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REACTION OF 2,3-TETRAMETHYLEN-3,4-DIHYDROQUINAZOL-4-ONE AND ITS DERIVATIVES WITH AROMATIC ALDEHYDES AND FURFUROL

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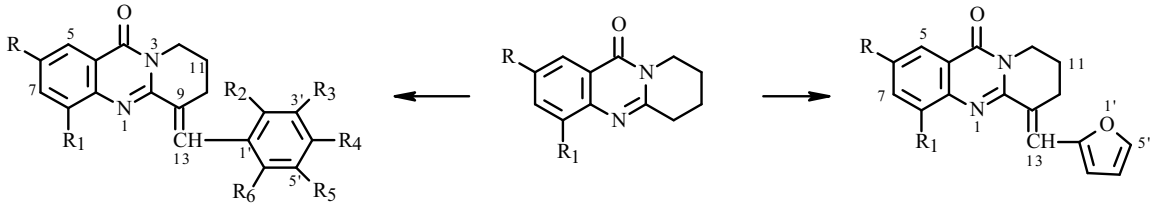
α-Aryliden-6H(nitro)- and 6,8-dibromo-2,3-tetramethylen-3,4-dihydroquinazol-4-ones were synthesized by condensation of 6H(nitro)- and 6,8-dibromo-2,3-tetramethylen-3,4-dihydroquinazol-4-ones with aromatic aldehydes, furfurol, and of α-formyl-2,3-tetramethylen-3,4-dihydroquinazol-4-one with benzaldehyde and 4-nitrobenzaldehyde in glacial acetic acid.

Key words: alkaloids, 6H(nitro)-, 6,8-dibromo-2,3-tetramethylen-3,4-dihydroquinazol-4-ones, aromatic aldehydes, condensation.

2,3-Tetramethylen-3,4-dihydroquinazol-4-one (alkaloid 6,7,8,9-tetrahydropyrido[2,1-b]quinazolin-11-one from *Mackinlaya subulata* Philipson, **1**, R = R_1 = H) and its derivatives are interesting from a theoretical and practical point of view [1-4].

We have previously studied the condensation of 2,3-trimethylen-3,4-dihydroquinazol-4-one (deoxyvacisinone) and its 6-bromo(nitro) derivatives with various aliphatic, aromatic, and heterocyclic aldehydes. It was found that the corresponding α-aryliden- or α-hydroxyarylmethyl derivatives could be formed depending on the conditions and duration of the reaction and the nature of the substituents in the quinazolone and aldehyde ring [5-11].

We studied the condensation of **1**-**3** with benzaldehyde; 4-hydroxy-, -dimethylamino-, -nitro-, and 3,4-dimethoxybenzaldehydes; 2-bromoisovanillin, 5-bromovanillins, and furfurol in order to find biologically active compounds and to determine the reactivity of **1** and its 6-nitro- (**2**) and 6,8-dibromo (**3**) derivatives in reactions with aromatic and heterocyclic aldehdyes in addition to the influence of the size of the cycloalkane ring and substituents on the course of the reactions. The reaction proceeded according to the scheme below and gave α-aryliden(furfuryliden)-2,3-tetramethylen-3,4-dihydroquinazol-4-ones (**4**-**25**).



4 - 10, 12 - 18, 20 - 24 **1 - 3** **11, 19, 25**

1: R = R_1 = H; **2:** R = NO_2, R_1 = H; **3:** R = R_1 = Br; **4 - 10:** R = R_1 = H; **12 - 18:** R = NO_2, R_1 = H
20 - 24: R = R_1 = Br; **11:** R = R_1 = H; **19:** R = NO_2, R_1 = H; **25:** R = R_1 = Br; **4, 12, 20:** R_2 = R_3 = R_4 = R_5 = R_6 = H
5, 13, 21: R_2 = R_3 = R_5 = R_6 = H, R_4 = OH; **6, 14, 22:** R_2 = R_3 = R_5 = R_6 = H, R_4 = $N(CH_3)_2$
7, 15, 23: R_2 = R_3 = R_5 = R_6 = H, R_4 = NO_2; **8, 16, 24:** R_2 = R_5 = R_6 = H, R_3 = R_4 = OCH_3
9, 17: R_5 = R_6 = H, R_2 = Br, R_3 = OH, R_4 = OCH_3; **10, 18:** R_2 = R_6 = H, R_3 = OCH_3, R_4 = OH, R_5 = Br

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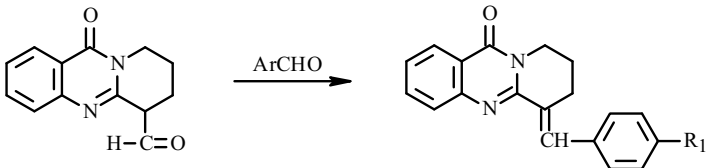
The reactions were carried out in glacial acetic acid under reflux for 3-5 h [12, 13].

Reactions of **1**-**3** with carbonyl compounds (aldehydes, acid chlorides, disubstituted formamides in the presence of inorganic acid chlorides) have not been reported. Furthermore, although 2,3-trimethylen-3,4-dihydroquinazol-4-one underwent acylation, 2,3-tetramethylen-3,4-dihydroquinazol-4-one reacted difficultly with acylating agents [14]. These compounds behaved similarly in formylation reactions [3, 15].

