Synthesis of a Novel Series of 2,3-Disubstituted Quinazolin-4(3*H*)-ones as a Product of a Nucleophilic Attack at C(2) of the Corresponding 4*H*-3,1-Benzoxazin-4-one

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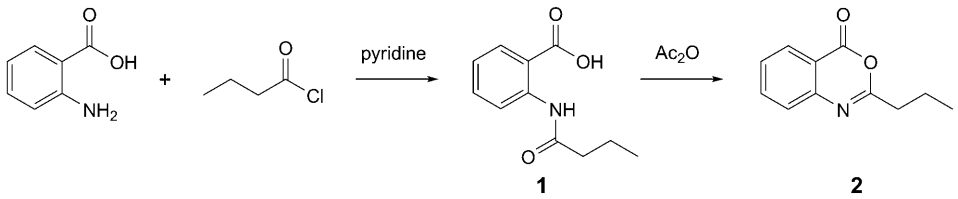
A new series of 2,3-disubstituted quinazolin-4(3*H*)-one derivatives was synthesized by nucleophilic attack at C(2) of the corresponding key starting material 2-propyl-4*H*-3,1-benzoxazin-4-one (*Scheme 2*). The reaction proceeded *via* amidinium salt formation (*Scheme 3*) rather than *via* an *N*-acylanthranilimide. The structure of the prepared compounds were elucidated by physical and spectral data like FT-IR, ^{1}H-NMR, and mass spectroscopy.

Introduction. – The 2,3-disubstituted quinazolin-4(3*H*)-one derivatives possess a broad spectrum of biological and pharmaceutical activities [1–4] such as sedative-hypnotic [5], anticonvulsant [6], phosphorylation-inhibition [7][8], EGFR-inhibition [9][10], and antidiabetic activity [11]. The most common approach toward quinazolinones is based on acylation of anthranilic acid (=2-aminobenzoic acid) and ring closure with Ac_2O to afford corresponding benzoxazinones [12], which are then submitted to react with various primary amines (as N-nucleophiles) to give a series of new 2,3-disubstituted quinazolin-4(3*H*)-ones.

It was envisioned that the nucleophilic attack of the 4*H*-3,1-benzoxazin-4-one takes place at C(2) as well as at C(4), even if the electrophilicity at C(2) is weaker than at C(4).

Results and Discussion. – The key starting material 2-propyl-4*H*-3,1-benzoxazin-4-one (**2**) was synthesized from butanoyl chloride and anthranilic acid in the presence of pyridine *via N*-acylanthranilic acid **1**, which on dehydration with Ac_2O afforded the desired benzoxazinone (*Scheme 1*).

