Lithiation of 3-(Acylamino)-2-unsubstituted-, 3-(Acylamino)-2-ethyl-, and 3-(Acylamino)-2-propyl-4(3*H*)-quinazolinones: Convenient Syntheses of More Complex Quinazolinones[1]

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3-(Pivaloylamino)- and 3-(acetylamino)-4(3*H*)-quinazolinones react with alkyllithium reagents to give 1,2-addition products in very good yields. Lithiation takes place with LDA and is regioselective at position 2. The lithium reagents thus obtained react with a variety of electrophiles to give the corresponding substituted derivatives in very good yields. Reactions of the lithium reagents with iodine give oxidatively dimerized cyclic structures. 3-(Pivaloylamino)- and 3-(acetylamino)-2-ethyl-4(3*H*)-quinazolinones and 3-(pivaloylamino)- and 3-(acetylamino)-2-propyl-4(3*H*)-quinazolinones are lithiated at the benzylic position with LDA. The lithium reagents so produced also react with a variety of electrophiles to give the corresponding 2-substituted-4(3*H*)-quinazolinone derivatives in very good yields. However, lithiation of 3-(acylamino)-2-(1-methylethyl)-4(3*H*)-quinazolinones was unsuccessful, as were lithiations of compounds having a diacetylamino group at position 3. The amide groups have been cleaved in good yield under basic or acidic conditions from some of the products to provide access to the free amino compounds.

Introduction

Metalation of aromatic substrates is an important strategy for the synthesis of regiospecifically substituted benzenes and heterocycles.[2−5] However, the high reactivity of diazines toward nucleophilic addition renders the metalation of these compounds more difficult than for aromatic compounds which are less prone to such reactions.[5] Nevertheless, metalations of several pyrimidine derivatives have been reported.[6−10] Wolfe has shown that double lithiation provides a useful method for side-chain elaboration of 3-unsubstituted- or 3-aryl-2-methyl-4(3*H*)-quinazolinones.[11,12] In a continuation of our own interests in heterocyclic chemistry,[13] particularly in the use of lithiation for heterocyclic synthesis,[14] we have recently shown that 3-(acylamino)-2-methyl-4(3*H*)-quinazolinones also undergo lithiation at the methyl group with *n*-butyllithium.[1] We now report the synthesis of 2-substituted quinazolinone derivatives *via* lithiation of 3-(acylamino)-2-unsubstituted-, 3-(acylamino)-2-ethyl-, and 3-(acylamino)-2-propyl-4(3*H*)-quinazolinones. Compounds possessing this ring system show a variety of biological activities.[15]

Results and Discussion

3-(Pivaloylamino)-4(3*H*)-quinazolinone (**4**) and 3-(acetylamino)-4(3*H*)-quinazolinone (**5**) were synthesized according to Scheme 1.[16]

It was hoped that ortho-lithiation would take place as for (pivaloylamino)benzenes[2] or various (pivaloylami-

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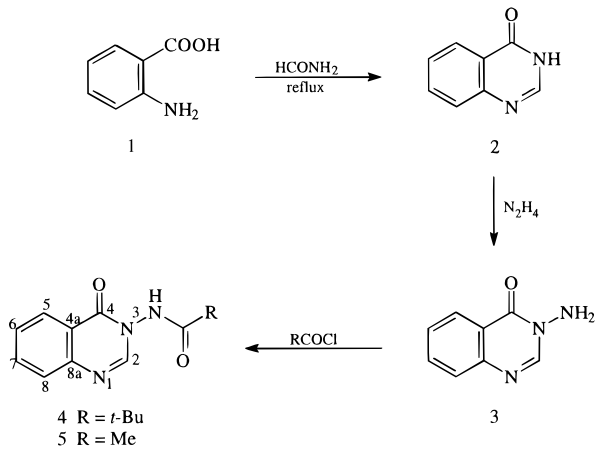
Scheme 1



Scheme 2

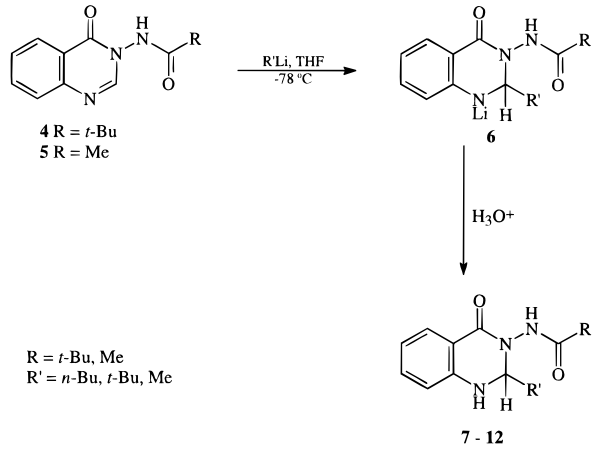


Table 1. Synthesis of 2-Alkyl-1,2-dihydro-4(3*H*)-quinazolinone Derivatives 7−12 According to Scheme 2

product	R	R′	yield, %[a]
7	*t*-Bu	*n*-Bu	96
8	*t*-Bu	*t*-Bu	98
9	*t*-Bu	Me	90
10	Me	*n*-Bu	82
11	Me	*t*-Bu	84
12	Me	Me	70

[a] Yields reported are for isolated and purified materials.

no)pyridines,[17] so that substitution of the hydrogen at position 2 could be achieved. However, it was found that lithiation of **4** and **5** did not take place with alkyllithiums. Instead, nucleophilic attack occurred at the imine bond to give 1,2-addition products (Scheme 2). The reactions of **4** and **5** with 1 equiv of alkyllithiums were complete within 5 min to give very good yields of 2-alkyl-1,2-dihydro-3-(acylamino)-4(3*H*)-quinazolinones **7**−**12** (Table 1).

The compounds **7**−**12** are fluorescent. Their ^{1}H NMR spectra show a characteristic H-2 signal in the δ 4.4−5.1 region, and their ^{13}C NMR spectra show that C-2 appears in the δ 68−80 region.

Chemoselective lithiation of 3-(acylamino)-4(3*H*)-quinazolinones **4** and **5** was achieved by use of LDA at −78 °C, and the reaction was regioselective at position

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Scheme 3

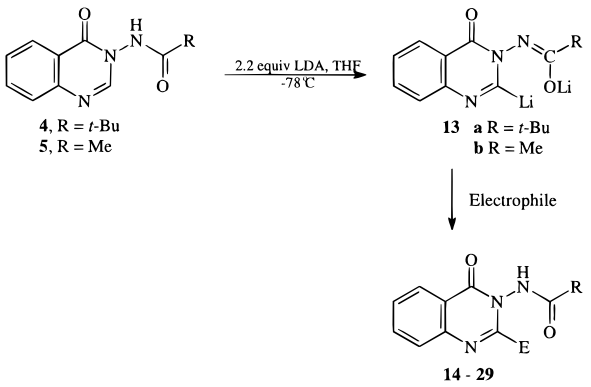

Table 2. Products from Reaction of Dilithio Compounds 13a and 13b with Electrophiles

Products	R	Electrophile	E	Yield %[a]
14	*t*-Bu	$(C_6H_5)_2CO$	$(C_6H_5)_2C(OH)$	85
15,16,17	*t*-Bu	MeI	Me, Et, *i*-Pr	89[b,c]
18	*t*-Bu	D_2O	D	88
19	*t*-Bu			87
20	*t*-Bu	$C_6H_5COCH_3$	$C_6H_5C(OH)(CH_3)$	85
21	*t*-Bu	C_6H_5NCO	C_6H_5NHCO	76
22	Me	$(C_6H_5)_2CO$	$(C_6H_5)_2C(OH)$	80
23,24,25	Me	MeI	Me, Et, *i*-Pr	92[b,d]
26	Me	D_2O	D	79
27	Me			81
28	Me	$C_6H_5COCH_3$	$C_6H_5C(OH)(CH_3)$	80
29	Me	C_6H_5NCO	C_6H_5NHCO	80

[a] Yields reported are for isolated and purified materials. [b] Overall yield obtained with MeI; see text for discussion. [c] **15** (67%); **16** (16%); **17** (6%). [d] **23** (59%); **24** (28%); **25** (5%).