Our research showed that reactions of 6H(nitro)- and 6,8-dibromo-2,3-tetramethylen-3,4-dihydroquinazol-4-ones (**1**-**3**) with aromatic aldehydes occurred exclusively at the α-C atom. Performing the reaction with 1:2 ratios of (**1**-**3**):aromatic aldehyde and with prolonged (10-12 h) heating in glacial acetic acid did not affect the β-, γ-, and δ-C atoms, i.e., 6H(nitro)-, 6,8-dibromo-, $\beta(\gamma,\delta)$-aryliden-; or bisaryliden- derivatives were not observed. Therefore, it seemed interesting to study the condensation of an α-substituted derivative of 2,3-tetramethylen-3,4-dihydroquinazol-4-one, in particular, α-formyl-2,3-tetramethylen-3,4-dihydroquinazol-4-one (**26**) with benzaldehyde and 4-nitrobenzaldehyde. It was expected that the α-formyl-(β,γ,δ)- (more probably β-)-aryliden-substituted quinazol-4-ones would form:



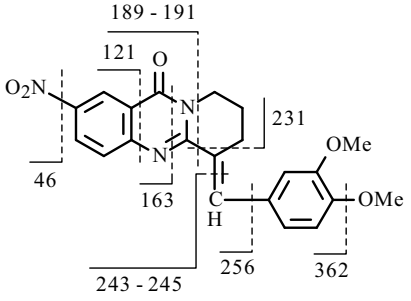
26 **4, 7**

Ar = C_6H_5, C_6H_4-NO_2-4 **4:** R_1 = H; **7:** R_1 = NO_2

The reactions of **26** with benzaldehyde and *p*-nitrobenzaldehyde were carried out in glacial acetic acid under reflux for 5 h. The formyl group in **26** had no electron-acceptor affect on the methylene groups in the β-, γ-, or δ-positions. The corresponding α-benzyliden(4′-nitrobenzyliden)-2,3-tetramethylen-3,4-dihydroquinazol-4-ones (**4** and **7**) were formed. The structures of the α-arylidene derivatives **4** and **7** that were prepared by this method were proved using mass and PMR spectra. Thus, we observed anomalous behavior of α-formyl-2,3-tetramethylen-3,4-dihydroquinazol-4-one (**26**) in reactions with carbonyl compounds that consisted of exchange of the formyl group by an aromatic aldehyde. Such behavior of **26** could be explained by cleavage of the formyl group in acetic acid to form **1**, which reacted with the aromatic aldehydes to form the corresponding α-arylidene derivatives **4** and **7**.

The structures of the synthesized compounds **4**-**25** were confirmed by IR, PMR, and mass spectra. Their IR spectra had stretching vibrations $\nu_{C=O}$ at 1650-1717 cm^{-1}; $\nu_{C=N}$, 1591-1618; ν_{C-N}, 1531-1590; ν_{C-NO2} for **12**-**19**, 1495-1516.

Mass spectra of the synthesized compounds showed principal fragmentation according to the following scheme (using **16** as an example):



16

PMR spectra showed methylene protons in the β-position had chemical shifts (CS) at 2.65-2.75 ppm (2H, triplet); in the γ-position, 1.84-1.87 (2H, multiplet); in the δ-position, 3.84-3.96 (2H, triplet); methyl protons of $N(CH_3)_2$ of **6** and **14**, 3.066-3.1 (6H, singlet); of OCH_3 for **8**-**10** and **16**-**18**, 3.38-3.62 (3H, singlet); aromatic protons, 6.31-8.85 ppm. The appearance of the β- and δ-methylene protons as triplets and the γ-methylene protons as multiplets and the lack of protons on the α-C atom at 2.8-3.0 ppm confirmed that the condensation occurred at the α-C atom.

Bactericidal properties of **4**-**25** were studied toward various Gram-positive and Gram-negative strains *Staphylococcus* T50a, *Klebsiella pneumoniae* T3a, *S. aureus* T48a, *Acinetobacter* sp. T16, *Enterococcus hormaechei* T2, *Escherichia coli* T60a, *Enterococcus hormaechei* T10, *Proteus rettgerri* T33a, *B. cereus* T80, *Citrobacter freundii* T1a, *Enterococcus feaecalis* T23a, *Pseudomonas aureginosa* T31a, *Proteus agglomerans* T26, *A. faecalis* T3, *Micrococcus luteus* T52a, *Pseudomonas aureginosa* T145, *S. saprophyticus* T415, *Klebsiella oxitoca* T4a, and *A. haumanii* T15a at concentrations of 0.01%, 0.1 and 1%. The results showed that they had low bactericidal activity.

EXPERIMENTAL

Mass spectra were recorded in an MS-30 (Kratos) instrument; IR spectra in mineral oil, on an IR-Fourier System 2000 spectrometer; PMR spectra in TFA, TFA+CD_3COOD, and $CDCl_3$ solutions, on a Unity 400+ instrument (operating frequency 400 MHz, TMS internal standard, δ scale). The purity of products and course of reactions were monitored using TLC on Silufol UV-254 plates and solvent systems benzene:MeOH (3:1, system A; 5:1, system B) and $CHCl_3$:MeOH (15:1, system C; 20:1, system D).

