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Application of Organolithium in Organic Synthesis: A Simple and Convenient Procedure for the Synthesis of More Complex 6-Substituted 3*H*-Quinazolin-4-ones

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Summary. 6-Methyl-3*H*-quinazolin-4-one reacted with alkyllithium reagents at −78°C in *THF* to give 2-alkyl-1,2-dihydro-6-methyl-3*H*-quinazolin-4-ones in high yields. However, no reaction took place when *LDA* was used as the lithium reagent. 6-Bromo-3*H*-quinazolin-4-one reacted with excessive butyllithium to give 2-butyl-1,2-dihydro-3*H*-quinazolin-4-ones in very good yields. However, the lithiation of 6-bromo-3*H*-quinazolin-4-one was achieved by the use of a combination of methyllithium (1.1 equivalents) and *tert*-butyllithium (2.2 equivalents) at −78°C in *THF*. The dilithio reagent thus obtained reacted with a variety of electrophiles (H_2O, iodoethane, benzaldehyde, anisaldehyde, cyclohexanone, 2-hexanone, benzophenone, phenyl isothiocyanate, *TITD*) to give the corresponding 6-substituted 3*H*-quinazolin-4-ones in excellent yields. Reaction of the dilithio reagent with 1,3-dibromopropane gave 6,6′-(propanediyl)bis(3*H*-quinazolin-4-one).

Keywords. 3*H*-Quinazolin-4-one; Nucleophilic addition; Bromine-lithium exchange; Dilithio reagent; Electrophiles.

Introduction

Recently, it was observed that lithiation of various heterocyclic compounds using lithium reagents at low temperature followed by reactions with electrophiles resulted in the production of substituted heterocycles in good yields [1]. Literature reveals that current attention is focused on the preparation of substituted quinazoline derivatives *via* directed lithiation in order to improve their biological activities

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[2–5]. More recent work involved successful lithiation of 3-*tert*-butoxycarbonyl-3*H*-quinazolin-4-one using lithium diisopropylamide (*LDA*) [6]. The reactions of the dilithio reagent thus formed with electrophiles followed by removal of the *tert*-butoxycarbonyl group afforded the corresponding 2-substituted derivatives [6].

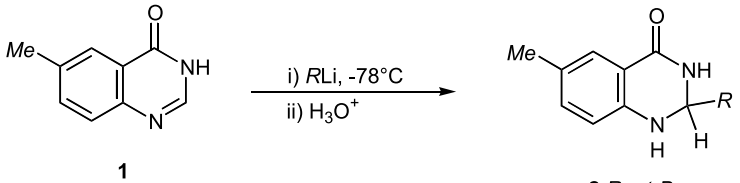
As a part of our own interest in heterocyclic chemistry [7], particularly in the use of directed lithiation in organic synthesis [8], we have shown that lithiation of various 3*H*-quinazolin-4-ones produced a wide range of more complex 2-substituted 3*H*-quinazolin-4-one derivatives in very good yields [9, 10]. Synthesis of the 3*H*-quinazolin-4-one ring system, which provides the backbone for compounds having numerous pharmacological activities [11], is an interesting challenge. We now report on the successful synthesis of 6-substituted 3*H*-quinazolin-4-ones *via* bromine–lithium exchange of 6-bromo-3*H*-quinazolin-4-one.

Results and Discussion

6-Methyl-3*H*-quinazolin-4-one (**1**) was prepared according to Ref. [12]. It was hoped that lithiation of **1** would take place as for 2-methyl-3*H*-quinazolin-4-one [11], so that substitution of the hydrogen of the methyl group at position 6 by lithium could be achieved, followed by reactions with electrophiles to give the corresponding 6-substituted derivatives. However, it was found that lithiation of **1** did not take place with alkyllithiums. Instead, nucleophilic attack by alkyllithiums occurred at the imine bond to give 1,2-addition products. The reactions of **1** with one equivalent of alkyllithiums (*tert*-butyllithium, *n*-butyllithium, methyllithium) at −78°C in *THF* took place within 15 minutes to give 2-alkyl-1,2-dihydro-6-methyl-3*H*-quinazolin-4-ones (**2**–**4**) (Scheme 1) in high yields (85–90%).

The compounds **2**–**4** are fluorescent. Their structures were confirmed by ^{1}H NMR, ^{13}C NMR, mass spectra, and high resolution mass spectral data. Their ^{1}H NMR spectra showed a characteristic H-2 signal in the $\delta = 4.31$–4.77 ppm region, and their ^{13}C NMR spectra showed that C-2 appears in the $\delta = 61$–72 ppm region (see Experimental for details).