2. Two molar equivalents of LDA were used, the first to remove the NH proton and the other one to remove the hydrogen from position 2 to form the dilithio derivatives **13** (Scheme 3). It is interesting that no deprotonation of the methyl group occurred for the case of compound **5** (R = Me), in view of the acidic character of the α-protons.[18] Such side reactions take place with simple acetanilides and account for the preferred use of the pivaloylamino group in directed lithiation reactions.[2] However, we have observed a similar phenomenon with the corresponding 2-methylquinazolinones.[1]

Reactions of the dilithio reagents **13a** and **13b** with a range of electrophiles (benzophenone, methyl iodide, D_2O, cyclohexanone, acetophenone, phenyl isocyanate) resulted in the production of the corresponding 2-substituted-4(3*H*)-quinazolinone derivatives **14**−**29** in very good yields (Table 2).

As can be seen from Table 2, there is little difference between the yields in the acetylamino series and those in the pivaloylamino series. The reactions with excess (4 equiv) methyl iodide resulted in almost quantitative yields of alkylated products, but as mixtures of 2-methyl-, 2-ethyl-, and 2-(1-methylethyl)quinazolinone derivatives.

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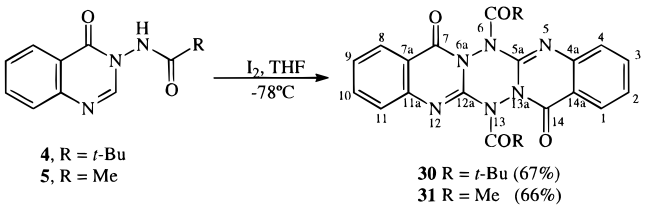
Scheme 4



It appears, therefore, that the 2-methylquinazolinone derivatives initially produced undergo lithiation by the excess LDA present in the reaction mixture and then methylate to give the 2-ethyl derivatives. These in turn react further to give the 2-(1-methylethyl) derivatives. The overall yields of products reflect the facts that production of ethyl compounds requires 2 equiv of base, that propyl derivatives require 3 equiv of base, and that a total of *ca.* 1.2 equiv of base are available after 1 equiv has been used for deprotonation of the acylamino derivative. We have not attempted to optimize the yield of any individual product from these reactions, but it is likely that control of the total amount of base and/or methyl iodide would be helpful in this respect. For our own purposes it was useful to have samples of compounds **16**, **17**, **24**, and **25** available for further study.

The ^{1}H NMR spectra of all of the products except **15**, **18**, **23**, and **26** show interesting diastereotopic features (see Experimental Section). For example, in the spectra of compounds **14** and **22** the two phenyl groups appear with separated signals, and for compounds **19** and **27** the two sides of the cyclohexane ring appear with separated signals. Similarly, for compounds **16** and **24**, the two hydrogen atoms of the CH_2 group at position 2 occur as independent, coupled signals, and for compounds **17** and **25**, the two methyl groups of the isopropyl group occur as two separate doublets. For compounds **20** and **28**, the extra complication of the presence of an asymmetric carbon atom results in the appearance in the NMR of two distereoisomers with unequal proportions. This phenomenon results from the orthogonal arrangement of the two ends of the hydrazine system and a high barrier to rotation about the N−N bond, as was also seen with products from 3-(acylamino)-2-methyl-4(3*H*)-quinazolinones.[1]

Reactions of the dilithio species **13** with iodine proceeded in an interesting manner. Instead of 2-iodoquinazolinone derivatives being formed, oxidative dimerization took place to give the pentacyclic compounds **30** and **31** (Scheme 4).

The ^{1}H NMR spectra of compounds **30** and **31** are characterized by the lack of NH protons. The FAB mass spectra for these compounds show pseudomolecular ion peaks (MH^+) at 487 and 403, respectively, and base peaks at 244 and 202, respectively.

Ethyl, *n*-propyl, and isopropyl groups were selected as representative alkyl groups for incorporation at position 2 of the 4(3*H*)-quinazolinone system, in order that lithiation of such compounds could be studied. Thus, compounds **16**, **17**, **24**, **25**, **35**, and **36** were prepared from **34** according to Scheme 5.[19] The yields of all compounds were excellent (Table 3).

Attempts to lithiate 3-(pivaloylamino)-2-ethyl-4(3*H*)-quinazolinone (**16**) and 3-(acetylamino)-2-ethyl-4(3*H*)-quinazolinone (**24**) with butyllithium gave only low

(19) Klosa, J. *J. Prakt. Chem.* **1961**, *31*, 3.

Scheme 5

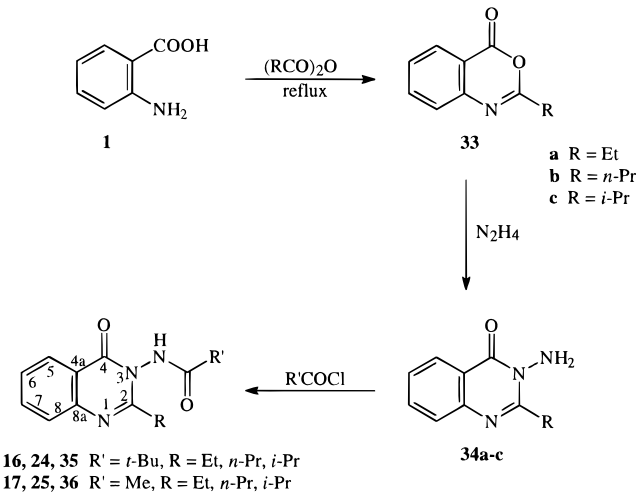
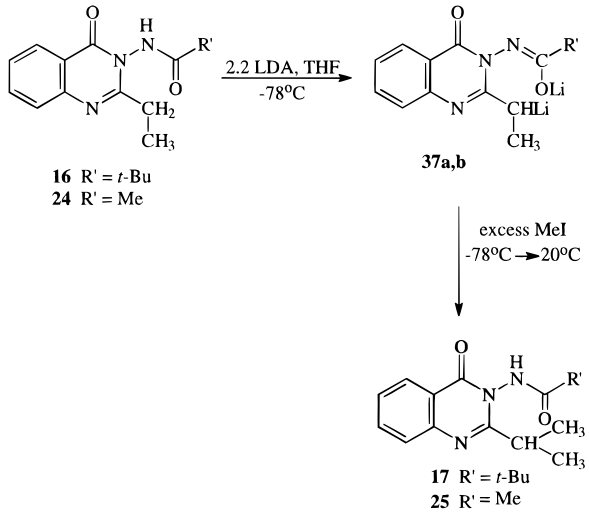


Table 3. 3-(Acylamino)-2-alkyl-4(3*H*)-quinazolinones 16, 17, 24, 25, 35, and 36 Prepared[a] According to Scheme 5

compd	R	R′	yield, %[b]
16	Et	*t*-Bu	90
17	*i*-Pr	*t*-Bu	90
24	Et	Me	81
25	*i*-Pr	Me	89
35	*n*-Pr	*t*-Bu	91
36	*n*-Pr	Me	87

[a] See Experimental Section for details. [b] Yields reported are for isolated and purified materials.

Scheme 6

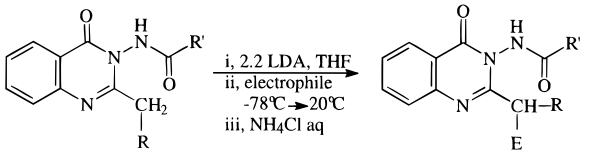


yields. However, successful lithiation was achieved with 2.2 molar equiv of LDA in THF at −78 °C for 1 h. Initial addition of LDA provided a yellow solution when approximately 1 equiv had been added and then gave a deep red solution as the remaining LDA was added. Addition of methyl iodide gave compound **17** from compound **16** and compound **25** from **24** in 92% and 84% isolated yields, respectively (Scheme 6).

In order to test the versatility of the intermediate dilithio compounds **37**, they were reacted with several electrophiles (Scheme 7, R = Me). The results are shown in Table 4.