Scheme 1

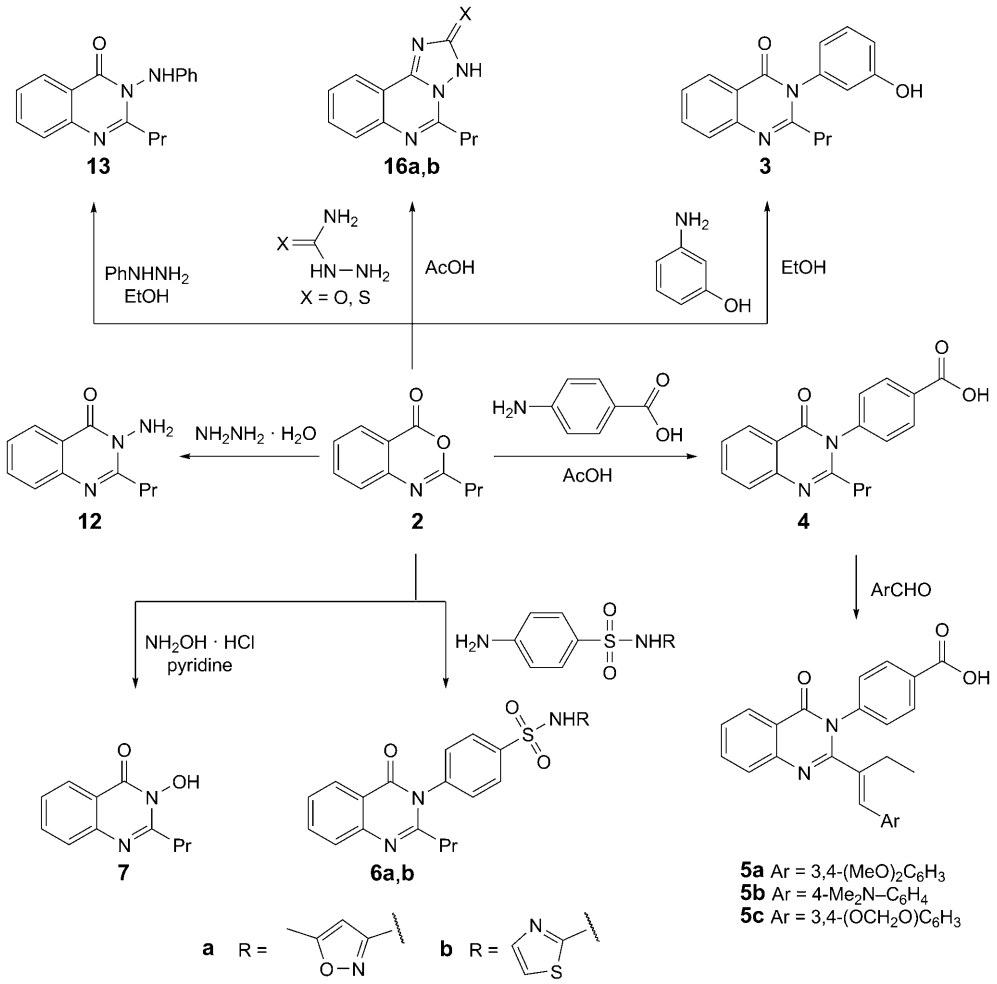


1 **2**

Considering the structure of 4*H*-3,1-benzoxazin-4-one derivatives, there are two sites available for nucleophilic attack, C(2) and C(4), *i.e.*, two different sites with partial positive charge that can lead to the opening of the oxazinone moiety by different nucleophiles. In most cases, reclosure of the heterocyclic part of the molecule is favored and provides a new compound with interesting chemical and biological properties [13].

The reaction of benzoxazinone **2** with a substituted aniline, namely 3-aminophenol or 4-aminobenzoic acid, was chosen as model reaction which resulted in 3-aryl-2-propylquinazolin-4(3*H*)-one derivative **3** or **4**, respectively (*Scheme 2*). The structure of **4** was confirmed chemically by its condensation with aromatic aldehydes like veratraldehyde (= 3,4-dimethoxybenzaldehyde), 4-(dimethylamino)benzaldehyde, and piperonal (= 1,3-benzodioxole-5-carboxaldehyde) in boiling glacial AcOH leading

Scheme 2

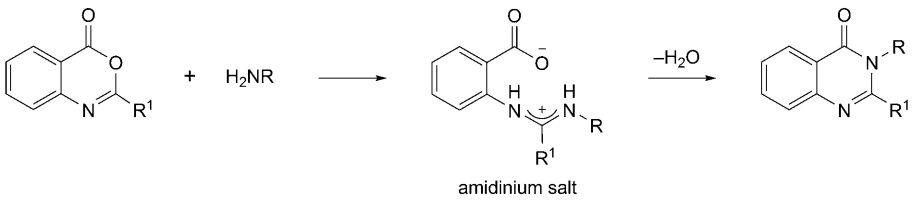


to the corresponding 4-{2-[1-(arylmethylidene)propyl]-4-oxoquinazolin-3(4*H*)-yl}benzoic acids **5a**–**5c**.

Moreover, 4*H*-3,1-benzoxazin-4-one **2** reacted with sulfanilamide (=4-aminobenzenesulfonamide) derivatives like sulfamethoxazol (=4-amino-*N*-(5-methylisoxazol-3-yl)benzenesulfonamide) or sulfathiazol (=4-amino-*N*-(thiazol-2-yl)benzenesulfonamide) to afford the corresponding sulfonamides **6a** or **6b**, respectively (*Scheme 2*).

One can interpret these results as follows: The N-nucleophiles are attacking the benzoxazinone **2** in a fashion in which the amino group first undergoes H-bonding to the N-atom of the heterocycle. Then, the amino group reacts by nucleophilic addition at the 'azavinylic' C(2) to form an inner amidinium salt, which subsequently is dehydrated to give the quinazolinone derivative (*Scheme 3*).