2,3-Tetramethylen-3,4-dihydroquinazol-4-one (1) was prepared by the literature method [16].

6-Nitro-2,3-tetramethylen-3,4-dihydroquinazol-4-one (2) was synthesized by a modified method [3].

2,3-Tetramethylen-3,4-dihydroquinazol-4-one (10 g, 0.05 mol) was dissolved with vigorous stirring in cold (0-2°C) conc. H_2SO_4 (95.72%, ρ = 1.835 g/cm^3, 20 mL), treated dropwise with a nitrating mixture consisting of nitric (7.5 mL, 59.69%, ρ = 1.365 g/cm^3) and sulfuric (7.5 mL, ρ = 1.835 g/cm^3) acids, stirred at room temperature for 2 h, and poured onto ice. The resulting precipitate was filtered off, washed with water until neutral, and dried. Recrystallization from MeOH produced **2** (9.5 g, 79%), mp 183-184°C, in agreement with the literature [3].

6,8-Dibromo-2,3-tetramethylen-3,4-dihydroquinazol-4-one (3) was synthesized by the literature method [17].

α-Oxymethyliden-2,3-tetramethylen-3,4-dihydroquinazol-4-one (26) was prepared by the literature method [3].

α-Benzyliden-2,3-tetramethylen-3,4-dihydroquinazol-4-one (4). Method A. Compound **1** (1.0 g, 5 mmol) was dissolved in glacial acetic acid (10 mL), treated with benzaldehyde (0.53 mL, 0.56 g, 5.3 mmol, ρ = 1.0498 g/cm^3), and refluxed for 3-5 h. Solvent was distilled off. The solid was recrystallized from aqueous DMF to afford **4** (1.05 g, 73%). $C_{19}H_{16}N_2O$, mp 146-147°C, R_f 0.83 (system C).

Method B. Compound **26** (0.456 g, 2 mmol) was dissolved in glacial acetic acid (5 mL), treated with benzaldehyde (0.21 mL, 0.22 g, 2.1 mmol, ρ = 1.0498 g/cm^3), and refluxed for 5 h. Solvent was distilled off. The solid was recrystallized from aqueous DMF to afford **4** (0.37 g, 64%). $C_{19}H_{16}N_2O$, mp 146-147°C, R_f 0.83 (system C).

A mixed melting point with an authentic sample did not show depression.

PMR spectrum (δ, ppm, J/Hz): 8.01 (1H, dd, J = 8.0, 1.0, H-5), 7.65 (1H, ddd, J = 8.0, 7,7, 1.0, H-7), 7.53 (1H, s, H-13), 7.42 (1H, d, J = 7.7, H-8), 7.40 (1H, t, J = 8.0, H-6), 7.11-7.17 (5H, m, H-2′,3′,4′,5′,6′), 3.93 (2H, t, J = 5.6, H-12), 2.75 (2H, td, J = 6.6, 1.8, H-10), 1.85 (2H, m, H-11).

IR spectrum (ν, cm^{-1}): 1717 ($\nu_{C=O}$), 1605 ($\nu_{C=N}$), 1531 (ν_{C-N}).

α-(4′-Hydroxybenzylidene)-2,3-tetramethylen-3,4-dihydroquinazol-4-one (5) was synthesized analogously as above from **1** (1.0 g, 5 mmol) and 4-hydroxybenzaldehyde (0.7 g, 5.3 mmol) to afford **5** (0.97 g, 64%). $C_{19}H_{16}N_2O_2$, mp 246-247°C (alcohol), R_f 0.61 (system C).

PMR spectrum (δ, ppm, J/Hz): 8.0 (1H, dd, J = 8.0, 1,2, H-5), 7.63 (1H, td, J = 8.6, 1.2, H-7), 7.47 (1H, s, H-13), 7.35-7.40 (2H, m, H-6,8), 7.18 (2H, d, J = 8.6, H-2′,6′), 6.68 (2H, d, J = 8.6, H-3′,5′), 3.92 (2H, t, J = 5.4, H-12), 2.72 (2H, t, J = 6.8, H-10), 1.85 (2H, m, H-11).

IR spectrum (ν, cm^{-1}): 1684 ($\nu_{C=O}$), 1606 ($\nu_{C=N}$), 1532 (ν_{C-N}).

α-(4′-Dimethylaminobenzylidene)-2,3-tetramethylen-3,4-dihydroquinazol-4-one (6) was synthesized analogously as above from **1** (1.0 g, 5 mmol) and 4-dimethylaminobenzaldehyde (0.79 g, 5.3 mmol) to afford **6** (1.01 g, 61%). $C_{21}H_{21}N_3O$, mp 174-175°C (alcohol), R_f 0.91 (system D).