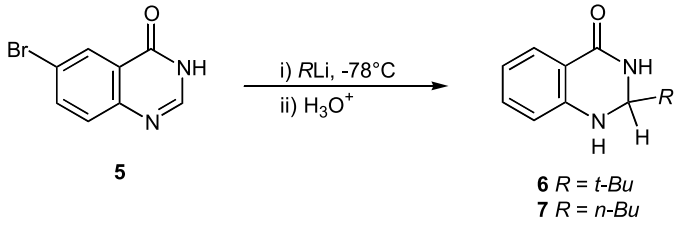
It was found that lithiation of **1** with a less nucleophilic lithium reagent, such as lithium diisopropylamide (*LDA*) did not take place and only starting material was recovered, indicating that no reaction took place under the conditions tried. No further attempts were made to try to find conditions under which lithiation of **1** could be effected.



1

2 *R* = *t-Bu*
3 *R* = *n-Bu*
4 *R* = *Me*

Scheme 1



5

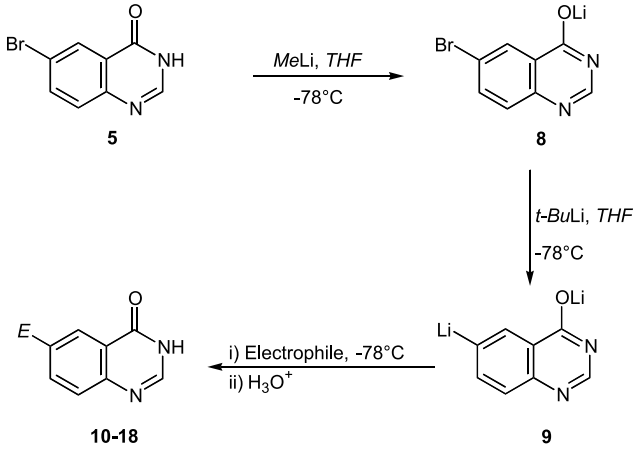
6 *R* = *t-Bu*
7 *R* = *n-Bu*

Scheme 2

Unfortunately, lithiation of **1** was not successful; therefore attention was turned next to replacing the methyl group at position 6 with bromine that could be replaced with lithium *via* bromine-lithium exchange. Initially, lithiations of 6-bromo-3*H*-quinazolin-4-one (**5**) [13] using *tert*- and *n*-butyllithium in *THF* at $-78°C$ were attempted. Unfortunately, reactions with a number of electrophiles (H_2O, iodoethane and benzaldehyde) produced low yields of the desired products along with 2-butyl-1,2-dihydro-3*H*-quinazolin-4-ones **6** and **7**. However, if 4 equivalents of *tert*- and *n*-butyllithium were used, **6** and **7** were obtained in 88 and 79% isolated yields (Scheme 2).

Compounds **6** and **7** are also fluorescent. The ^1H NMR spectra of **6** and **7** showed a characteristic H-2 signal at $\delta = 4.35$ and $\delta = 5.50$ ppm. Their ^{13}C NMR spectra showed that C-2 appears at $\delta = 72.55$ and $\delta = 67.38$ ppm (see Experimental for details).

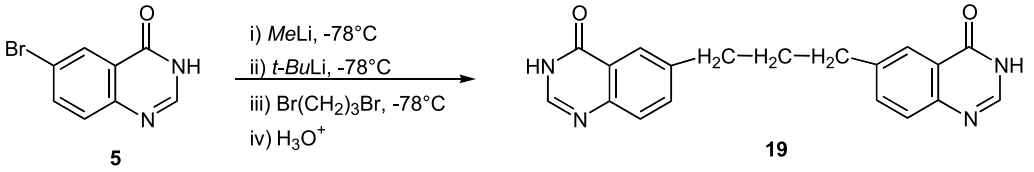
However, compound **5** was successfully lithiated using a combination of methyllithium and *tert*-butyllithium in *THF* at $-78°C$. Lithiation of **5** took place on nitrogen to form the monolithio reagent **8** using methyllithium (1.1 equivalents), followed by bromine-lithium exchange using *tert*-butyllithium (2.2 equivalents) to give the dilithio reagent **9** (Scheme 3). To test the extent to which the dilithio reagent **9** had formed, it was protonated using aqueous saturated ammonium chloride solution to give 3*H*-quinazolin-4-one (**10**) in 91% isolated yield. In order to



5 **8** **9** **10-18**

E = H (**10**), *Et* (**11**), *Ph*CH(OH) (**12**), 4-*Me*OC$_6$H$_4$CH(OH) (**13**), cyclohexyl-1-ol (**14**), *Me*C(OH)*Bu* (**15**), Ph_2C(OH) (**16**), *Ph*NHCS (**17**), SCSN^i*Pr*$_2$ (**18**)

Scheme 3



Scheme 4

test the versatility of the intermediate dilithio reagent **9**, it was reacted with other electrophiles (iodoethane, benzaldehyde, anisaldehyde, cyclohexanone, 2-hexanone, benzophenone, phenyl isothiocyanate, tetra-*iso*-propylthiuram disulfide (*TITD*)) to give the corresponding 6-substituted 3*H*-quinazolin-4-ones (**11**–**18**) (Scheme 3) in good yields (81–91%).

