}C nmr: δ 46.79 (NCH_2), 120.28, 124.93, 126.34, 126.76, 127.32, 129.92, 135.62, 139.88, 148.58, 149.79, 148.98, 156.85 (C quinazoline, phenyl, N=CH), 158.76 (C_5=O), 166.30 (C_2=O).

Anal. Calcd. for $C_{17}H_{11}N_5O_4$: C, 58.46; H, 3.17; N, 20.05. Found: C, 58.77; H, 3.37; N, 20.16.

N-(2,5-Dioxo-2,3-dihydroimidazo[2,1-*b*]quinazolin-1(5*H*)-yl)acetamide (**7a**).

A mixture of compound **4** (1.08 g, 5 mmol), acetic anhydride (0.61 g, 0.57 ml, 6 mmol) and acetic acid (15 mL) was heated at reflux for 8 h. After cooling to room temperature the solid was collected by filtration, washed with cold methanol and recrystallized from ethanol to yield 1.01 g (78%) of **7a**, mp 152-154°; ir: 3420, 3184 (NH), 1790, 1694, 1652 cm^{-1} (CO); ^{1}H nmr: δ 2.12 (s, 3H, CH_3), 4.81 (m, 2H, CH_2), 7.46 (m, 1H, Ar-H), 7.60 (d, 1H, Ar-H, J = 8.2 Hz), 7.81 (m, 1H, Ar-H), 8.14 (d, 1H, Ar-H, J = 7.9 Hz), 11.00 (s, 1H, NH); ^{13}C nmr: δ 21.0 (CH_3), 46.46 (NCH_2), 120.34, 126.08, 126.87, 126.93, 135.63, 148.58, 149.26 (C quinazoline), 158.76 (C_5=O), 167.15 (C=O), 169.13 (C_2=O).

Anal. Calcd. for $C_{12}H_{10}N_4O_3$: C, 55.80; H, 3.88; N, 21.70. Found: C, 55.71; H, 3.83; N, 21.59.

N-(2,5-Dioxo-2,3-dihydroimidazo[2,1-*b*]quinazolin-1(5*H*)-yl)-2-phenylacetamide (**7b**).

To a suspension of compound **4** (0.54 g, 2.5 mmol) in dry pyridine-acetonitrile (1:1) solution (20 mL) phenylacetyl chloride (0.46 g, 0.4 mL, 3 mmol) was added and the reaction mixture was heated at reflux for 5 h. The solvent was removed *in vacuo*, and

the residue was diluted with water (30 mL). The resulting precipitate was collected by filtration and recrystallized from ethanol to yield 0.66 g (79%) of **7b**, mp 125-126°; ir: 3346 (NH), 1787, 1694, 1651 cm^{-1} (CO); ^1H nmr: δ 3.77 (s, 2H, $CH_2C_6H_5$), 4.82 (m, 2H, CH_2), 7.43 (m, 6H, Ar-H), 7.58 (d, 1H, Ar-H, J = 7.8 Hz), 7.82 (m, 1H, Ar-H), 8.15 (d, 1H, Ar-H, J = 8.9 Hz), 11.00 (s, 1H, NH); ^{13}C nmr: δ 46.53 (NCH_2), 120.36, 126.13, 126.89, 126.95, 127.49, 129.07, 129.82, 135.19, 135.68, 148.54, 149.19 (C quinazoline, phenyl), 158.73 (C_5=O), 167.09 (C=O), 170.13 (C_2=O).

Anal. Calcd. for $C_{18}H_{14}N_4O_3$: C, 64.67; H, 4.22; N, 16.76. Found: C, 64.71; H, 4.23; N, 16.58.

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