PMR spectrum (δ, ppm, J/Hz): 8.03 (1H, br.d, J = 7.8, H-5), 7.66 (1H, br.t, J = 8.1, H-7), 7.57 (1H, s, H-13), 7.46 (1H, d, J = 8.1, H-8), 7.42 (1H, t, J = 7.8, H-6), 7.36-7.39 (4H, m, H-2′,3′,5′,6′), 3.94 (2H, t, J = 5.7, H-12), 3.07 [6H, s, $N(CH_3)_2$], 2.68 (2H, t, J = 6.9, H-10), 1.86 (2H, m, H-11).

IR spectrum (ν, cm^{-1}): 1662 ($\nu_{C=O}$), 1599 ($\nu_{C=N}$), 1535 (ν_{C-N}).

α-(4′-Nitrobenzylidene)-2,3-tetramethylen-3,4-dihdyroquinazol-4-one (7). Method A. The reaction was carried out analogously as above from **1** (1.0 g, 5 mmol) and 4-nitrobenzaldehyde (0.8 g, 5.3 mmol) to afford **7** (1.36 g, 82%). $C_{19}H_{15}N_3O_3$, mp 226-227°C (EtOAc), R_f 0.91 (system C).

Method B. Compound **26** (0.456 g, 2 mmol) was dissolved in glacial acetic acid (5 mL), treated with 4-nitrobenzaldehyde (0.306 g, 2.1 mmol), and refluxed for 5 h. The resulting crystals were filtered off, washed thoroughly with water, and dried. Recrystallization from EtOAc afforded **7** (0.526 g, 72%). $C_{19}H_{15}N_3O_3$, mp 226-227°C (EtOAc), R_f 0.91 (system C).

A mixed melting point with an authentic sample did not show depression.

PMR spectrum (δ, ppm, J/Hz): 8.03 (1H, d, J = 7.7, H-5), 7.98 (2H, d, J = 8.9, H-3′,5′), 7.67 (1H, t, J = 8.4, H-7), 7.61 (1H, s, H-13), 7.44 (1H, d, J = 8.4, H-8), 7.42 (1H, t, J = 7.4, H-6), 7.34 (2H, d, J = 8.9, H-2′,6′), 3.95 (2H, t, J = 5.7, H-12), 2.71 (2H, td, J = 1.5, 6.6, H-10), 1.87 (2H, m, H-11).

IR spectrum (ν, cm^{-1}): 1717 ($\nu_{C=O}$), 1607 ($\nu_{C=N}$), 1541 (ν_{C-N}), 1509 (ν_{C-NO2}).

α-(3′,4′-Dimethoxybenzylidene)-2,3-tetramethylen-3,4-dihdyroquinazol-4-one (8) was synthesized analogously as above from **1** (0.5 g, 2.5 mmol) and 3,4-dimethoxybenzaldehyde (0.415 g, 2.5 mmol) to afford **8** (0.61 g, 70%). $C_{21}H_{20}N_2O_3$, mp 156-157°C (MeOH), R_f 0.85 (system A).

PMR spectrum (δ, ppm, J/Hz): 8.0 (1H, d, J = 7.0, H-5), 7.63 (1H, t, J = 8.4, H-7), 7.46 (1H, s, H-13), 7.36-7.41 (2H, m, H-6,8), 6.96 (1H, dd, J = 8.4, 1.7, H-6′), 6.81 (1H, d, J = 1.7, H-2′), 6.71 (1H, d, J = 8.4, H-5′), 3.92 (2H, t, J = 5.6, H-12), 3.58 [6H, d, 2(OCH_3)], 2.75 (2H, t, J = 5.2, H-10), 1.86 (2H, m, H-11).

IR spectrum (ν, cm^{-1}): 1672 ($\nu_{C=O}$), 1609 ($\nu_{C=N}$), 1539 (ν_{C-N}).

α-(2′-Bromo-3′-hydroxy-4′-methoxybenzylidene)-2,3-tetramethylen-3,4-dihdyroquinazol-4-one (9) was synthesized from **1** (0.5 g, 2.5 mmol) and 2-bromoisovanillin (0.58 g, 2.5 mmol) to afford **9** (0.55 g, 54%). $C_{20}H_{17}N_2O_3Br$, mp 178-180°C (benzene), R_f 0.41 (system B).

PMR spectrum (δ, ppm, J/Hz): 8.02 (1H, dd, J = 8.1, 1.2, H-5), 7.64 (2H, td, J = 8.4, 1.2, H-7,8), 7.45 (1H, d, J = 8.1, H-6), 7.4 (2H, dd, J = 7.8, H-5′,6′), 6.91 (1H, s, H-13), 3.94 (2H, t, J = 5.4, H-12), 3.55 (3H, s, OCH_3), 2.62 (2H, t, J = 6.0, H-10), 1.85 (2H, m, H-11).

IR spectrum (ν, cm^{-1}): 3183 (ν_{O-H}), 1669 ($\nu_{C=O}$), 1594 ($\nu_{C=N}$), 1564 (ν_{C-N}).

α-(3′-Methoxy-4′-hydroxy-5′-bromobenzylidene)-2,3-tetramethylen-3,4-dihydroquinazol-4-one (10) was synthesized analogously as above from **1** (0.34 g, 1.7 mmol) and 5-bromovanillin (0.4 g, 1.7 mmol) to afford **10** (0.46 g, 66%). $C_{20}H_{17}N_2O_3Br$, mp 202-204°C (aq. DMF), R_f 0.76 (system B).