No N-substitution was observed, even with excessive iodoethane (2 equivalents) as electrophile. The structures of **10**–**18** were confirmed by ^{1}H NMR, ^{13}C NMR, mass spectra, and high resolution mass spectral data (see Experimental for details). The ^{1}H NMR spectrum of **18** showed that the methyl and CH protons of the *iso*-propyl groups appeared as broad signals at room temperature and as doublet and heptet signals at 80°C indicating that there is restricted rotation about the C–S and C–N bonds at room temperature. Similar observations have been made previously for 3-amino- and 3-acylamino-3*H*-quinazolin-4-one derivatives [14].

Finally, reaction of the dilithio reagent of **5** with 1,3-dibromopropane (0.55 equivalent) in *THF* at −78°C gave **19** (Scheme 4) in 71% isolated yield. The NMR and mass spectra confirmed the structure of **19**.

In conclusion, the reaction accommodates a range of more complex substitutents into the benzene ring of the 3*H*-quinazolin-4-one system. Therefore, it represents a convenient, clean, and simple procedure for the high yield synthesis of 6-substituted 3*H*-quinazolin-4-ones, which might be difficult to prepare by other means.

Experimental

Melting points were determined on an electrothermal melting MEL-TEMP II apparatus. ^{1}H and ^{13}C NMR spectra were recorded in *DMSO*-d_6 using a Bruker AC400 spectrometer operating at 400 MHz for ^{1}H and 100 MHz for ^{13}C. Chemical shifts are reported in parts per million relative to tetramethylsilane. Low-resolution mass spectra were recorded on a Quattro II triple quadrupole mass spectrometer (electron impact: 70 eV; chemical ionization: ammonia). Accurate mass data were obtained on a MAT 900 instrument. UV and visible spectra were recorded in $CHCl_3$ using a Unicam UV300 UV-visible spectrometer. Fluorescence spectra were recorded in $CHCl_3$ using a Perkin Elmer LS50B luminescence spectrometer. Butyllithium and methyllithium were obtained from Aldrich and were estimated prior to use by the method of *Watson* and *Eastham* [15]. *THF* was distilled from sodium benzophenone ketyl. Compounds **1** and **5** were prepared according to Refs. [12, 13]. Their analytical data agreed with the published work.

Synthesis of 2-Alkyl-6-methyl-1,2-dihydro-3H-quinazolin-4-ones ***2–4***

To a cold (−78°C), stirred solution of 0.32 g of **1** (2.0 mmol) in 50 cm^3 of dry *THF* under N_2 was added a solution of 2.2 mmol of alkyllithium. The yellow solution obtained was stirred at −78°C for 15 min and then allowed to warm to room temperature. The mixture was quenched with 20 cm^3 of aq. sat.

NH_4Cl. The organic layer was washed with $2 \times 20\,cm^3$ of H_2O, dried ($MgSO_4$), and the solvent was evaporated under reduced pressure. The products were recrystallised form methanol to give **2**–**4**.

2-tert-Butyl-6-methyl-1,2-dihydro-3H-quinazolin-4-one (**2**, $C_{13}H_{18}N_2O$)

Yield 90%; mp 197–189°C; ^{1}H NMR: $\delta = 0.88$ (s, $C(CH_3)_3$), 2.15 (s, CH_3), 4.31 (t, $J = 2.2$ Hz, H-2), 6.33 (s, exch., NH), 6.71 (d, $J = 8.2$ Hz, H-8), 7.02 (dd, $J = 8.2$, 1.6 Hz, H-7), 7.36 (d, $J = 1.6$ Hz, H-5), 7.75 (s, exch., NH) ppm; ^{13}C NMR: $\delta = 20.40$ (q, $C(CH_3)_3$), 24.90 (q, CH_3), 37.57 (s, $C(CH_3)_3$), 72.65 (d, C-2), 114.18 (d), 114.47 (s, C-4a), 124.93 (s, C-6), 127.27 (d), 134.29 (d), 146.60 (s, C-8a), 164.13 (s, C-4) ppm; EI-MS: m/z (%) = 218 (M^+, 59), 201 (100), 187 (41), 174 (63), 161 (85), 57 (44); CI-MS: m/z (%) = 219 (MH^+, 100), 161 (12), 57 (5); HRCI-MS: $C_{13}H_{19}N_2O$ (MH^+), calcd 219.1497, found 219.1496; UV-Vis ($CHCl_3$): $\lambda_{max} = 345$ nm; Fluorescence ($CHCl_3$): $\lambda_{max} = 421$ nm.