As can be seen from Table 4, the dianions **37** react with a variety of electrophiles to form the corresponding substituted products **38**−**49** in good yields. In the reactions of the dianion of **24** (*i.e.*, **37b**) with benzophe-

Scheme 7



16 R' = *t*-Bu, R = Me
24 R' = Me, R = Me
35 R' = *t*-Bu, R = Et
36 R' = Me, R = Et

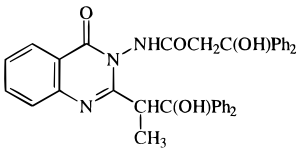
38 - 49, R = Me
52 - 57, R = Et

Table 4. Products from Reactions According to Scheme 7 (R = Me)[a]

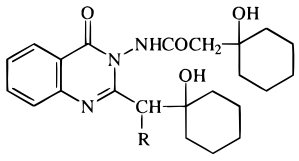
Product	Electrophile	E	R′	Yield %[b]
17	MeI	Me	*t*-Bu	92
38	$(C_6H_5)_2CO$	$(C_6H_5)_2C(OH)$	*t*-Bu	90
39	D_2O	D	*t*-Bu	88
40			*t*-Bu	82
41			*t*-Bu	84
42	$C_6H_5COCH_3$	$C_6H_5C(OH)(CH_3)$	*t*-Bu	81
43	I_2	I	*t*-Bu	70
25	MeI	Me	Me	84
44	$(C_6H_5)2CO$	$(C_6H_5)_2C(OH)$	Me	80
45	D_2O	D	Me	81
46			Me	82
47			Me	80
48	$C_6H_5COCH_3$	$C_6H_5C(OH)(CH_3)$	Me	77
49	I_2	I	Me	70

[a] See Experimental Section for details. [b] Yields reported are for isolated and purified products.

none and cyclohexanone a small quantity (3−4% yield) of a byproduct was isolated. This resulted in each case from attack of a further equivalent of the electrophile on the methyl group of the acetylamino unit, giving rise to the products **50** and **51** respectively.



50



51 R = Me
58 R = Et

Apparently, the excess of LDA was giving rise to a small quantity of trianion, which in turn led to **50** and **51**. However, by use of 2.0 equiv of LDA instead of 2.2 equiv it was possible to eliminate the byproduct completely.

Attention was next turned to lithiation of 3-(acylamino)-2-propyl-4(3*H*)-quinazolinones. It was hoped that lithiation of **35** and **36** would take place as for **16** and **24**, which would suggest that the process was tolerant of a variety of primary alkyl groups at position 2. It was found that lithiation of **35** and **36** with LDA did indeed take place smoothly and that the dilithio reagents produced reacted with representative electrophiles (methyl iodide, benzophenone, cyclohexanone) to give the corresponding 2-substituted-4(3*H*)-quinazolinones **52**−**57** (Scheme 7, R = Et) in very good yields (Table 5).

Table 5. Products from Reactions According to Scheme 7 (R = Et)[a]

Product	Electrophile	E	R′	Yield %[b]
52	MeI	Me	*t*-Bu	90
53	$(C_6H_5)_2CO$	$(C_6H_5)_2C(OH)$	*t*-Bu	92
54			*t*-Bu	88
55	MeI	Me	Me	86
56	$(C_6H_5)_2CO$	$(C_6H_5)_2C(OH)$	Me	87
57			Me	85

[a] See Experimental Section for details. [b] Yields reported are for isolated and purified products.

A side product obtained (5% yield) in the reaction of the dianion of **36** with cyclohexanone was identified as 2-[1-(1-hydroxycyclohexyl)propyl]-3-[[(1-hydroxycyclohexyl)-acetyl]amino]-4(3*H*)-quinazolinone (**58**), evidently formed again by further lithiation in the acetyl group. This side product was eliminated when 2.0 equiv of lithiating agent were used instead of 2.2 equiv.

In order to discover whether the reaction was applicable to cases in which there was a secondary alkyl group at position 2 of the quinazolinone system, lithiations of 3-(pivaloylamino)-2-(1-methylethyl)-4(3*H*)-quinazolinone (**17**) and 3-(acetylamino)-2-(1-methylethyl)-4(3*H*)-quinazolinone (**25**) with LDA were attempted. However, after attempted trapping with methyl iodide **17** and **25** were recovered unchanged. Similarly, attempts to lithiate 2-alkyl-3-(diacetylamino)-4(3*H*)-quinazolinones and 2-unsubstituted-3-(diacetylamino)-4(3*H*)-quinazolinone met with failure.

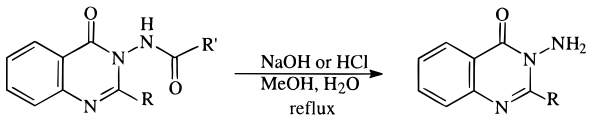
We have previously shown that it is possible to hydrolyze the acylamino group of 2-ethyl-3-(acylamino)-4(3*H*)-quinazolinones under basic conditions to provide access to the corresponding 3-amino compound.[1] In order to demonstrate whether the hydrolysis is possible in acidic conditions too and also for other 2-substituents, we have hydrolyzed **15**, **17**, **23**, and **25** under acidic and/or basic conditions. We found that addition of hydrochloric acid or aqueous sodium hydroxide to a methanolic solution of these compounds, followed by a period of reflux, removed the acyl group to give 3-amino-2-methyl-4(3*H*)-quinazolinone (**32**)[20] or 3-amino-2-(1-methylethyl)-4(3*H*)-quinazolinone (**34c**)[21] in good yield (Scheme 8).

Conclusion

Direct lithiation of 3-(acylamino)-4(3*H*)-quinazolinones with LDA is a facile, practical, and regiospecific process

(20) Bogert, M. T.; Gortner, R. A. *J. Am. Chem. Soc.* **1909**, *31*, 943.
(21) Fahmy, A. F. M.; El-Hashash, M. A.; Habashy, M. A.; El-Wannise, S. A. *Rev. Roum. Chim.* **1978**, *23*, 1567; *Chem. Abstr.* **1978**, *91*, 20422.

Scheme 8



15 R = Me, R' = t-Bu
17 R = *i*-Pr, R' = Me
23 R = Me, R' = Me
25 R = *i*-Pr, R' = Me

32 R = Me (75%)
34c R = *i*-Pr (75%)

providing access to a broad variety of 2-substituted derivatives. A similar metalation procedure allows regiospecific electrophilic substitution of 3-(acylamino)-2-*n*-alkyl-4(3*H*)-quinazolinones at the benzylic position of the *n*-alkyl group. These procedures provide efficient syntheses of more complicated 3-(acylamino)-2-substituted-4(3*H*)-quinazolinone derivatives, which are not easily synthesized by other routes. The facility with which the acylamino group can be cleaved, as exemplified by the syntheses of 3-amino-2-alkyl-4(3*H*)-quinazolinones, makes the process even more attractive for the elaboration of structures with potential pharmacological significance.

Experimental Section

Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz for ^{1}H and 100 MHz for ^{13}C. Low-resolution mass spectra were recorded at 70 ev (EI) or by the use of ammonia as ionization gas (CI). Elemental analyses were obtained from the Laboratories of the University of Wales, Cardiff. Column chromatography was carried out using Merck Kieselgel 60 (230−400 mesh). Alkyllithiums were estimated prior to use by the method of Watson and Eastham.[22] THF was distilled from sodium benzophenone ketyl. Other solvents were purified by standard procedures.[23,24] Other chemicals were used without further purification. All compounds gave microanalyses and accurately mass measured molecular ions (or MH^+ ions) which confirmed their elemental composition. IR and mass spectra were in agreement with the assigned structures.

3-(Pivaloylamino)-4(3*H*)-quinazolinone (4). A mixture of **3** (5.00 g, 31.0 mmol), pivaloyl chloride (4.00 g, 32.0 mmol), and Et_3N (4 mL) in dry toluene (60 mL) was heated under reflux for 30 min with stirring. The organic layer was washed twice with a saturated $NaHCO_3$ solution (20 mL) and H_2O (25 mL), dried ($MgSO_4$), and evaporated *in vacuo*. Crystallization from EtOAc/Et_2O gave cotton-like white crystals (6.46 g, 26.0 mmol; 85%): mp 136 °C; ^{1}H NMR ($CDCl_3$) δ 8.91 (s, exch, 1H), 8.19 (d, J = 8.2 Hz, 1H), 7.91 (s, 1H), 7.74 (t, J = 8.2 Hz, 1H), 7.67 (d, J = 8.2 Hz, 1H), 7.47 (t, J = 8.2 Hz, 1H), 1.34 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 179.3, 159.4, 147.4, 147.1, 134.8, 127.8, 127.5, 126.7, 122.0, 38.9, 27.2; HRMS calcd for $C_{13}H_{16}N_3O_2$ 246.1243, found 246.1243. Anal. Calcd for $C_{13}H_{15}N_3O_2$: C, 63.67; H, 6.12; N, 17.14. Found: C, 63.45; H, 6.28; N, 17.23.