PMR spectrum (δ, ppm, J/Hz): 8.0 (1H, dd, J = 7.3, 1.0, H-5), 7.63 (1H, td, J = 7.3, 1.4, H-7), 7.37-7.41 (3H, m, H-6,8,13), 7.05 (1H, d, J = 1.7, H-6′), 6.70 (1H, d, J = 1.7, H-2′), 3.92 (2H, t, J = 5.6, H-12), 3.56 (3H, s, OCH_3), 2.73 (2H, t, J = 5.6, H-10), 1.86 (2H, m, H-11).

IR spectrum (ν, cm^{-1}): 3183 (ν_{O-H}), 1650 ($\nu_{C=O}$), 1594 ($\nu_{C=N}$), 1545 (ν_{C-N}).

α-(Furfurylidene-1′)-2,3-tetramethylen-3,4-dihydroquinazol-4-one (11) was synthesized analogously as above from **1** (0.5 g, 2.5 mmol) and furfurol (0.22 mL, 0.24 g, 2.65 mmol, ρ = 1.1598 g/cm^3) to afford **11** (0.56 g, 80%). $C_{17}H_{14}N_2O_2$, mp 136-138°C (aq. alcohol), R_f 0.76 (system B).

PMR spectrum (δ, ppm, J/Hz): 7.98 (1H, dd, J = 8.1, 1.2, H-5), 7.61 (1H, td, J = 7.2, 1.2, H-7), 7.32-7.39 (4H, m, H-6,8,13,5′), 6.71 (1H, d, J = 3.9, H-3′), 6.30 (1H, dd, J = 3.9, H-4′), 3.94 (2H, m, H-12), 2.79 (2H, td, J = 6.6, 1.8, H-10), 1.83 (2H, m, H-11).

IR spectrum (ν, cm^{-1}): 1715 ($\nu_{C=O}$), 1608 ($\nu_{C=N}$), 1550 (ν_{C-N}).

6-Nitro-α-benzyliden-2,3-tetramethylen-3,4-dihydroquinazol-4-one (12). A mixture of **2** (0.5 g, 2.0 mmol) was dissolved in glacial acetic acid (5 mL), treated with benzaldehyde (0.23 mL, 0.24 g, 2.3 mmol, ρ = 1.0498 g/cm^3), and refluxed for 5 h. Solvent was distilled off. The solid was recrystallized from benzene to afford **12** (0.54 g, 80%). $C_{19}H_{15}N_3O_3$, mp 200-202°C, R_f 0.86 (system A).

PMR spectrum (δ, ppm, J/Hz): 8.83 (1H, d, J = 2.4, H-5), 8.38 (1H, dd, J = 8.9, 2.4, H-7), 7.65 (1H, d, J = 8.9, H-8), 7.63 (1H, s, H-13), 7.13-7.19 (5H, m, H-2′,3′,4′,5′,6′), 3.93 (2H, t, J = 5.4, H-12), 2.76 (2H, t, J = 5.9, H-10), 1.86 (2H, m, H-11).

IR spectrum (ν, cm^{-1}): 1653 ($\nu_{C=O}$), 1604 ($\nu_{C=N}$), 1560 (ν_{C-N}), 1505 (ν_{NO2}).

6-Nitro-α-(4′-hydroxybenzylidene)-2,3-tetramethylen-3,4-dihydroquinazol-4-one (13) was synthesized analogously as above from **2** (0.5 g, 2.0 mmol) and 4-hydroxybenzaldehyde (0.28 g, 2.3 mmol) to afford **13** (0.53 g, 75%). $C_{19}H_{15}N_3O_4$, mp 262-264°C (aq. DMF), R_f 0.73 (system A).

PMR spectrum (δ, ppm, J/Hz): 8.82 (1H, d, J = 2.6, H-5), 8.37 (1H, dd, J = 8.8, 2.6, H-7), 7.60 (1H, d, J = 8.8, H-8), 7.57 (1H, s, H-13), 7.22 (2H, d, J = 8.8, H-2′,6′), 6.7 (2H, d, J = 8.8, H-3′,5′), 3.92 (2H, t, J = 5.6, H-12), 2.73 (2H, t, J = 5.6, H-10), 1.86 (2H, m, H-11).

Mass spectrum (*m*/*z*, *I*rel, %): 349 (15.4) $[M]^+$, 348 (46) $[M - 1]^+$, 332 (3.5) $[M - OH]^+$, 318 (100), 317 (57.3), 303 (4.8) $[M - NO_2]^+$, 302 (42.6), 243 (7), 122 (2.5), 76 (4.8).

IR spectrum (ν, cm^{-1}): 1653 ($\nu_{C=O}$), 1604 ($\nu_{C=N}$), 1560 (ν_{C-N}), 1505 (ν_{NO2}).