2-Butyl-6-methyl-1,2-dihydro-3H-quinazolin-4-one (**3**, $C_{13}H_{18}N_2O$)

Yield 85%; mp 129–130°C; ^{1}H NMR: $\delta = 0.88$ (t, $J = 7.2$ Hz, CH_3), 1.30 (sextet, $J = 7.2$ Hz, CH_2), 1.39 (m, CH_2), 1.61 (m, CH_2), 2.18 (s, CH_3), 4.63 (t, $J = 5.3$ Hz, H-2), 6.37 (s, exch., NH), 6.67 (d, $J = 8.2$ Hz, H-8), 7.05 (dd, $J = 8.2$, 1.6 Hz, H-7), 7.40 (d, $J = 1.6$ Hz, H-5), 7.85 (s, exch., NH) ppm; ^{13}C NMR: $\delta = 14.30$ (q, CH_3), 20.44 (q, CH_3), 22.45 (t, CH_2), 25.84 (t, CH_2), 34.98 (t, CH_2), 64.90 (d, C-2), 114.87 (d), 115.44 (s, C-4a), 125.86 (s, C-6), 127.57 (d), 134.19 (d), 146.73 (s, C-8a), 164.42 (s, C-4) ppm; EI-MS: m/z (%) = 218 (M^+, 47), 201 (100), 187 (45), 161 (80), 105 (22), 57 (51); CI-MS: m/z (%) = 219 (MH^+, 100), 161 (32); HRCI-MS: $C_{13}H_{19}N_2O$ (MH^+), calcd 219.1497, found 219.1497; UV-Vis ($CHCl_3$): $\lambda_{max} = 317$ nm; Fluorescence ($CHCl_3$): $\lambda_{max} = 413$ nm.

2,6-Dimethyl-1,2-dihydro-3H-quinazolin-4-one (**4**, $C_{10}H_{12}N_2O$)

Yield 87%; mp 211–213°C; ^{1}H NMR: $\delta = 1.30$ (d, $J = 6.0$ Hz, CH_3), 2.18 (s, CH_3), 4.77 (q, $J = 6.0$ Hz, H-2), 6.43 (s, exch., NH), 6.61 (d, $J = 8.0$ Hz, H-8), 7.07 (dd, $J = 8.0$, 2.0 Hz, H-7), 7.41 (d, $J = 2.0$ Hz, H-5), 7.87 (s, exch., NH) ppm; ^{13}C NMR: $\delta = 20.45$ (q, CH_3), 21.51 (q, CH_3), 61.32 (d, C-2), 114.78 (d), 115.59 (s, C-4a), 126.17 (s, C-6), 127.67 (d), 134.21 (d), 147.00 (s, C-8a), 164.60 (s, C-4) ppm; EI-MS: m/z (%) = 176 (M^+, 17), 161 (100), 134 (18), 106 (16), 104 (22), 77 (31); CI-MS: m/z (%) = 194 ($M^+ + NH_4$, 6), 177 (MH^+, 100), 161 (6); HRCI-MS: $C_{10}H_{13}N_2O$ (MH^+), calcd 177.1028, found 177.1027; UV-Vis ($CHCl_3$): $\lambda_{max} = 337$ nm; Fluorescence ($CHCl_3$): $\lambda_{max} = 417$ nm.

*Synthesis of 2-Butyl-1,2-dihydro-3H-quinazolin-4-ones **6** and **7***

To a cold (−78°C), stirred solution of 0.45 g of **5** (2.0 mmol) in 50 cm^3 of dry *THF* under N_2 was added a solution of 8.0 mmol of butyllithium. The yellow solution obtained was stirred at −78°C for 30 min. It was then allowed to warm to room temperature and quenched with 20 cm^3 of aq. sat. NH_4Cl. The organic layer was separated, washed with $2 \times 20\,cm^3$ of H_2O, dried ($MgSO_4$), and the solvent was evaporated under reduced pressure. The products were recrystallised form methanol to give **6** and **7**.