Scheme 3

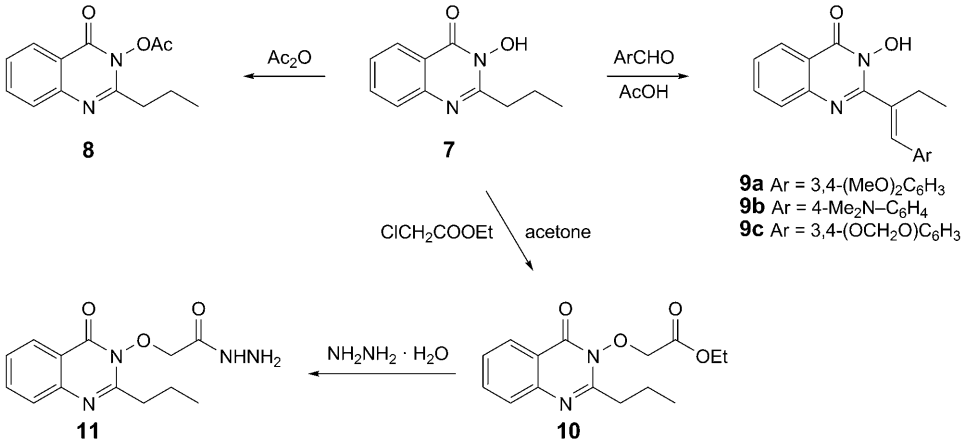


In the case of the reaction of **2** with a substituted aniline derivative, we rejected the nucleophilic attack at C(4) as the second possible pathway which would lead to the *N*-acylanthranilamides. The supposed *N*-acylanthranilamide is reported [14] to be difficult to recyclize and requires temperatures above 200° to affect cyclization which does not correspond with our reaction conditions.

It was reported that 4*H*-3,1-benzoxazin-4-one derivatives react with $NH_2OH \cdot HCl$ in boiling dry pyridine and undergo heterocycle opening and recyclization to give hydroxyquinazolinone derivatives [15]. Thus, treatment of 2-propyl-4*H*-3,1-benzoxazin-4-one (**2**) with $NH_2OH \cdot HCl$ in dry pyridine at 110° afforded 3-hydroxy-2-propylquinazolin-4(3*H*)-one (**7**) (*Scheme 2*). The structure of **7** was inferred chemically by studying its behavior towards C-electrophiles. In this context, treatment of compound **7** with boiling Ac_2O afforded 3-(acetyloxy)quinazolin-4(3*H*)-one (**8**) (*Scheme 4*). The 3-hydroxyquinazolinone **7** underwent also condensation with aromatic aldehydes such as veratraldehyde, 4-(dimethylamino)benzaldehyde, and piperonal in boiling glacial AcOH to give the corresponding 2-[1-(arylmethylidene)-propyl]-3-hydroxyquinazolin-4(3*H*)-ones **9a**–**9c**. Moreover, the conversion of **7** into ethyl 2-{[4-oxo-2-propylquinazolin-3(4*H*)-yl]oxy}acetate (**10**) was achieved *via* the interaction with $ClCH_2COOEt$ in the presence of anhydrous K_2CO_3 in boiling dry acetone. The structure of compound **10** was established chemically by the reaction with $NH_2NH_2 \cdot H_2O$ in boiling EtOH affording 2-[(4-oxo-2-propylquinazolin-3(4*H*)-yl)oxy]-acetohydrazide (**11**) (*Scheme 4*).

Heating 4*H*-3,1-benzoxazin-4-one **2** in neat $NH_2NH_2 \cdot H_2O$ or in $NH_2NH_2 \cdot H_2O$/pyridine produced the 3-amino-2-propylquinazolin-4(3*H*)-one (**12**) (*Scheme 2*). On the other hand, hydrazinolysis of benzoxazinone **2** with $PhNHNH_2$ provided the quinazolinone derivative **13** (*Scheme 2*). It has been reported that compounds having

Scheme 4

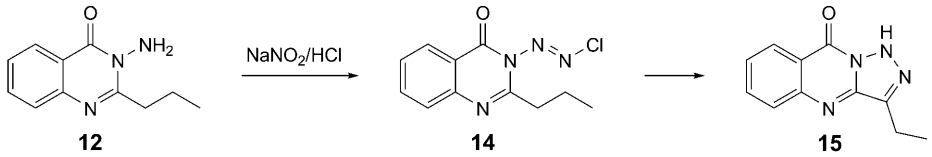


the structure of quinazolinone derivative **13** are key starting materials for synthesizing some interesting triazino-quinazoline derivatives [16].

The above results are in agreement with our assumption of a nucleophilic attack at C(2). On the other hand, they are in disagreement with previous results which account for the formation of 3-aminoquinazoline to rationalize the hydrazinolysis reaction in the presence of anhydrous $ZnCl_2$ [17] or when the substituent at C(2) is sterically bulky [18].

When 3-aminoquinazolin-4(3*H*)-one **12** was treated with HNO_2, it gave 3-(chlorodiazenyl) compound **14** as a fleeting intermediate (not isolated), followed by coupling with different active-methylene-containing compounds such as malononitrile, $ClCH_2COOEt$, and diethyl malonate resulting in the same sole product 3-ethyl[1,2,3]-triazolo[5,1-*b*]quinazolin-9(1*H*)-one (**15**) (*Scheme 5*). When the fleeting intermediate **14** was treated with AcONa in the absence of active-methylene containing compounds under identical reaction and work-up conditions, the product obtained was also **15**.