6-Nitro-α-(4′-dimethylaminobenzylidene)-2,3-tetramethylen-3,4-dihydroquinazol-4-one (14) was synthesized analogously as above from **2** (0.5 g, 2.0 mmol) and 4-dimethylaminobenzaldehyde (0.34 g, 2.3 mmol) to afford **14** (0.55 g, 72%). $C_{21}H_{20}N_4O_3$, mp 242-243°C (aq. DMF), R_f 0.87 (system A).

PMR spectrum (δ, ppm, J/Hz): 8.85 (1H, br.s, H-5), 8.40 (1H, d , J = 8.8, H-7), 7.69 (1H, d, J = 8.8, H-8), 7.68 (1H, s, H-13), 7.42 (2H, d, J = 8.8, H-2′,6′), 7.38 (2H, d, J = 8.8, H-3′,5′), 3.94 (2H, t, J = 5.5, H-12), 3.07 [6H, s, $N(CH_3)_2$], 2.7 (2H, t, J = 6.6, H-10), 1.87 (2H, m, H-11).

IR spectrum (ν, cm^{-1}): 1674 ($\nu_{C=O}$), 1614 ($\nu_{C=N}$), 1580 (ν_{C-N}), 1505 (ν_{NO2}).

6-Nitro-α-(4′-nitrobenzylidene)-2,3-tetramethylen-3,4-dihydroquinazol-4-one (15) was synthesized analogously as above from **2** (0.5 g, 2.0 mmol) and 4-nitrobenzaldehyde (0.34 g, 2.3 mmol) to afford **15** (0.67 g, 87%). $C_{19}H_{14}N_4O_5$, mp 243-244°C (aq. DMF), R_f 0.88 (system A).

PMR spectrum (δ, ppm, J/Hz): 8.84 (1H, d, J = 2.4, H-5), 8.4 (1H, dd, J = 8.9, 2.4, H-7), 7.99 (2H, d, J = 8.6, H-3′,5′), 7.70 (1H, d, J = 8.9, H-8), 7.69 (1H, s, H-13), 7.35 (2H, d, J = 8.6, H-2′,6′), 3.95 (2H, t, J = 5.4, H-12), 2.73 (2H, t, J = 6.6, H-10), 1.88 (2H, m, H-11).

Mass spectrum (*m*/*z*, *I*rel, %): 378 (100) $[M]^+$, 332 (14) $[M - NO_2]^+$, 331 (73), 317 (73), 302 (16.8), 286 (14) $[M - (NO_2)_2]^+$, 243 (5.6), 164 (2.8), 151 (2.8), 143 (4.2), 120 (4.2), 77 (12.6).

IR spectrum (ν, cm^{-1}): 1681 ($\nu_{C=O}$), 1614 ($\nu_{C=N}$), 1588 (ν_{C-N}), 1512 (ν_{NO2}).

6-Nitro-α-(3′,4′-dimethoxybenzylidene)-2,3-tetramethylen-3,4-dihydroquinazol-4-one (16) was synthesized analogously as above from **2** (0.5 g, 2.0 mmol) and 3,4-dimethoxybenzaldehyde (0.332 g, 2.0 mmol) to afford **16** (0.62 g, 77%). $C_{21}H_{19}N_3O_5$, mp 230-231°C (aq. DMF), R_f 0.86 (system A).

PMR spectrum (δ, ppm, J/Hz): 8.83 (1H, d, J = 2.6, H-5), 8.38 (1H, dd, J = 9.1, 2.6, H-7), 7.62 (1H, d, J = 9.1, H-8), 7.58 (1H, s, H-13), 7.01 (1H, dd, J = 8.8, 1.9, H-6′), 6.84 (1H, d, J = 1.9, H-2′), 6.73 (1H, d, J = 8.8, H-5′), 3.92 (2H, t, J = 5.6, H-12), 3.58 [6H, d, $(OCH_3)_2$], 2.77 (2H, t, J = 5.9, H-10), 1.88 (2H, m, H-11).

Mass spectrum (*m*/*z*, *I*rel, %): 393 (12.6) $[M]^+$, 363 (93) $[M - OCH_3]^+$, 362 (100), 348 (28) $[M - NO_2]^+$, 332 (12.6), 317 (4.2), 244 (2), 231 (3.5), 219 (4.2), 191 (4.2), 165 (2.8), 151 (1.7), 149 (23), 145 (3.5), 130 (5), 121 (4.2), 101 (5.6), 76 (12).

IR spectrum (ν, cm^{-1}): 1673 ($\nu_{C=O}$), 1610 ($\nu_{C=N}$), 1578 (ν_{C-N}), 1506 (ν_{NO2}).

6-Nitro-α-(2′-bromo-3′-hydroxy-4′-methxoybenzylidene)-2,3-tetramethylen-3,4-dihydroquinazol-4-one (17) was synthesized from **2** (0.4 g, 1.6 mmol) and 2-bromoisovanillin (0.39 g, 1.7 mmol) to afford **17** (0.45 g, 60%). $C_{20}H_{16}N_3O_5Br$, mp 248-250°C (aq. DMF), R_f 0.63 (system B).