2-tert-Butyl-1,2-dihydro-3H-quinazolin-4-one (**6**, $C_{12}H_{16}N_2O$)

Yield 86%; mp 190–191°C; ^{1}H NMR: $\delta = 0.86$ (s, $C(CH_3)_3$), 4.35 (t, $J = 2.2$ Hz, H-2), 6.47 (s, exch., NH), 6.58 (dt, $J = 8.0$, 1.9 Hz, 1H), 6.78 (d, $J = 8.0$ Hz, 1H), 7.18 (dt, $J = 8.0$, 1.9 Hz, 1H), 7.55 (dd, $J = 8.0$, 1.9 Hz, 1H), 7.82 (s, exch., NH) ppm; ^{13}C NMR: $\delta = 24.84$ (q, $C(CH_3)_3$), 37.38 (s, $C(CH_3)_3$), 72.55 (d, C-2), 113.98 (d), 114.45 (s, C-4a), 116.37 (d), 127.40 (d), 133.43 (d), 148.70 (s, C-8a), 163.99 (s, C-4) ppm; EI-MS: m/z (%) = 204 (M^+, 2), 187 (3), 147 (100), 130 (10), 92 (15), 65 (16), 57 (26); CI-MS: m/z (%) = 222 ($M^+ + NH_4$, 5), 205 (MH^+, 100), 187 (2), 147 (20); HRCI-MS: $C_{12}H_{17}N_2O$

(MH^+), calcd 205.1341, found 205.1339; UV-Vis ($CHCl_3$): $\lambda_{max} = 334$ nm; Fluorescence ($CHCl_3$): $\lambda_{max} = 406$ nm.

2-Butyl-1,2-dihydro-3H-quinazolin-4-one (**7**, $C_{12}H_{16}N_2O$)

Yield 79%; mp 125–126°C; ^{1}H NMR: $\delta = 1.67$ (t, $J = 7.2$ Hz, CH_3), 2.09 (sextet, $J = 7.2$ Hz, CH_2), 2.19 (m, CH_2), 2.46 (m, CH_2), 5.46 (s, exch., NH), 5.49 (t, $J = 4.3$ Hz, H-2), 7.40 (t, $J = 8.1$ Hz, 1H), 7.35 (d, $J = 8.1$ Hz, 1H), 8.03 (dt, $J = 8.1$, 1.5 Hz, 1H), 8.41 (dd, $J = 8.1$, 1.5 Hz, 1H), 8.71 (s, exch., NH) ppm; ^{13}C NMR: $\delta = 16.62$ (q, CH_3), 25.07 (t, CH_2), 28.34 (t, CH_2), 37.70 (t, CH_2), 67.43 (d, C-2), 117.31 (d), 117.85 (s, C-4a), 119.98 (d), 130.31 (d), 136.12 (d), 151.51 (s, C-8a), 167.34 (s, C-4) ppm; EI-MS: m/z (%) = 204 (M^+, 2), 160 (10), 147 (100), 130 (16), 119 (20), 92 (36), 65 (22), 41 (95); CI-MS: m/z (%) = 222 ($M^+ + NH_4$, 6), 205 (MH^+, 100), 147 (11); HRCI-MS: $C_{12}H_{17}N_2O$ (MH^+), calcd 205.1341, found 205.1340; UV-Vis ($CHCl_3$): $\lambda_{max} = 309$ nm; Fluorescence ($CHCl_3$): $\lambda_{max} = 407$ nm.

General Procedure for the Synthesis of 6-Substituted 3H-Quinazolin-4-ones ***10–19***

A solution of methyllithium in ether (2.2 cm^3, 1.0 *M*, 2.2 mmol) was added to a cold (−78°C), stirred solution of 0.45 g of **5** (2.0 mmol) in 50 cm^3 of dry *THF* under N_2. After 5 min a solution of *tert*-butyllithium in pentane (2.6 cm^3, 1.7 *M*, 4.4 mmol) was added and the resultant yellow solution obtained was stirred at −78°C for 1 h to complete the formation of the dilithio reagent **9**. An electrophile (2.2 mmol), in 8 cm^3 of dry *THF* if solid, otherwise neat, was added. The reaction mixture was stirred for 2 h at −78°C, then removed from the cooling bath and allowed to warm to room temperature. The mixture was diluted with 20 cm^3 of ethyl acetate and quenched with 20 cm^3 of aq. sat. NH_4Cl. The organic layer was separated, washed with 2×20 cm^3 of H_2O, dried ($MgSO_4$), and the solvent was evaporated under reduced pressure. The products were recrystallised form methanol or ethyl acetate to give **10–19**. Compound **19** was obtained using 1,3-dibromopropane (1.1 mmol) as the electrophile.

3H-Quinazolin-4-one (**10**)

Yield 91%; mp 217°C (Ref. [16] 215.5–216.5°C).