Scheme 5



Finally, 2-propyl-4*H*-3,1-benzoxazinone **2**, when treated with semicarbazide (= hydrazinecarboxamide) or thiosemicarbazide (= hydrazinecarbothioamide) in boiling glacial AcOH, afforded 5-propyl[1,2,4]triazolo[1,5-*c*]quinazolin-2(3*H*)-one (**16a**) or 5-propyl[1,2,4]triazolo[1,5-*c*]quinazolin-2(3*H*)-thione (**16b**), respectively (*Scheme 2*).

Conclusions. – We successfully converted the prepared 4*H*-3,1-benzoxazin-4-one **2** into the more stable and the higher functionalized 2,3-disubstituted quinazoline derivatives (*Scheme 2*). The nucleophilic attack at C(2) of **2** by the NH_2 moiety was established, suggesting that the ring reclosure occurred readily *via* an amidinium intermediate under mild reaction conditions (*Scheme 3*).

Experimental Part

General. M.p.: *Stuart* electric melting-point apparatus; uncorrected. IR Spectra: λ FT-IR *8201PC Shimadzu* (Japan, 1995); KBr pellets; $\tilde{\nu}$ in cm^{-1}. ^{1}H-NMR Spectra: *Varian* 300 MHz (Germany, 1999); in $CDCl_3$ or (D_6)DMSO; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. EI-MS: GC/MS-*Qploopx Shimadzu* (Japan, 1990); in *m*/*z* (rel. %). Elemental analysis were carried out in the Micro Analytical Center, Cairo University, Giza, Egypt.

*2-Propyl-4*H*-3,1-benzoxazin-4-one* (**2**). A suspension of 2-[(1-oxobutyl)amino]benzoic acid (**1**; 2.07 g, 0.01 mol) in freshly dist. Ac_2O (50 ml) was heated under reflux for 3 h and then concentrated. The residue was crystallized from petroleum ether (40–60°): **2** (78%). Colorless crystals. M.p. 59°. IR (KBr): 1614 (C=N), 1764 (CO). ^{1}H-NMR ($CDCl_3$): 1.07 (*t*, *J* = 6.9, Me); 1.69 ('*sext.*', *J* = 6.4, $MeCH_2$); 2.58 (*t*, *J* = 13.4, $MeCH_2CH_2$); 7.22–7.98 (*m*, 4 arom. H). Anal. calc. for $C_{11}H_{11}NO_2$: C 69.84, H 5.82; found: C 69.76, H 5.92.

*3-(3-Hydroxyphenyl)-2-propylquinazolin-4(3*H*)-one* (**3**). A mixture of **2** (1.89 g, 0.01 mol) and 3-aminophenol (1.09 g, 0.01 mol) in boiling EtOH (20 ml) was refluxed for 3 h. The mixture was allowed to stand overnight, and the solid obtained was filtered off and recrystallized from toluene: **3** (66%). M.p. 216–218°. IR (KBr): 1605 (C=N), 1672 (CO), 2870, 2931, 2962 (CH, aliph.), 3055 (CH, arom.). ^{1}H-NMR ((D_6)DMSO): 0.96 (*t*, *J* = 6.9, Me); 1.82 ('*sext.*', *J* = 6.4, $MeCH_2$); 2.33 (*t*, *J* = 13.6, $MeCH_2CH_2$); 5.3 (*s*, OH); 7.53–8.12 (*m*, 8 arom. H). MS: 280 (M^+), 251, 159, 145, 119, 105. Anal. calc. for $C_{17}H_{16}N_2O_2$: C 72.81, H 5.75; found: C 73.04, H 5.68.

*4-[4-Oxo-2-propylquinazolin-3(4*H*)-yl]benzoic Acid* (**4**). A soln. of **2** (1.89 g, 0.01 mol) and 4-aminobenzoic acid (1.37 g, 0.01 mol) in glacial AcOH (30 ml) was refluxed for 3 h. The solid, separated after cooling, was filtered off and crystallized from EtOH: **4** (69%). M.p. 225–226°. IR (KBr): 1605 (C=N), 1674, 1685 (CO), 2870, 2931, 2962 (CH, aliph.), 3055 (CH, arom.), 3400 (OH). ^{1}H-NMR ((D_6)DMSO): 0.97 (*t*, *J* = 6.9, Me); 1.76 ('*sext.*', *J* = 6.4, $MeCH_2$); 2.48 (*t*, *J* = 13.6, $MeCH_2CH_2$); 7.42–8.04 (*m*, 8 arom. H); 11.81 (*s*, OH). MS: 308 (M^+), 293, 280, 279, 159, 122. Anal. calc. for $C_{18}H_{16}N_2O_3$: C 70.12, H 5.23; found: C 69.84, H 5.41.