3-(Acetylamino)-4(3*H*)-quinazolinone (5). Compound **5** was prepared according to the literature method as white crystals: mp 210−211 °C (lit. mp 168−170 °C, shrinks at 120−125 °C);[16] ^{1}H NMR (DMSO-d_6) δ 11.26 (s, exch, 1H), 8.22 (s, 1H), 8.19 (d, J = 8.1 Hz, 1H), 7.87 (t, J = 8.1 Hz, 1H), 7.73 (d, J = 8.1 Hz, 1H), 7.59 (t, J = 8.1 Hz, 1H), 2.11 (s, 3H); ^{13}C NMR (DMSO-d_6) δ 169.4, 158.4, 148.8, 147.2, 134.7, 127.4, 127.3, 126.3, 122.0, 20.4; HRMS calcd for $C_{10}H_9N_3O_2$ 203.0695, found 203.0695. Anal. Calcd for $C_{10}H_9N_3O_2$: C, 59.11; H, 4.43; N, 20.69. Found: C, 59.22; H, 4.16; N, 20.85

General Procedure for the Synthesis of 3-(Acylamino)-2-alkyl-1,2-dihydro-4(3*H*)-quinazolinones. To a cooled (−78 °C), stirred solution of **4** or **5** (2.0 mmol) in THF (20 mL) under N_2 was added a solution of alkyllithium (2.7 mL of 1.6 M, 2.2 mmol). The yellow solution obtained was allowed to stir at −78 °C for 5 min; then the temperature was raised to 0 °C. The mixture was quenched with aqueous saturated NH_4Cl (20 mL) and diluted with Et_2O (20 mL). The organic layer was washed with H_2O (2 × 20 mL), dried ($MgSO_4$), and evaporated. The products obtained were recrystallized from EtOAc to give white crystals.

2-Butyl-3-(pivaloylamino)-1,2-dihydro-4(3*H*)-quinazolinone (7): mp 157−158 °C; ^{1}H NMR ($CDCl_3$) δ 8.54 (s, exch, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.23 (t, J = 8.0 Hz, 1H), 6.75 (t, J = 8.0 Hz, 1H), 6.63 (d, J = 8.0 Hz, 1H), 4.97 (m, 1H), 4.92 (s, exch, 1H), 1.64 (m, 2H), 1.32 (s, 9H), 1.27−1.16 (m, 4H), 0.81 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 178.2, 163.5, 146.2, 133.9, 128.6, 118.9, 115.5, 115.0, 71.4, 38.5, 32.0, 26.5, 22.3, 27.4, 13.9; HRMS calcd for $C_{17}H_{26}N_3O_2$ 304.2025, found 304.2025. Anal. Calcd for $C_{17}H_{25}N_3O_2$: C, 67.32; H, 8.25; N, 13.86. Found: C, 67.43; H, 8.48; N, 13.79.

2-(1,1-Dimethylethyl)-3-(pivaloylamino)-1,2-dihydro-4(3*H*)-quinazolinone (8): mp 200−202 °C; ^{1}H NMR ($CDCl_3$) δ 8.58 (s, exch, 1H), 7.71 (d, J = 7.8 Hz, 1H), 7.17 (t, J = 7.8 Hz, 1H), 6.66 (t, J = 7.8 Hz, 1H), 6.56 (d, J = 7.8 Hz, 1H), 5.25 (d, J = 4.5 Hz, exch, 1H), 4.70 (d, J = 4.5 Hz, 1H), 1.32 (s, 9H), 0.89 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 177.2, 162.5, 146.9, 137.1, 128.2, 117.8, 114.6, 114.2, 79.1, 40.8, 38.4, 27.3, 25.8; HRMS calcd for $C_{17}H_{26}N_3O_2$ 304.2025, found 304.2021. Anal. Calcd for $C_{17}H_{25}N_3O_2$: C, 67.32; H, 8.25; N, 13.86. Found: C, 67.34; H, 8.30; N, 13.79.

2-Methyl-3-(pivaloylamino)-1,2-dihydro-4(3*H*)-quinazolinone (9): mp 235 °C; ^{1}H NMR (DMSO-d_6) δ 9.70 (s, exch, 1H), 7.61 (d, J = 7.9 Hz, 1H), 7.27 (t, J = 7.9 Hz, 1H), 6.73 (s, exch, 1H), 6.71−6.69 (m, 2H), 5.64 (q, J = 5.7 Hz, 1H), 1.32 (d, J = 5.7 Hz, 3H), 1.18 (s, 9H); ^{13}C NMR (DMSO-d_6) δ 176.6, 162.8, 148.0, 133.5, 128.0, 117.5, 114.5, 114.3, 67.4, 37.6, 27.2, 19.2; HRMS calcd for $C_{14}H_{20}N_3O_2$ 262.1556, found 262.1556. Anal. Calcd for $C_{14}H_{19}N_3O_2$: C, 64.36; H, 7.28; N, 16.09. Found: C, 64.15; H, 7.36; N, 15.96.

3-(Acetylamino)-2-butyl-1,2-dihydro-4(3*H*)-quinazolinone (10): mp > 250 °C; ^{1}H NMR ($CDCl_3$) δ 9.08 (br s, exch, 1H), 7.82 (d, J = 7.9 Hz, 1H), 7.32 (t, J = 7.9 Hz, 1H), 6.82 (t, J = 7.9 Hz, 1H), 6.66 (d, J = 7.9 Hz, 1H), 5.04 (m, 1H), 4.74 (br s, exch, 1H), 2.10 (s, 3H), 1.84−1.77 (m, 2H), 1.34−1.26 (m, 4H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 169.8, 163.5, 146.0, 134.3, 128.7, 119.1, 115.6, 114.9, 71.9, 32.9, 26.6, 22.4, 20.9, 13.9; HRMS calcd for $C_{14}H_{20}N_3O_2$ 262.1556, found 262.1556. Anal. Calcd for $C_{14}H_{19}N_3O_2$: C, 64.36; H, 7.28; N, 16.09. Found: C, 64.44; H, 7.38; N, 16.03.

3-(Acetylamino)-2-(1,1-dimethylethyl)-1,2-dihydro-4(3*H*)-quinazolinone (11): mp > 250 °C; ^{1}H NMR (DMSO-d_6) δ 10.24 (s, exch, 1H), 7.50 (d, J = 7.8 Hz, 1H), 7.18 (t, J = 7.8 Hz, 1H), 7.01 (d, exch, J = 3.1 Hz, 1H), 6.67 (d, J = 7.8 Hz, 1H), 6.54 (t, J = 7.8 Hz, 1H), 4.43 (d, J = 3.1 Hz, 1H), 1.89 (s, 3H), 0.85 (s, 9H); ^{13}C NMR (DMSO-d_6) δ 167.7, 161.2, 147.6, 133.5, 127.5, 115.7, 113.4, 113.2, 79.0, 40.7, 25.2, 20.6; HRMS calcd for $C_{14}H_{20}N_3O_2$ 262.1556, found 262.1556. Anal. Calcd for $C_{14}H_{19}N_3O_2$: C, 64.36; H, 7.28; N, 16.09. Found: C, 64.56; H, 7.38; N, 16.02.