6-Ethyl-3H-quinazolin-4-one (**11**, $C_{10}H_{10}N_2O$)

Yield 84%; mp 183–185°C; ^{1}H NMR: $\delta = 1.20$ (t, $J = 7.6$ Hz, CH_3), 2.71 (q, $J = 7.6$ Hz, CH_2), 7.57 (d, $J = 8.1$ Hz, H-8), 7.65 (dd, $J = 8.1$, 2.0 Hz, H-7), 7.91 (d, $J = 2.0$ Hz, H-5), 8.03 (s, H-2), 12.18 (s, exch., NH) ppm; ^{13}C NMR: $\delta = 15.72$ (q, CH_3), 28.16 (t, CH_2), 122.67 (s, C-4a), 124.21 (d), 127.48 (d), 134.04 (d), 143.04 (d), 144.93 (s, C-6), 147.19 (s, C-8a), 161.17 (s, C-4) ppm; EI-MS: m/z (%) = 174 (M^+, 69), 159 (100), 146 (12), 132 (10), 118 (8), 104 (13), 91 (13), 77 (18); CI-MS: m/z (%) = 192 ($M^+ + NH_4$, 7), 175 (MH^+, 100), 147 (18), 52 (15); HRCI-MS: $C_{10}H_{11}N_2O$ (MH^+), calcd 175.0871, found 175.0870.

6-(Hydroxyphenylmethyl)-3H-quinazolin-4-one (**12**, $C_{15}H_{12}N_2O_2$)

Yield 81%; mp 178–179°C; ^{1}H NMR: $\delta = 5.87$ (s, CH), 6.12 (s, exch., OH), 7.22 (t, $J = 7.3$ Hz, $1H_{arom}$), 7.33 (t, $J = 7.3$ Hz, $2H_{arom}$), 7.41 (d, $J = 7.3$ Hz, $2H_{arom}$), 7.62 (d, $J = 8.3$ Hz, H-8), 7.81 (dd, $J = 8.3$, 1.5 Hz, H-7), 8.06 (s, H-2), 8.13 (d, $J = 1.5$ Hz, H-5), 12.22 (s, exch., NH) ppm; ^{13}C NMR: $\delta = 74.00$ (d, CH), 122.56 (s, C-4a), 123.18 (d), 126.19 (d), 127.31 (d), 128.59 (d), 132.98 (d), 134.68 (d), 144.74 (s, C_{arom}), 145.42 (s, C-6), 145.52 (d, C-2), 148.04 (s, C-8a), 161.16 (s, C-4) ppm; EI-MS: m/z (%) = 252 (M^+, 24), 173 (66), 147 (100), 105 (62), 90 (30), 77 (82), 51 (48); CI-MS: m/z

(%) = 270 ($M^+ + NH_4$, 2), 253 (MH^+, 61), 237 (12), 147 (100), 98 (25); HRCI-MS: $C_{15}H_{13}N_2O_2$ (MH^+), calcd 253.0977, found 253.0976.

6-[Hydroxy(4-methoxyphenyl)methyl]-3H-quinazolin-4-one (**13**, $C_{16}H_{14}N_2O_3$)

Yield 83%; mp 221–222°C; ^{1}H NMR: $\delta = 3.72$ (s, CH_3), 5.81 (s, CH), 6.01 (s, exch., OH), 6.89 (d, $J = 7.7$ Hz, $2H_{arom}$), 7.31 (d, $J = 7.7$ Hz, $2H_{arom}$), 7.60 (d, $J = 8.5$ Hz, H-8), 7.77 (dd, $J = 8.5$, 1.9 Hz, H-7), 8.06 (s, H-2), 8.11 (d, $J = 1.9$ Hz, H-5), 12.20 (s, exch., NH) ppm; ^{13}C NMR: $\delta = 55.37$ (q, CH_3), 73.58 (d, CH), 113.95 (d), 122.51 (s, C-4a), 123.04 (d), 127.38 (d), 127.96 (d), 132.96 (d), 137.64 (s, C_{arom}), 145.07 (s, C-6), 145.36 (d, C-2), 147.95 (s, C-8a), 158.60 (s, C_{arom}), 161.19 (s, C-4) ppm; EI-MS: m/z (%) = 282 (M^+, 41), 265 (10), 173 (52), 147 (91), 135 (61), 109 (100), 90 (43), 77 (88), 63 (38); CI-MS: m/z (%) = 300 ($M^+ + NH_4$, 5), 383 (MH^+, 91), 265 (100), 147 (18), 52 (14); HRCI-MS: $C_{16}H_{15}N_2O_3$ (MH^+), calcd 283.1082, found 283.1078.