*4-{2-[1-(Arylmethylidene)propyl]-4-oxoquinazolin-3(4*H*)-yl}benzoic Acids* **5a**–**5c**. A soln. of **4** (3.08 g, 0.01 mol) and veratraldehyde, 4-(dimethylamino)benzaldehyde, or piperonal (0.01 mol) in glacial AcOH was heated under reflux for 10 h. After cooling, the mixture was poured into cooled water. The precipitated solid was collected, filtered off, and crystallized from EtOH: **5a**–**5c**.

*4-{2-{1-[(3,4-Dimethoxyphenyl)methylidene]propyl}4-oxoquinazolin-3(4*H*)-yl}benzoic Acid* (**5a**): Yield 54%. M.p. 188–189°. IR (KBr): 1597, 1605 (C=N), 1675 (CO), 2870, 2931, 2962 (CH, aliph.), 3055 (CH, arom.), 3450 (OH). ^{1}H-NMR ((D_6)DMSO): 1.13 (*t*, *J* = 7.5, Me); 2.48 (*q*, *J* = 16.7, CH_2); 4.10 (*s*, 2 MeO); 6.64 (*s*, =CH); 6.94–7.83 (*m*, 11 arom. H); 11.83 (*s*, OH). Anal. calc. for $C_{27}H_{24}N_2O_5$: C 71.04, H 5.30; found: C 71.37, H 5.52.

*4-{2-{1-{[(4-Dimethylamino)phenyl]methylidene}propyl}-4-oxoquinazolin-3(4*H*)-yl}benzoic Acid* (**5b**): Yield 61%. M.p. 173°. IR (KBr): 1599, 1605 (C=N), 1674 (CO), 2870, 2931, 2964 (CH, aliph.), 3050 (CH, arom.), 3450 (OH). ^{1}H-NMR ((D_6)DMSO): 1.13 (*t*, *J* = 7.5, Me); 2.49 (*q*, *J* = 16.9, CH_2); 3.11 (*s*, 2 Me); 6.52 (*s*, =CH); 6.85–7.97 (*m*, 12 arom. H); 11.89 (*s*, OH). Anal. calc. for $C_{27}H_{25}N_3O_3$: C 73.78, H 5.73; found: C 73.51, H 5.60.

*4-{2-{1-[(1,3-benzodioxol-5-yl)methylidene]propyl}-4-oxoquinazolin-3(4*H*)-yl}benzoic Acid* (**5c**): Yield 71%. M.p. 201–203°. IR (KBr): 1603 (C=N), 1677 (CO), 2870, 2930, 2965 (CH, aliph.), 3050 (CH, arom.), 3450 (OH). ^{1}H-NMR ((D_6)DMSO): 1.13 (*t*, *J* = 7.5, Me); 2.33 (*q*, *J* = 16.9, CH_2); 5.85 (*s*, OCH_2O); 6.77 (*s*, =CH); 7.03–7.84 (*m*, 11 arom. H); 11.47 (*s*, OH). Anal. calc. for $C_{26}H_{20}N_2O_5$: C 70.90, H 4.58; found: C 71.29, H 4.82.

*4-[4-Oxo-2-propylquinazolin-3(4*H*)-yl]benzenesulfonamides* (**6a** *and* **6b**). A mixture of **2** (0.01 mol) and sulfamethoxazol or sulfathiazol (0.01 mol) in glacial AcOH (20 ml) was refluxed for 3 h. The mixture was concentrated and the formed precipitate washed with water, filtered off, and crystallized from the proper solvent: **6a** and **6b**.

N-*(5-Methylisoxazol-3-yl)-4-[4-oxo-2-propylquinazolin-3(4*H*)-yl]benzenesulfonamide* (**6a**): Yield 86%. M.p. 185° (EtOH). IR (KBr): 1597, 1629 (C=N), 1674 (CO), 2870, 2931, 2962 (CH, aliph.), 3054 (CH, arom.), 3200 (NH). ^{1}H-NMR ((D$_6$)DMSO): 0.94 (*t*, *J* = 6.9, Me); 1.68 ('*sext.*', *J* = 6.3, MeC*H*$_2$); 1.93 (*s*, Me); 2.48 (*t*, *J* = 13.6, MeCH$_2$C*H*$_2$); 6.21 (*s*, =CH); 7.34–7.95 (*m*, 8 arom. H); 8.92 (*s*, NH). MS: 424 (*M*$^+$), 395, 298, 159, 145, 119, 115. Anal. calc. for $C_{21}H_{20}N_4O_4S$: C 59.42, H 4.75; found: C 59.73, H 4.71.