PMR spectrum (δ, ppm, J/Hz): 8.84 (1H, d, J = 2.6, H-5), 8.38 (1H, dd, J = 8.8, 2.6, H-7), 7.77 (1H, s, H-13), 7.65 (1H, d, J = 8.8, H-8), 6.82 (1H, d, J = 8.5, H-6′), 6.65 (1H, d, J = 8.5, H-5′), 3.93 (2H, t, J = 5.6, H-12), 3.61 (3H, s, OCH_3), 2.64 (2H, t, J = 6.2, H-10), 1.85 (2H, m, H-11).

IR spectrum (ν, cm^{-1}): 3464 (ν_{O-H}), 1689 ($\nu_{C=O}$), 1614 ($\nu_{C=N}$), 1583 (ν_{C-N}), 1506 (ν_{NO2}).

6-Nitro-α-(3′-methoxy-4′-hydroxy-5′-bromobenzylidene)-2,3-tetramethylen-3,4-dihydroquinazol-4-one (18) was synthesized analogously as above from **2** (0.4 g, 1.6 mmol) and 5-bromovanillin (0.39 g, 1.7 mmol) to afford **18** (0.55 g, 74%). $C_{20}H_{16}N_3O_5Br$, mp 278-280°C (aq. DMF), R_f 0.47 (system B).

PMR spectrum (δ, ppm, J/Hz): 8.83 (1H, d, J = 2.6, H-5), 8.38 (1H, dd, J = 9.1, 2.6, H-7), 7.63 (1H, d, J = 9.1, H-8), 7.49 (1H, s, H-13), 7.10 (1H, d, J = 1.6, H-6′), 6.72 (1H, d, J = 1.6, H-2′), 3.93 (2H, t, J = 5.2, H-12), 3.58 (3H, s, OCH_3), 2.75 (2H, t, J = 5.9, H-10), 1.88 (2H, m, H-11).

IR spectrum (ν, cm^{-1}): 3422 (ν_{O-H}), 1659 ($\nu_{C=O}$), 1618 ($\nu_{C=N}$), 1570 (ν_{C-N}), 1495 (ν_{NO2}).

6-Nitro-α-(furfuryliden-1′)-2,3-tetramethylen-3,4-dihydroquinazol-4-one (19) was synthesized analogously as above from **2** (0.3 g, 1.2 mmol) and furfurol (0.11 mL, 0.12 g, 1.3 mmol, ρ = 1.1598 g/cm^3) to afford **19** (0.37 g, 93%). $C_{17}H_{13}N_3O_4$, mp 236-238°C (benzene), R_f 0.87 (system A).

PMR spectrum (δ, ppm, J/Hz): 8.81 (1H, d, J = 2.3, H-5), 8.36 (1H, dd, J = 9.0, 2.3, H-7), 7.58 (1H, d, J = 9.0, H-8), 7.46 (1H, d, J = 1.6, H-3′), 7.45 (1H, s, H-13), 6.81 (1H, d, J = 3.7, H-5′), 6.34 (1H, dd, J = 3.7, 1.6, H-4′), 3.94 (2H, m, H-12), 2.8 (2H, t, J = 6.4, H-10), 1.85 (2H, m, H-11).

6,8-Dibromo-α-benzyliden-2,3-tetramethylen-3,4-dihydroquinazol-4-one (20). A mixture of **3** (0.4 g, 1.12 mmol) was dissolved in glacial acetic acid (5 mL), treated with benzaldehyde (0.16 mL, 0.168 g, 1.66 mmol, ρ = 1.0498 g/cm^3), and refluxed for 6 h. Solvent was distilled off. The solid was recrystallized from cyclohexane to afford **20** (0.36 g, 72%). $C_{19}H_{14}N_2OBr_2$, mp 168-170°C, R_f 0.89 (system B).

PMR spectrum (δ, ppm, J/Hz): 8.1 (1H, d, J = 2.0, H-5), 8.0 (1H, d, J = 2.0, H-7), 7.13-7.19 (3H, m, H-2′,6′,13), 6.93-6.96 (3H, m, H-3′,4′,5′), 3.9 (2H, t, J = 5.7, H-12), 2.74 (2H, t, J = 1.7, H-10), 1.82 (2H, m, H-11).

IR spectrum (ν, cm^{-1}): 1681 ($\nu_{C=O}$), 1572 ($\nu_{C=N}$), 1543 (ν_{C-N}).

6,8-Dibromo-α-(4′-hydroxybenzylidene)-2,3-tetramethylen-3,4-dihydroquinazol-4-one (21) was synthesized analogously as above from **3** (0.2 g, 0.56 mmol) and 4-hydroxybenzaldehyde (0.087 g, 0.72 mmol) to afford **21** (0.164 g, 64%). $C_{19}H_{14}N_2O_2Br_2$, mp 288-289°C (aq. DMF), R_f 0.72 (system A).

PMR spectrum (δ, ppm, J/Hz): 8.08 (1H, d, J = 2.0, H-5), 7.94 (1H, d, J = 2.0, H-7), 7.48 (1H, s, H-13), 7.22 (2H, d, J = 8.4, H-2′,6′), 6.69 (2H, d, J = 8.4, H-3′,5′), 3.89 (2H, t, J = 5.6, H-12), 2.72 (2H, t, J = 6.6, H-10), 1.85 (2H, m, H-11).