3-(Acetylamino)-2-methyl-1,2-dihydro-4(3*H*)-quinazolinone (12): mp > 250 °C; ^{1}H NMR ($CDCl_3$) δ 9.30 (s, exch, 1H), 7.78 (d, J = 7.9 Hz, 1H), 7.24 (t, J = 7.9 Hz, 1H), 6.76 (t, J = 7.9 Hz, 1H), 6.62 (d, J = 7.9 Hz, 1H), 5.21−5.17 (m, 1H), 5.03 (d, J = 5.9 Hz, exch, 1H), 2.05 (s, 3H), 1.41 (d, J = 5.9 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 170.3, 164.0, 146.6, 134.3, 128.7, 119.2, 115.4, 114.6, 68.2, 20.7, 19.2; HRMS calcd for $C_{11}H_{14}N_3O_2$ 220.1086, found 220.1086. Anal. Calcd for $C_{11}H_{13}N_3O_2$: C, 60.27; H, 5.93; N, 19.18. Found: C, 60.43; H, 5.99; N, 19.09.

General Procedure for the Synthesis of 3-(Acylamino)-2-substituted-4(3*H*)-quinazolinones 14−31. A solution of LDA in heptane (2.7 mL of 1.6 M, 4.4 mmol) was added in a dropwise manner to a stirred solution of **4** or **5** (2.0 mmol) in THF (20 mL, N_2 atmosphere) maintained at −78 °C. Formation of the dianion was observed as a yellowish brown solution. The mixture was stirred at −78 °C for an additional 1 h, after

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which an electrophile (2.2 mmol) (in THF (8 mL) if solid, otherwise neat) was added. The mixture was stirred for 4 h and then removed from the cooling bath and allowed to warm to room temperature, diluted with Et_2O (15 mL), and quenched with aqueous saturated NH_4Cl (15 mL). The organic layer was washed with H_2O (2 × 20 mL), dried ($MgSO_4$), and evaporated. The products obtained were recrystallized from EtOAc to give white crystals.

2-(Hydroxydiphenylmethyl)-3-(pivaloylamino)-4(3*H*)-quinazolinone (14): mp 149−151 °C; ^{1}H NMR ($CDCl_3$) δ 8.25 (d, J = 8.1 Hz, 1H), 7.82 (t, J = 8.1 Hz, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.55 (t, J = 8.1 Hz, 1H), 7.47−7.31 (m, 10H), 6.86 (s, exch, 1H), 6.21 (s, exch, 1H), 0.97 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 176.6, 160.0, 158.4, 144.8, 142.4, 141.9, 135.0, 128.3, 128.2, 128.12, 128.07, 127.9, 127.83, 127.79, 127.7, 127.3, 121.1, 81.0, 38.6, 26.7; HRMS calcd for $C_{26}H_{26}N_3O_3$ 428.1974, found 428.1974. Anal. Calcd for $C_{26}H_{25}N_3O_3 \cdot H_2O$: C, 70.11; H, 6.06; N, 9.40. Found: C, 70.12; H, 6.18; N, 9.40.

2-Methyl-3-(Pivaloylamino)-4(3*H*)-quinazolinone (15): mp 161−163 °C (lit. mp 161−163 °C).[1]

2-Ethyl-3-(pivaloylamino)-4(3*H*)-quinazolinone (16): mp 194−195 °C (lit. mp 194−195 °C).[1]

2-(1-Methylethyl)-3-(pivaloylamino)-4(3*H*)-quinazolinone (17): mp 174−175 °C; ^{1}H NMR ($CDCl_3$) δ 8.45 (s, exch, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.70 (t, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 3.04 (hept, J = 6.7 Hz, 1H), 1.36 (s, 9H), 1.27, 1.19 (2 d, J = 6.7 Hz, 6H); ^{13}C NMR ($CDCl_3$) δ 179.2, 161.83, 160.6, 147.1, 134.6, 127.6, 126.5, 126.4, 120.5, 38.9, 31.0, 27.2, 21.0, 20.1; HRMS calcd for $C_{16}H_{21}N_3O_2$ 287.1634, found 287.1634. Anal. Calcd for $C_{16}H_{21}N_3O_2$: C, 66.90; H, 7.32; N, 14.63. Found: C, 66.68; H, 7.51; N, 14.48.

2-Deuterio-3-(pivaloylamino)-4(3*H*)-quinazolinone (18): mp 136 °C; ^{1}H NMR ($CDCl_3$) δ 8.85 (s, exch, 1H), 8.19 (d, J = 8.0 Hz, 1H), 7.75 (t, J = 8.0 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.47 (t, J = 8.0 Hz, 1H), 1.34 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 179.3, 159.41, 159.38, 147.1, 134.8, 127.8, 127.5, 127.0, 122.0, 38.9, 27.2; HRMS calcd for $C_{13}H_{14}N_3O_2D$ 246.1227, found 246.1227.

2-(1-Hydroxycyclohexyl)-3-(pivaloylamino)-4(3*H*)-quinazolinone (19): mp 208 °C; ^{1}H NMR ($CDCl_3$) δ 8.40 (s, exch, 1H), 8.13 (d, J = 8.0 Hz, 1H), 7.70 (t, J = 8.0 Hz, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.42 (t, J = 8.0 Hz, 1H), 4.79 (s, exch, 1H), 2.15−1.18 (m, 10H), 1.35 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 178.7, 160.5, 159.9, 145.3, 134.9, 127.7, 127.2, 127.0, 120.5, 73.9, 39.0, 35.0, 34.7, 25.4, 21.7, 21.6, 21.1; HRMS calcd for $C_{19}H_{26}N_3O_3$, 344.1974, found 344.1974. Anal. Calcd for $C_{19}H_{25}N_3O_3$: C, 66.47; H, 7.29; N, 12.24. Found: C, 66.51; H, 7.30; N, 12.21.

2-(1-Hydroxy-1-phenylethyl)-3-(pivaloylamino)-4(3*H*)-quinazolinone (20): mp 175−176 °C. Compound **20** appears in its NMR spectra as a mixture of two isomers, **a** and **b**, with a ratio of 3:5. ^{1}H NMR ($CDCl_3$): **20a**, δ 8.19 (d, J = 8.0 Hz, 1H), 7.77 (t, J = 8.0 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.35−7.24 (m, 7H), 4.78 (s, exch, 1H), 1.93 (s, 3H), 1.04 (s, 9H); **20b**, δ 8.19 (d, J = 8.0 Hz, 1H), 7.77 (t, J = 8.0 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.35−7.24 (m, 7H), 5.73 (s, exch, 1H), 1.88 (s, 3H), 1.07 (s, 9H). ^{13}C NMR ($CDCl_3$): **20a**, δ 177.9, 160.6, 158.5, 145.3, 143.9, 134.9, 128.4, 127.9, 127.5, 127.3, 127.1, 124.8, 121.1, 75.1, 38.7, 29.7, 26.8; **20b**, δ 176.9, 160.0, 159.5, 145.0, 143.1, 134.9, 128.7, 127.9, 127.8, 127.3, 127.1, 125.5, 121.1, 75.9, 38.6, 29.7, 26.8. HRMS: calcd for $C_{21}H_{24}N_3O_3$ 366.1818, found 366.1818. Anal. Calcd for $C_{21}H_{23}N_3O_3$: C, 69.04; H, 6.30; N, 11.50. Found: C, 69.09; H, 6.38; N, 11.40.

2-[(Phenylamino)carbonyl]-3-(pivaloylamino)-4(3*H*)-quinazolinone (21): mp 266−268 °C; ^{1}H NMR (DMSO-d_6) δ 11.02 (s, exch, 1H), 10.87 (s, exch, 1H), 8.21 (d, J = 8.0 Hz, 1H), 7.95 (t, J = 8.0 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.70−7.67 (m, 3H), 7.36 (t, J = 8.1 Hz, 2H), 7.13 (t, J = 8.1 Hz, 1H), 1.14 (s, 9H); ^{13}C NMR (DMSO-d_6) δ 176.9, 158.6, 158.4, 151.1, 146.0, 137.9, 137.8, 135.4, 128.9, 128.4, 127.9, 126.6, 124.5, 121.9, 119.9, 37.9, 26.8; HRMS calcd for $C_{20}H_{21}N_4O_3$ 365.1614, found 365.1614. Anal. Calcd for $C_{20}H_{20}N_4O_3$: C, 65.93; H, 5.49; N, 15.38. Found: C, 65.77; H, 5.68; N, 15.38.