6-(1-Hydroxycyclohexyl)-3H-quinazolin-4-one (**14**, $C_{14}H_{16}N_2O_2$)

Yield 85%; mp 217–219°C; ^{1}H NMR: $\delta = 1.28$–1.98 (m, $5CH_2$), 4.95 (s, exch., OH), 7.61 (d, $J = 8.3$ Hz, H-8), 7.91 (dd, $J = 8.3$, 2.0 Hz, H-7), 8.06 (s, H-2), 8.24 (d, $J = 2.0$ Hz, H-5), 12.19 (s, exch., NH) ppm; ^{13}C NMR: $\delta = 22.05$ (t, CH_2), 25.41 (t, CH_2), 38.59 (t, CH_2), 71.89 (s, C–OH), 121.70 (d), 122.22 (s, C-4a), 127.03 (d), 131.96 (d), 145.18 (d, C-2), 147.54 (s, C-6), 150.20 (s, C-8a), 161.35 (s, C-4) ppm; EI-MS: m/z (%) = 244 (M^+, 19), 226 (17), 201 (100), 188 (41), 159 (19), 145 (31), 115 (22), 90 (33), 77 (40), 63 (42), 55 (69); CI-MS: m/z (%) = 262 ($M^+ + NH_4$, 2), 245 (MH^+, 51), 227 (22), 147 (100), 116 (53), 98 (70), 84 (39); HRCI-MS: $C_{14}H_{17}N_2O_2$ (MH^+), calcd 245.1290, found 245.1286.

6-(1-Hydroxy-1-methylpentyl)-3H-quinazolin-4-one (**15**, $C_{14}H_{18}N_2O_2$)

Yield 88%; mp 128–129°C; ^{1}H NMR: $\delta = 0.76$ (t, $J = 7.2$ Hz, CH_3), 0.88–1.25 (m, $2CH_2$), 1.46 (s, CH_3), 1.66–1.76 (m, CH_2), 5.09 (s, exch., OH), 7.60 (d, $J = 8.5$ Hz, H-8), 7.84 (dd, $J = 8.5$, 1.8 Hz, H-7), 8.06 (s, H-2), 8.18 (d, $J = 1.8$ Hz, H-5), 12.16 (s, exch., NH) ppm; ^{13}C NMR: $\delta = 14.33$ (q, CH_3), 22.89 (t, CH_2), 26.15 (t, CH_2), 30.51 (q, CH_3), 43.99 (t, CH_2), 73.16 (s, C–OH), 122.00 (d), 122.17 (s, C-4a), 126.97 (d), 132.03 (d), 145.13 (d, C-2), 147.41 (s, C-6), 148.47 (s, C-8a), 161.34 (s, C-4) ppm; EI-MS: m/z (%) = 246 (M^+, 2), 189 (100), 173 (12), 147 (30), 57 (18); CI-MS: m/z (%) = 264 ($M^+ + NH_4$, 4), 247 (MH^+, 78), 231 (24), 189 (18), 164 (17), 147 (100), 111 (26), 98 (30); HRCI-MS: $C_{14}H_{19}N_2O_2$ (MH^+), calcd 247.1446, found 247.1448.

6-(Hydroxydiphenylmethyl)-3H-quinazolin-4-one (**16**, $C_{21}H_{16}N_2O_2$)

Yield 88%; mp 182–183°C; ^{1}H NMR: $\delta = 6.55$ (s, exch., OH), 7.07–7.19 (m, $10H_{arom}$), 7.47 (d, $J = 8.1$ Hz, H-8), 7.53 (dd, $J = 8.1$, 1.9 Hz, H-7), 7.76 (s, H-2), 7.92 (d, $J = 1.9$ Hz, H-5), 11.94 (s, exch., NH) ppm; ^{13}C NMR: $\delta = 80.79$ (s, C–OH), 121.91 (s, C-4a), 124.75 (d), 126.99 (d), 127.11 (d), 127.60 (d), 128.10 (d), 134.58 (d), 145.78 (d, C-2), 146.78 (s, C-6), 147.57 (s, C_{arom}), 147.99 (s, C-8a), 161.19 (s, C-4) ppm; EI-MS: m/z (%) = 328 (M^+, 12), 312 (14), 251 (68), 223 (52), 173 (53), 145 (22), 105 (91), 90 (23), 77 (100), 51 (26); CI-MS: m/z (%) = 346 ($M^+ + NH_4$, 5), 329 (MH^+, 72), 311 (75), 200 (27), 147 (100); HRCI-MS: $C_{21}H_{17}N_2O_2$ (MH^+), calcd 329.1290, found 329.1291.