*4-[4-Oxo-2-propylquinazolin-3(4*H*)-yl]-*N*-(thiazol-2-yl)benzenesulfonamide* (**6b**): Yield 76%. M.p. 171° (toluene). IR (KBr): 1598 (C=N), 1668 (CO), 2872, 2930, 2962 (CH, aliph.), 3054 (CH, arom.), 3200 (NH). ^{1}H-NMR ((D$_6$)DMSO): 1.05 (*t*, *J* = 6.9, Me); 1.64 ('*sext.*', *J* = 6.3, MeC*H*$_2$); 2.53 (*t*, *J* = 13.6, MeCH$_2$C*H*$_2$); 6.83 (*d*, =CH); 7.38–7.86 (*m*, 8 arom. H, =CH); 9.3 (*s*, NH). Anal. calc. for $C_{20}H_{18}N_4O_3S$: C 56.32, H 4.25; found: C 56.16, H 4.37.

*3-Hydroxy-2-propylquinazolin-4(3*H*)-one* (**7**). A soln. of **2** (1.89 g, 0.01 mol) and $NH_2OH \cdot HCl$ in boiling EtOH (25 ml) was refluxed for 3 h. The mixture was concentrated and the residue cooled and recrystallized from EtOH: **7** (84%). M.p. 168°. IR (KBr): 1614 (C=N), 1679 (CO), 2890, 2973 (CH, aliph.), 3060 (CH, arom.), 3410 (OH). ^{1}H-NMR ($CDCl_3$): 0.94 (*t*, *J* = 6.8, Me); 1.95 ('*sext.*', *J* = 6.4, MeC*H*$_2$); 2.63 (*t*, *J* = 13.6, MeCH$_2$C*H*$_2$); 7.51–7.81 (*m*, 4 arom. H); 12.30 (*s*, OH). Anal. calc. for $C_{11}H_{12}N_2O_2$: C 64.69, H 5.92; found: C 65.12, H 5.71.

*3-(Acetyloxy)-2-propylquinazolin-4(3*H*)-one* (**8**). A soln. of **7** (2.04 g, 0.01 mol) in freshly dist. Ac_2O (10 ml) was refluxed for 3 h. The mixture was concentrated and the residue cooled and recrystallized from petroleum ether (60–80°): **8** (79%). M.p. 80°. IR (KBr): 1605 (C=N), 1676, 1728, 1800 (CO), 2877, 2931, 2970 (CH, aliph.), 3055 (CH, arom.). ^{1}H-NMR ($CDCl_3$): 0.97 (*t*, *J* = 6.9, Me); 1.64 ('*sext.*', *J* = 6.2, MeC*H*$_2$); 2.31 (*s*, MeCOO); 2.71 (*t*, *J* = 13.5, MeCH$_2$C*H*$_2$); 7.43–7.79 (*m*, 4 arom. H). MS: 246 (*M*$^+$); 217, 175, 159, 105, 77. Anal. calc. for $C_{13}H_{14}N_2O_3$: C 63.41, H 5.73; found: C 63.42, H 5.79.

*2-[1-(Arylmethylidene)propyl]-3-hydroxyquinazolin-4(3*H*)-ones* **9a**–**9c**. A mixture of **7** (2.04 g, 0.01 mol) and an aromatic aldehyde (0.01 mol) namely, veratraldehyde, 4-(dimethylamino)benzaldehyde, or piperonal, in glacial AcOH (10 ml) was refluxed for 8 h. The excess solvent was distilled off, and the residue was poured on ice water. The produced solid was filtered off and recrystallized from the proper solvent: **9a**–**9c**.

*2-[1-[(3,4-Dimethoxyphenyl)methylidene]propyl}-3-hydroxyquinazolin-4(3*H*)-one* (**9a**): Yield 53%. M.p. 122–123° (MeOH). IR (KBr): 1605 (C=N), 1672 (CO), 2870, 2931, 2962 (CH, aliph.), 3055 (CH, arom.), 3430 (OH). ^{1}H-NMR ($CDCl_3$): 1.40 (*t*, *J* = 7.4, Me); 2.45 (*q*, *J* = 17.2, MeC*H*$_2$); 3.42 (*s*, 2 MeO); 6.60 (*s*, =CH); 6.82–7.94 (*m*, 7 arom. H); 11.72 (*s*, OH). MS: 352 (*M*$^+$), 337, 324, 176, 145, 105. Anal. calc. for $C_{20}H_{20}N_2O_4$: C 68.17, H 5.72; found: C 68.32, H 5.84.

*2-{1-{[4-Dimethylamino)phenyl]methylidene}propyl}-3-hydroxyquinazolin-4(3*H*)-one* (**9b**): Yield 64%. M.p. 113–116° (MeOH). IR (KBr): 1602 (C=N), 1677 (CO), 2870, 2931, 2959 (CH, aliph.), 3055 (CH, arom.), 3430 (OH). ^{1}H-NMR ($CDCl_3$): 1.17 (*t*, *J* = 7.5, Me); 2.61 (*q*, *J* = 16.9, MeC*H*$_2$); 2.83 (*s*, Me_2N); 6.48 (*s*, =CH); 6.78–8.05 (*m*, 8 arom. H); 11.61 (*s*, OH). Anal. calc. for $C_{20}H_{21}N_3O_2$: C 71.62, H 6.31; found: C 71.76, H 6.38.