3-(Acetylamino)-2-(hydroxydiphenylmethyl)-4(3*H*)-quinazolinone (22): mp 197−198 °C; ^{1}H NMR (DMSO-d_6) δ 10.22 (s, exch, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.99 (t, J = 8.0 Hz, 1H), 7.55 (t, J = 8.0 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.36−7.19 (m, 10H), 5.78 (s, exch, 1H), 1.37 (s, 3H); ^{13}C NMR (DMSO-d_6) δ 166.6, 159.4, 158.4, 144.9, 143.1, 134.7, 128.2, 128.0, 127.8, 127.7, 127.6, 127.0, 126.7, 126.5, 126.3, 121.2, 81.5, 19.7; HRMS calcd for $C_{23}H_{20}N_3O_3$ 386.1505, found 386.1505. Anal. Calcd for $C_{23}H_{19}N_3O_3$: C, 71.69; H, 4.93; N, 10.91. Found: C, 71.49; H, 5.06; N, 10.71.

3-(Acetylamino)-2-methyl-4(3*H*)-quinazolinone (23): mp 175−176 °C (lit. mp 176.5 °C).[20]

3-(Acetylamino)-2-ethyl-4(3*H*)-quinazolinone (24): mp 135−136 °C (lit. mp 136−138 °C).[19]

3-(Acetylamino)-2-(1-methylethyl)-4(3*H*)-quinazolinone (25): mp 122 °C; ^{1}H NMR ($CDCl_3$) δ 9.32 (s, exch, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.72 (t, J = 8.0 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.40 (t, J = 8.0 Hz, 1H), 3.18 (hept, J = 6.8 Hz, 1H), 2.27 (s, 3H), 1.32, 1.27 (2 d, J = 6.8 Hz, 6H); ^{13}C NMR ($CDCl_3$) δ 170.9, 161.9, 147.3, 134.9, 127.7, 126.59, 126.58, 120.4, 31.0, 21.3, 21.0, 20.1; HRMS calcd for $C_{13}H_{15}N_3O_2$ 245.1164, found 245.1164. Anal. Calcd for $C_{13}H_{15}N_3O_2 \cdot H_2O$: C, 59.31; H, 6.44; N, 15.97. Found: C, 59.04; H, 6.63; N, 15.96.

3-(Acetylamino)-2-deuterio-4(3*H*)-quinazolinone (26): mp 211 °C; ^{1}H NMR (DMSO-d_6) δ 11.45 (s, exch, 1H), 8.32 (d, J = 8.0 Hz, 1H), 7.99 (t, J = 8.0 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.70 (t, J = 8.0 Hz, 1H), 2.25 (s, 3H); ^{13}C NMR (DMSO-d_6) δ 169.2, 158.3, 158.0, 147.3, 134.5, 127.4, 127.1, 126.3, 122.1, 20.4; HRMS calcd for $C_{10}H_8N_3O_2D$ 204.0758, found 204.0758.

3-(Acetylamino)-2-(1-hydroxycyclohexyl)-4(3*H*)-quinazolinone (27): mp 170 °C; ^{1}H NMR (DMSO-d_6) δ 11.62 (s, exch, 1H), 8.09 (d, J = 8.0 Hz, 1H), 7.84 (t, J = 8.0 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.53 (t, J = 8.0 Hz, 1H), 5.12 (s, exch, 1H), 2.07 (s, 3H), 2.00−1.25 (m, 10H); ^{13}C NMR (DMSO-d_6) δ 169.3, 160.9, 159.7, 145.5, 134.8, 127.5, 127.1, 126.4, 120.7, 73.7, 35.4, 34.8, 25.2, 21.6, 21.5, 21.0; HRMS calcd for $C_{16}H_{20}N_3O_3$ 302.1505, found 302.1505. Anal. Calcd for $C_{16}H_{19}N_3O_3 \cdot H_2O$: C, 60.18; H, 6.58; N, 13.16. Found: C, 60.02; H, 6.39; N, 13.04.

3-(Acetylamino)-2-(1-hydroxy-1-phenylethyl)-4(3*H*)-quinazolinone (28): mp 189−190 °C. Compound **28** appears in its NMR spectra as a mixture of two isomers **a** and **b** with a ratio of 1:3. ^{1}H NMR (DMSO-d_6): **28a**, δ 9.85 (s, exch, 1H), 8.09 (d, J = 8.0 Hz, 1H), 7.87 (t, J = 8.0 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.56 (t, J = 8.0 Hz, 1H), 7.32−7.12 (m, 5H), 6.09 (s, exch, 1H), 1.69 (s, 3H), 1.37 (s, 3H); **28b**, δ 10.23 (s, exch, 1H), 8.09 (d, J = 8.0 Hz, 1H), 7.87 (t, J = 8.0 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.57 (t, J = 8.0 Hz, 1H), 7.32−7.12 (m, 5H), 6.41 (s, exch, 1H), 1.81 (s, 3H), 1.37 (s, 3H). ^{13}C NMR (DMSO-d_6): **28a**, δ 168.4, 159.7, 159.2, 145.4, 144.7, 135.0, 127.9, 127.7, 127.3, 126.6, 126.2, 124.7, 121.0, 75.3, 29.9, 20.4; **28b**, δ 166.0, 160.0, 159.2, 145.5, 144.7, 134.8, 127.8, 127.7, 127.4, 126.6, 126.5, 123.9, 121.3, 76.4, 32.6, 19.7. HRMS: calcd for $C_{18}H_{18}N_3O_3$ 324.1548, found 324.1548. Anal. Calcd for $C_{18}H_{17}N_3O_3$: C, 66.87; H, 5.26; N, 13.00. Found: C, 66.61; H, 5.43; N, 12.88.

3-(Acetylamino)-2-[(phenylamino)carbonyl]-4(3*H*)-quinazolinone (29): mp 251−252 °C; ^{1}H NMR (DMSO-d_6) δ 11.19 (s, exch, 1H), 10.72 (s, exch, 1H), 8.23 (d, J = 8.0 Hz, 1H), 7.90 (t, J = 8.0 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 8.0 Hz, 2H), 7.58 (t, J = 8.0 Hz, 1H), 7.32 (t, J = 8.0 Hz, 2H), 7.10 (t, J = 8.0 Hz, 1H), 2.05 (s, 3H); ^{13}C NMR (DMSO-d_6) δ 169.0, 158.7, 158.3, 150.5, 145.9, 138.0, 134.8, 128.6, 128.4, 127.8, 127.7, 126.8, 124.3, 124.2, 122.1, 120.1, 20.5; HRMS calcd for $C_{17}H_{14}N_4O_3$ 322.1066, found 322.1066. Anal. Calcd for $C_{17}H_{14}N_4O_3$: C, 63.35; H, 4.34; N, 17.39. Found: C, 63.26; H, 4.58; N, 17.45.

6,13-Dipivaloyl-1,2,4,5-tetrazino[3,2-*b*:6,5-*b*′]bisquinazoline-7,14(6*aH*,13*aH*)-dione (30): mp 155−157 °C; ^{1}H NMR ($CDCl_3$) δ 8.40 (d, J = 8.0 Hz, 2H), 7.78 (t, J = 8.0 Hz, 2H), 7.70 (d, J = 8.0 Hz, 2H), 7.47 (t, J = 8.0 Hz, 2H), 1.52 (s, 18H); ^{13}C NMR ($CDCl_3$) δ 168.3, 155.7, 151.7, 147.1, 135.0, 127.5, 126.7, 125.4, 118.9, 33.2, 27.3; HRMS calcd for $C_{26}H_{27}N_6O_4$ 487.2093, found 487.2098. Anal. Calcd for $C_{26}H_{26}N_6O_4$: C, 64.19; H, 5.35; N, 17.28. Found: C, 64.38; H, 5.71; N, 17.31.