6-(Phenylaminothiocarbonyl)-3H-quinazolin-4-one (**17**, $C_{15}H_{11}N_3SO$)

Yield 82%; mp 262–264°C; ^{1}H NMR: $\delta = 7.30$ (t, $J = 7.4$ Hz, $1H_{arom}$), 7.46 (t, $J = 7.4$ Hz, $2H_{arom}$), 7.74 (d, $J = 8.1$ Hz, H-8), 7.83 (d, $J = 7.4$ Hz, $2H_{arom}$), 8.21 (s, H-2), 8.31 (dd, $J = 8.1$, 2.2 Hz, H-7), 8.57 (d,

$J = 2.2$ Hz, H-5), 12.09 (s, exch., NH), 12.41 (s, exch., NH) ppm; ^{13}C NMR: $\delta = 122.17$ (s, C-4a), 124.65 (d), 124.98 (d), 126.78 (d), 127.33 (d), 128.92 (d), 134.11 (d), 140.29 (s, C_{arom}), 140.33 (s, C-6), 147.15 (d, C-2), 150.69 (s, C-8a), 161.06 (s, C-4), 196.09 (s, CS) ppm; EI-MS: m/z (%) = 281 (M^+, 22), 248 (16), 189 (100), 172 (14), 162 (13), 134 (12), 110 (22), 90 (18), 77 (47), 65 (27), 51 (23); CI-MS: m/z (%) = 282 (MH^+, 100), 252 (15), 189 (8), 161 (16), 147 (7), 94 (40), 52 (33); HRCI-MS: $C_{15}H_{12}N_3SO$ (MH^+), calcd 282.0701, found 282.0704.

6-(Diisopropyldithiocarbamoyl)-3H-quinazolin-4-one (**18**, $C_{15}H_{19}N_3S_2O$)

Yield 81%; mp 245–246°C; ^{1}H NMR (80°C): $\delta = 1.49$ (d, $J = 6.8$ Hz, $4CH_3$), 4.83 (heptet, $J = 6.8$ Hz, 2CH), 7.66 (d, $J = 8.4$ Hz, H-8), 7.74 (dd, $J = 8.4$, 2.1 Hz, H-7), 8.08 (s, H-2), 8.12 (d, $J = 2.1$ Hz, H-5), 11.89 (s, exch., NH) ppm; ^{13}C NMR (80°C): $\delta = 19.13$ (q, CH_3), 53.18 (d, CH), 122.39 (s, C-4a), 126.73 (d), 129.38 (s, C-6), 133.51 (d), 141.24 (d), 145.57 (d, C-2), 148.75 (s, C-8a), 159.40 (s, C-4), 192.67 (s, CS) ppm; EI-MS: m/z (%) = 321 (M^+, 100), 278 (33), 221 (5), 177 (12), 144 (27), 102 (55), 60 (34), 43 (85); CI-MS: m/z (%) = 322 (MH^+, 7), 179 (12), 146 (100), 116 (9), 102 (13); HRCI-MS: $C_{15}H_{20}N_3S_2O$ (MH^+), calcd 322.1048, found 322.1045.

6,6′-(1,3-Propanediyl)bis(3H-quinazolin-4-one) (**19**, $C_{19}H_{16}N_4O_2$)

Yield 71%; mp >300°C; ^{1}H NMR: $\delta = 1.95$ (t, $J = 7.0$ Hz, CH_2), 2.74 (t, $J = 7.0$ Hz, $2CH_2$), 7.56 (d, $J = 8.2$ Hz, 2H-8), 7.65 (dd, $J = 8.2$, 2.0 Hz, 2H-7), 7.92 (d, $J = 2.0$ Hz, 2H-5), 8.11 (s, 2H-2), 12.10 (s, exch., 2NH) ppm; ^{13}C NMR: $\delta = 33.73$ (t, CH_2), 34.68 (t, CH_2), 122.66 (s, C-4a), 126.24 (d), 127.22 (d), 135.38 (d), 141.26 (s, C-6), 145.36 (d, C-2), 146.56 (s, C-8a), 161.01 (s, C-4) ppm; EI-MS: m/z (%) = 332 (M^+, 12), 290 (10), 173 (40), 160 (48), 159 (91), 146 (35), 132 (31), 117 (25), 104 (26), 90 (48), 77 (63), 64 (100), 51 (65); CI-MS: m/z (%) = 350 ($M^+ + NH_4$, 8), 333 (MH^+, 93), 293 (25), 161 (37), 147 (100), 137 (26), 112 (22), 98 (38); HRCI-MS: $C_{19}H_{17}N_4O_2$ (MH^+), calcd 333.1351, found 333.1351.

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