*2-{1-[(1,3-Benzodioxol-5-yl)methylidene]propyl}-3-hydroxyquinazolin-4(3*H*)-one* (**9c**): Yield 71%. M.p. 134–135° (MeOH). IR (KBr): 1605 (C=N), 1675 (CO), 2870, 2931, 2957 (CH, aliph.), 3057 (CH, arom.), 3424 (OH). ^{1}H-NMR ($CDCl_3$): 1.13 (*t*, *J* = 7.4, Me); 2.49 (*q*, *J* = 17.2, MeC*H*$_2$); 5.64 (*s*, OCH_2O); 6.68 (*s*, =CH); 7.05–8.07 (*m*, 7 arom. H); 11.65 (*s*, OH). Anal. calc. for $C_{19}H_{16}N_2O_4$: C 67.85, H 4.76; found: C 67.97, H 4.60.

*Ethyl 2-{[4-Oxo-2-propylquinazolin-3(4*H*)-yl]oxy}acetate* (**10**). A mixture of **7** (2.04 g, 0.01 mol), $ClCH_2COOEt$ (2.72 g, 0.02 mol), and anh. K_2CO_3 (0.04 mol) in dry acetone (50 ml) was refluxed for 24 h on a water bath. The excess solvent was removed by distillation, and the residue was poured on to cold water. The obtained solid was filtered off and recrystallized from benzene: **10** (89%). M.p. 110°. IR (KBr): 1597, 1600 (C=N), 1674, 1740 (CO), 2877, 2931, 2970 (CH, aliph.), 3024 (CH, arom.). ^{1}H-NMR ($CDCl_3$): 1.08 (*t*, *J* = 6.9, Me); 1.32 (*t*, *J* = 7.1, *Me*CH_2O); 1.73 ('*sext.*', *J* = 6.4, MeC*H*$_2$); 2.51 (*t*, *J* = 13.4,

$MeCH_2CH_2$); 3.94 (*q*, *J* = 7.1, $MeCH_2O$); 4.63 (*s*, OCH_2CO); 7.42–7.92 (*m*, 4 arom. H). MS: 290 (M^+), 261, 218, 190, 119, 105. Anal. calc. for $C_{15}H_{18}N_2O_4$: C 62.06, H 6.20; found: C 62.20, H 6.29.

*2-{[4-Oxo-2-propylquinazolin-3(4*H*)-yl]oxy}acetic Acid Hydrazide* (**11**). A soln. of **10** (2.90 g, 0.01 mol) and $NH_2NH_2 \cdot H_2O$ (0.75 g, 0.015 mol) in EtOH (50 ml) was refluxed for 3 h. The mixture was concentrated and then allowed to cool and the obtained solid filtered off and recrystallized from EtOH: **11** (68%). M.p. 180°. IR (KBr): 1597, 1600 (C=N), 1684 (CO), 2887, 2925, 2977 (CH, aliph.), 3045 (CH, arom.), 3298, 3322 (NH). ^{1}H-NMR ($CDCl_3$): 0.91 (*t*, *J* = 6.8, Me); 1.60 ('*sext.*', *J* = 6.2, $MeCH_2$); 2.49 (*t*, *J* = 13.4, $MeCH_2CH_2$); 4.72 (*s*, OCH_2CO); 7.46–7.84 (*m*, 4 arom. H); 8.84 (*s*, NH_2); 8.97 (*s*, NH). Anal. calc. for $C_{13}H_{16}N_4O_3$: C 56.53, H 5.79; found: C 56.81, H 5.90.

*3-Amino-2-propylquinazolin-4(3*H*)-one* (**12**). A mixture of **2** (1.89 g, 0.01 mol) and $NH_2NH_2 \cdot H_2O$ (5 ml) was heated in a water bath for 30 min, and then EtOH (50 ml) was added and the mixture heated under reflux for 3 h. The mixture was concentrated, and the residue was poured on cooled water and the formed precipitate dried and crystallized from petroleum ether (60–80°): **12** (75%). M.p. 85°. IR (KBr): 1596 (C=N), 1673 (CO), 2875, 2935, 2965 (CH, aliph.), 3055 (CH, arom.), 3212, 3309 (NH). ^{1}H-NMR ($CDCl_3$): 0.94 (*t*, *J* = 7.0, Me); 1.86 ('*sext.*', *J* = 6.5, $MeCH_2$); 2.68 (*t*, *J* = 13.4, $MeCH_2CH_2$); 7.49–7.79 (*m*, 4 arom. H); 8.8 (*s*, NH_2). MS: 203 (M^+), 174, 146, 120, 77. Anal. calc. for $C_{11}H_{13}N_3O$: C 65.02, H 6.40; found: C 64.81, H 6.54.