6,13-Diacetyl-1,2,4,5-tetrazino[3,2-*b*:6,5-*b*′]bisquinazoline-7,14(6*aH*,13*aH*)-dione (31): mp 255−257 °C; ^{1}H NMR (DMSO-d_6) δ 8.25 (d, J = 8.0 Hz, 2H), 7.84 (t, J = 8.0 Hz, 2H),

7.65 (d, J = 8.0 Hz, 2H), 7.50 (t, J = 8.0 Hz, 2H), 2.58 (s, 6H); ^{13}C NMR (DMSO-d_6) δ 160.0, 155.3, 152.1, 147.1, 135.1, 126.8, 126.5, 125.3, 118.7, 11.6; HRMS calcd for $C_{20}H_{15}N_6O_4$ 403.1155, found 403.1155. Anal. Calcd for $C_{20}H_{14}N_6O_4$: C, 59.70; H, 3.48; N, 20.89. Found: C, 59.54; H, 3.50; N, 20.68.

General Procedure for the Synthesis of 2-Alkyl-3-(pivaloylamino)-4(3*H*)-quinazolinones. A mixture of the appropriate compound **34**[21,25] (36.6 mmol), pivaloyl chloride (4.80 g, 39.4 mmol), and Et_3N (8 mL) in dry toluene (80 mL) was heated under reflux for 30 min, with stirring. The organic layer was washed with saturated $NaHCO_3$ (2 × 20 mL) and H_2O (25 mL), dried ($MgSO_4$), and evaporated. Crystallization from EtOAc gave white crystals. In the cases of compounds **16** and **17** the products were identical in all respects to the compounds obtained according to Scheme 3.

3-(Pivaloylamino)-2-propyl-4(3*H*)-quinazolinone (35): mp 152 °C; ^{1}H NMR ($CDCl_3$) δ 8.41 (s, exch, 1H, NH), 8.12 (d, J = 8.0 Hz, 1H), 7.71 (t, J = 8.0 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.39 (t, J = 8.0 Hz, 1H), 2.59−2.62 (m, 2H), 1.72 (sextet, J = 7.5 Hz, 2H), 1.37 (s, 9H), 0.97 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 179.0, 160.4, 157.8, 147.0, 134.8, 127.4, 126.54, 126.48, 120.5, 38.9, 35.5, 27.2, 19.9, 13.8; HRMS calcd for $C_{16}H_{22}N_3O_2$ 288.1712, found 288.1712. Anal. Calcd for $C_{16}H_{21}N_3O_2$: C, 66.90; H, 7.32; N, 14.63. Found: C, 67.08; H, 7.47; N, 14.83.

General Procedure for the Synthesis of 3-(Acetylamino)-2-alkyl-4(3*H*)-quinazolinones. Compounds **24** and **25** were prepared according to a literature procedure.[19] Compound 36 was prepared in similar manner.

3-(Acetylamino)-2-propyl-4(3*H*)-quinazolinone (36): mp 135−136 °C; ^{1}H NMR ($CDCl_3$) δ 9.38 (s, exch, 1H), 8.13 (d, J = 8.0 Hz, 1H), 7.73 (t, J = 8.0 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.39 (t, J = 8.0 Hz, 1H), 2.79−2.64 (m, 2H), 2.24 (s, 3H), 1.79 (sextet, J = 7.3 Hz, 2H), 1.02 (t, J = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 170.7, 160.9, 157.8, 147.1, 135.0, 127.5, 126.63, 126.62, 120.5, 35.4, 20.9, 19.9, 13.8; HRMS calcd for $C_{13}H_{16}N_3O_2$ 246.1243, found 246.1243. Anal. Calcd for $C_{13}H_{15}N_3O_2$: C, 63.67; H, 6.12; N, 17.14. Found: C, 63.82; H, 6.17; N, 17.43.

General Procedure for the Synthesis of 3-(Acylamino)-2-substituted-4(3*H*)-quinazolinones 38 −58. A solution of LDA in pentane (2.7 mL of 1.6 M, 4.4 mmol) was added dropwise under nitrogen to a stirred solution of the appropriate 3-(acylamino)-2-alkyl-4(3*H*)-quinazolinone (**16**, **24**, **35**, or **36**) (2.0 mmol) in THF (20 mL) at −78 °C. Formation of the dianion was observed as a very deep red solution. The mixture was stirred at −78 °C for 30 min, after which an electrophile (2.2 mmol) (as a solution in THF for solids) was added. The mixture was stirred for 2 h, then allowed to warm to room temperature, diluted with Et_2O (20 mL), and quenched with aqueous saturated NH_4Cl (20 mL). The organic layer was washed with H_2O (2 × 20 mL), dried ($MgSO_4$), and evaporated. The products were purified by column chromatography (Et_2O) and then crystallized, usually from EtOAc, to give white crystals.

2-(2-Hydroxy-2,2-diphenyl-1-methylethyl)-3-(pivaloylamino)-4(3*H*)-quinazolinone (38): mp 196−197 °C. Compound **38** appeared as a mixture of two isomers, **a** and **b**, in a ratio of 1:2 in its NMR spectra. ^{1}H NMR ($CDCl_3$): **38a**, δ 8.15 (d, J = 8.0 Hz, 1H), 7.78 (t, J = 8.0 Hz, 1H), 7.61−7.09 (m, 14H), 4.00 (q, J = 6.8 Hz, 1H), 1.46 (s, 9H), 1.22 (d, J = 6.8 Hz, 3H); **38b**, δ 8.06 (d, J = 8.0 Hz, 1H), 7.69 (t, J = 8.0 Hz, 1H), 7.61−7.01 (m, 14H), 4.33 (q, J = 6.8 Hz, 1H), 1.44 (s, 9H), 1.35 (d, J = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$): **38a**, δ 179.4, 161.5, 159.8, 147.8, 145.8, 145.1, 134.9, 128.3, 128.1, 127.0, 126.7, 126.3, 126.0, 125.5, 120.2, 79.3, 42.4, 39.2, 27.3, 14.6; **38b**, δ 179.4, 161.5, 159.6, 147.8, 145.4, 144.7, 135.0, 128.2, 128.0, 126.9, 126.8, 126.2, 126.0, 125.2, 120.3, 79.5, 42.1, 39.2, 27.3, 14.9. HRMS: calcd for $C_{28}H_{30}N_3O_3$ 456.2287, found 456.2287. Anal. Calcd for $C_{28}H_{29}N_3O_3$: C, 73.84; H, 6.37; N, 9.23. Found: C, 73.73; H, 6.49; N, 9.14.

2-(1-Deuterioethyl)-3-(pivaloylamino)-4(3*H*)-quinazolinone (39): mp 194−195 °C; ^{1}H NMR ($CDCl_3$) δ 8.44 (s, exch, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.71 (t, J = 8.0 Hz, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.40 (t, J = 8.0 Hz, 1H), 2.64−2.62 (m), 1.36, 1.20 (m, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 180.0, 160.4, 158.5, 147.0, 134.7, 127.5, 126.5, 126.5, 120.453, 38.951, 27.2, 26.6, 26.4, 26.2, 10.4; HRMS calcd for $C_{15}H_{19}N_3O_2D$ 275.1618, found 275.1618.

2-[1-(1-Hydroxycyclohexyl)ethyl]-3-(pivaloylamino)-4(3*H*)-quinazolinone (40): mp 174−175 °C. Compound **40** appears in its NMR spectra as a mixture of two isomers, **a** and **b**, in a ratio of 5:6. ^{1}H NMR ($CDCl_3$): **40a**, δ 8.24 (s, exch, 1H), 8.19 (d, J = 8.0 Hz, 1H), 7.75 (t, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.44 (t, J = 8.0 Hz, 1H), 5.79 (s, exch, 1H), 2.87 (q, J = 7.0 Hz, 1H), 1.40 (s, 9H), 1.30 (d, J = 7.0 Hz, 3H), 1.84−1.19 (m, 10H); **40b**, δ 8.29 (s, exch, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.75 (t, J = 8.0 Hz, 1H), 7.65 (d, J = 8.0Hz, 1H), 7.44 (t, J = 8.0 Hz, 1H), 5.02 (s, exch, 1H), 3.14 (q, J = 7.0 Hz, 1H), 1.41 (s, 9H), 1.34 (d, J = 7.0 Hz, 3H), 1.84−1.19 (m, 10H). ^{13}C NMR ($CDCl_3$): **40a**, δ 179.1, 162.4, 160.0, 145.5, 135.0, 127.1, 126.95, 126.9, 120.5, 72.2, 42.5, 39.0, 37.7, 35.4, 27.2, 25.7, 22.1, 21.9, 13.6; **40b**, δ 179.1, 161.8, 160.0, 145.9, 135.0, 127.3, 126.9, 126.8, 120.4, 72.7, 42.3, 39.0, 39.0, 34.8, 25.7, 21.8, 21.8, 27.2, 13.4. HRMS: calcd for $C_{21}H_{30}N_3O_3$ 372.2287, found 372.2287. Anal. Calcd for $C_{21}H_{29}N_3O_3$: C, 67.92; H, 7.81; N, 11.32. Found: C, 67.98; H, 7.94; N, 11.17.