IR spectrum (ν, cm^{-1}): 3070 (ν_{OH}), 1656 ($\nu_{C=O}$), 1580 ($\nu_{C=N}$), 1542 (ν_{C-N}).

6,8-Dibromo-α-(4′-dimethylaminobenzylidene)-2,3-tetramethylen-3,4-dihydroquinazol-4-one (22) was synthesized analogously as above from **3** (0.4 g, 1.12 mmol) and 4-dimethylaminobenzaldehyde (0.21 g, 1.44 mmol) to afford **22** (0.37 g, 68%). $C_{21}H_{19}N_3OBr_2$, mp 215-216°C (benzene), R_f 0.89 (system B).

PMR spectrum (δ, ppm, J/Hz): 8.12 (1H, d, J = 2.0, H-5), 7.97 (1H, d, J = 2.0, H-7), 7.58 (1H, s, H-13), 7.41 (2H, d, J = 9.0, H-2′,6′), 7.38 (2H, d, J = 9.0, H-3′,5′), 3.91 (2H, t, J = 5.7, H-12), 3.06 [6H, s, $N(CH_3)_2$], 2.69 (2H, t, J = 5.7, H-10), 1.86 (2H, m, H-11).

IR spectrum (ν, cm^{-1}): 1664 ($\nu_{C=O}$), 1601 ($\nu_{C=N}$), 1542 (ν_{C-N}), 1515 (ν_{NO2}).

6,8-Dibromo-α-(4′-nitrobenzylidene)-2,3-tetramethylen-3,4-dihydroquinazol-4-one (23) was synthesized analogously as above from **3** (0.4 g, 1.12 mmol) and 4-nitrobenzaldehyde (0.22 g, 1.5 mmol) to afford **23** (0.45 g, 82%). $C_{19}H_{13}N_3O_3Br_2$, mp 270-271°C (aq. DMF), R_f 0.86 (system B).

PMR spectrum (δ, ppm, J/Hz): 8.12 (1H, d, J = 2.0, H-5), 8.0 (2H, d, J = 9.0, H-3′,5′), 7.97 (1H, d, J = 2.0, H-7), 7.62 (1H, s, H-13), 7.36 (2H, d, J = 9.0, H-2′,6′), 3.92 (2H, t, J = 5.7, H-12), 2.72 (2H, td, J = 6.7, 1.7, H-10), 1.87 (2H, m, H-11).

IR spectrum (ν, cm-1): 1666 ($\nu_{C=O}$), 1584 ($\nu_{C=N}$), 1547 (ν_{C-N}), 1508 (ν_{NO2}).

6,8-Dibromo-α-(3′,4′-dimethoxybenzylidene)-2,3-tetramethylen-3,4-dihydroquinazol-4-one (24) was synthesized analogously as above from **3** (0.2 g, 0.56 mmol) and 3,4-dimethoxybenzaldehyde (0.12 g, 0.72 mmol) to afford **24** (0.19 g, 68%). $C_{21}H_{18}N_2O_3Br_2$, mp 192-193°C (benzene), R_f 0.85 (system B).

PMR spectrum (δ, ppm, J/Hz): 8.09 (1H, d, J = 2.0, H-5), 7.94 (1H, d, J = 2.02, H-7), 7.48 (1H, s, H-13), 7.0 (1H, dd, J = 8.4, 2.0, H-6′), 6.84 (1H, d, J = 2.0, H-2′), 6.73 (1H, d, J = 8.4, H-5′), 3.89 (2H, t, J = 5.7, H-12), 3.58 [6H, d, $(OCH_3)_2$], 2.75 (2H, t, J = 6.7, H-10), 1.86 (2H, m, H-11).

IR spectrum (ν, cm^{-1}): 1668 ($\nu_{C=O}$), 1585 ($\nu_{C=N}$), 1549 (ν_{C-N}).

6,8-Dibromo-α-(furfuryliden-1′)-2,3-tetramethylen-3,4-dihydroquinazol-4-one (25) was synthesized analogously as above from **3** (0.3 g, 0.84 mmol) and furfurol (0.1 mL, 0.115 g, 1.2 mmol, ρ = 1.1598 g/cm^3) to afford **25** (0.265 g, 73%). $C_{17}H_{12}N_2O_2Br_2$, mp 224-226°C (benzene), R_f 0.86 (system B).

PMR spectrum (δ, ppm, J/Hz): 8.26 (1H, d, J = 2.3, H-5), 8.12 (1H, t, J = 4.0, 2.0, H-13), 8.02 (1H, d, J = 2.3, H-7), 7.53 (1H, d, J = 1.8, H-5′), 6.65 (1H, d, J = 3.3, H-3′), 6.49 (1H, dd, J = 3.3, 1.8, H-4′), 4.09 (2H, m, H-12), 3.0 (2H, td, J = 6.6, 2.0, H-10), 2.0 (2H, m, H-11).

IR spectrum (ν, cm^{-1}): 1672 ($\nu_{C=O}$), 1572 ($\nu_{C=N}$), 1554 (ν_{C-N}).

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