*3-(Phenylamino)-2-propylquinazolin-4(3*H*)-one* (**13**). A mixture of **2** (1.89 g, 0.01 mol) and $PhNHNH_2$ (2.16 g, 0.02 mol) in EtOH (30 ml) was refluxed for 3 h. The mixture was concentrated, the residue poured over cold water, and the separated solid filtered off and recrystallized from benzene: **13** (79%). M.p. 136–138°. IR (KBr): 1597, 1605 (C=N), 1674 (CO), 2870, 2931, 2962 (CH, aliph.), 3055 (CH, arom.), 3200 (NH). ^{1}H-NMR ($CDCl_3$): 0.94 (*t*, *J* = 7.0, Me); 1.82 ('*sext.*', *J* = 6.4, $MeCH_2$); 2.53 (*t*, *J* = 13.7, $MeCH_2CH_2$); 6.68–7.94 (*m*, 9 arom. H); 8.92 (*s*, NH). MS: 279 (M^+), 264, 237, 236, 146, 120. Anal. calc. for $C_{17}H_{17}N_3O$: C 73.10, H 6.13; found: C 73.28, H 6.34.

*3-Ethyl[1,2,3]triazolo[5,1-*b*]quinazolin-9(1*H*)-one* (**15**). A soln. of **12** (2.03 g, 0.01 mol) in AcOH/conc. HCl soln. 1:3 (15 ml) was cooled to 0°, and an eq. soln. of $NaNO_3$ (1.38 g, 0.02 mol) was added. The mixture was stirred at 0° for 15 min then added to a soln. of malononitrile, acetyl acetone (= pentane-2,4-dione), or ethyl acetoacetate (= ethyl 3-oxobutanoate) (0.01 mol) in EtOH (5 ml) containing AcONa (4 g). The mixture was stirred overnight, and the obtained solid was dried and recrystallized from MeOH: **15** (62%). M.p. 198°. IR (KBr): 1620 (C=N), 1676 (CO), 2931, 2962 (CH, aliph.), 3167 (NH). ^{1}H-NMR ((D_6)DMSO): 2.10 (*t*, *J* = 7.3, Me); 2.62 (*q*, *J* = 13.9, CH_2); 7.24–7.86 (*m*, 4 arom. H); 12.1 (*s*, NH). Anal. calc. for $C_{11}H_{10}N_4O$: C 61.68, H 4.67; found: C 61.81, H 4.54.

*[1,2,4]Triazolo[1,5-*c*]quinazolin-2(3*H*)-one and -thione* **16a** *and* **16b**. A mixture of **2** (1.89 g, 0.01 mol) and semicarbazide or thiosemicarbazide (0.01 mol) in glacial AcOH (25 ml) in the presence of AcONa (0.05 mol) was heated under reflux for 4 h. The mixture was allowed to stand overnight, and the separated solid was crystallized from the proper solvent to give **16a** or **16b**.

*5-Propyl[1,2,4]triazolo[1,5-*c*]quinazolin-2(3*H*)-one* (**16a**): Yield 72%. M.p. 219–221° (EtOH). IR (KBr): 1605 (C=N), 1685 (CO), 2870, 2931, 2962 (CH, aliph.), 3055 (CH, arom.), 3310 (NH). ^{1}H-NMR ((D_6)DMSO): 0.93 (*t*, *J* = 6.8, Me); 1.84 ('*sext.*', *J* = 6.4, $MeCH_2$); 2.48 (*t*, *J* = 13.6, $MeCH_2CH_2$); 7.32–7.89 (*m*, 4 arom. H); 9.42 (*s*, NH). Anal. calc. for $C_{12}H_{12}N_4O$: C 63.14, H 5.30; found: C 63.38, H 5.38.

*5-Propyl[1,2,4]triazolo[1,5-*c*]quinazoline-2(3*H*)-thione* (**16b**): Yield 82%. M.p. 234° (EtOH). IR (KBr): 1161 (CS), 1604 (C=N), 2881, 2931, 2962 (CH, aliph.), 3055 (CH, arom.), 3361 (NH). ^{1}H-NMR ((D_6)DMSO): 0.93 (*t*, *J* = 6.9, Me); 1.58 ('*sext.*', *J* = 6.4, $MeCH_2$); 2.37 (*t*, *J* = 13.6, $MeCH_2CH_2$); 7.26–7.81 (*m*, 4 arom. H); 9.86 (*s*, NH). MS: 244 (M^+), 230, 217, 216, 203, 145, 119, 92, 77. Anal. calc. for $C_{12}H_{12}N_4S$: C 58.99, H 4.95; found: C 59.34, H 5.18.

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