2-[1-(1-Hydroxycyclopentyl)ethyl]-3-(pivaloylamino)-4(3*H*)-quinazolinone (41): mp 122−124 °C. Compound **41** appears as a mixture of two isomers, **a** and **b**, in a ratio of 5:8 in its NMR spectra. ^{1}H NMR ($CDCl_3$): **41a**, δ 8.32 (s, exch, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 8.0 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.44 (t, J = 8.0 Hz, 1H), 5.27 (s, exch, 1H), 3.10 (q, J = 7.0 Hz, 1H), 1.93−1.46 (m, 8H), 1.40 (s, 9H), 1.36 (d, J = 7.0 Hz, 3H); **41b**, δ 8.38 (s, exch, 1H), 8.16 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 8.0 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.44 (t, J = 8.0 Hz, 1H), 5.64 (s, exch, 1H), 2.76 (q, J = 7.0 Hz, 1H), 1.93−1.46 (m, 8H), 1.39 (s, 9H), 1.38 (d, J = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$): **41a**, δ 179.3, 162.2, 159.9, 145.8, 135.0, 127.1, 126.9, 126.8, 120.6, 83.4, 43.6, 40.1, 39.0, 38.2, 27.2, 24.1, 23.9, 15.0; **41b**, δ 179.3, 162.4, 159.9, 145.6, 135.0, 127.2, 126.9, 126.8, 120.6, 83.1, 44.0, 39.07, 38.8, 38.2, 27.2, 23.89, 23.86, 15.3. HRMS: calcd for $C_{20}H_{28}N_3O_3$ 358.2131, found 358.2131. Anal. Calcd for $C_{20}H_{27}N_3O_3$: C, 67.22; H, 7.56; N, 11.67. Found: C, 67.00; H, 7.60; N, 11.57.

2-(2-Hydroxy-1-methyl-2-phenylpropyl)-3-(pivaloylamino)-4(3*H*)-quinazolinone (42): mp 120−121 °C. Compound **42** appears in its NMR spectra as a mixture of two isomers, **a** and **b**, in a ratio of 3:4. ^{1}H NMR ($CDCl_3$): **42a**, δ 8.42 (s, exch, 1H), 8.20 (d, J = 8.0 Hz, 1H), 7.77 (t, J = 8.0 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.49−7.30 (m, 6H), 5.87 (s, exch, 1H), 3.47 (q, J = 7.0 Hz, 1H), 1.36 (s, 3H), 1.40 (s, 9H), 1.07 (d, J = 7.0 Hz, 3H); **42b**, δ 8.49 (s, exch, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.77 (t, J = 8.0 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.49−7.30 (m, 6H), 6.51 (s, exch, 1H), 3.20 (q, J = 7.0 Hz, 1H), 1.37 (s, 3H), 1.45 (s, 9H), 0.98 (d, J=8.0 Hz, 3H). ^{13}C NMR ($CDCl_3$): **42a**, δ 179.4, 162.3, 159.9, 146.0, 145.5, 135.2, 128.2, 128.0, 127.1, 126.9, 126.5, 124.8, 120.6, 75.6, 44.6, 39.1, 29.8, 27.2, 14.7; **42b**, 179.3, 162.3, 159.9, 146.5, 145.8, 135.2, 128.3, 128.2, 127.2, 127.0, 126.7, 124.7, 120.5, 75.6, 44.4, 39.1, 30.0, 27.2, 15.1. HRMS: calcd for $C_{23}H_{28}N_3O_3$ 394.2131, found 394.2131. Anal. Calcd for $C_{23}H_{27}N_3O_3$: C, 70.23; H, 6.87; N, 10.68. Found: C, 70.29; H, 7.09; N, 10.44.

2-(1-Iodoethyl)-3-(pivaloylamino)-4(3*H*)-quinazolinone (43): mp 167−168 °C; ^{1}H NMR ($CDCl_3$) δ 8.22 (d, J = 8.0 Hz, 1H), 8.09 (s, exch, 1H), 7.77−7.72 (m, 2H), 7.48 (t, J = 8.0 Hz, 1H), 4.93 (q, J = 6.9 Hz, 1H), 2.27 (d, J = 6.9 Hz, 3H), 1.43 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 178.8, 160.0, 156.8, 146.6, 134.9, 128.2, 127.4, 127.0, 121.1, 39.1, 27.1, 24.3, 16.4; HRMS calcd for $C_{15}H_{19}N_3O_2I$ 400.0522, found 400.0522. Anal. Calcd for $C_{15}H_{18}N_3O_2I$: C, 45.11; H, 4.51; N, 10.52. Found: C, 45.29; H, 4.63; N, 10.29.

3-(Acetylamino)-2-(2-hydroxy-2,2-diphenyl-1-methylethyl)-4(3*H*)-quinazolinone (44): mp 139−140 °C. Compound **44** appears in its NMR spectra as a mixture of two isomers, **a** and **b**, in a ratio of 1:2. ^{1}H NMR ($CDCl_3$): **44a**, δ 8.74 (s, exch, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.73−6.89 (m, 14H), 4.10 (q, J = 6.9 Hz, 1H), 3.32 (s, 3H), 1.34 (d, J = 6.9 Hz, 3H); **44b**, δ 8.76 (s, exch, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.73−6.89 (m, 14H), 4.42 (q, J = 6.9 Hz, 1H), 2.25 (s, 3H), 1.24 (d, J = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$): **44a**, δ 171.5, 161.8, 160.4, 147.9, 145.4, 144.7, 135.2, 128.1, 127.0, 126.6, 126.3, 125.6, 125.1, 120.1, 79.4, 42.5, 21.3, 14.7; **44b**, δ 171.5, 161.9, 160.3,

147.9, 145.53, 144.7, 135.4, 128.2, 127.2, 126.7, 126.4, 126.0, 125.5, 120.1, 79.7, 42.3, 21.2, 15.3. HRMS: calcd for $C_{25}H_{24}N_3O_3$ 414.1818, found 414.1818. Anal. Calcd for $C_{25}H_{23}N_3O_3$: C, 72.64; H, 5.57; N, 10.17. Found: C, 72.51; H, 5.70; N, 10.39.

3-(Acetylamino)-2-(1-deuterioethyl)-4(3*H*)-quinazolinone (45): mp 135−136 °C; ^{1}H NMR ($CDCl_3$) δ 9.12 (s, exch, 1H), 8.15 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 8.0 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H, H-8), 7.42 (t, J = 8.0 Hz, 1H, H-6), 2.84−2.78 (m, 1H, CH), 2.26 (s, 3H), 1.32 (m, J = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 170.2, 160.9, 158.6, 147.2, 135.0, 127.5, 126.71, 126.66, 120.5, 26.9, 26.6, 26.4, 21.0, 10.6; HRMS calcd for $C_{12}H_{13}N_3O_2D$ 233.1149, found 233.1149.

3-(Acetylamino)-2-[1-(1-hydroxycyclohexyl)ethyl]-4(3*H*)-quinazolinone (46): mp 139−140 °C. Compound **46** appears in its NMR spectra as a mixture of two isomers, **a** and **b**, in a ratio of 9:10. ^{1}H NMR ($CDCl_3$): **46a**, δ 9.50 (s, exch, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 8.0 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.41 (t, J = 8.0 Hz, 1H), 5.89 (s, exch, 1H), 2.96 (q, J = 7.0 Hz, 1H), 2.29 (s, 3H), 1.92−1.35 (m, 10H), 1.28 (d, J = 7.0 Hz, 3H); **46b**, δ 9.50 (s, exch, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 8.0 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.41 (t, J = 8.0 Hz, 1H), 5.18 (s, exch, 1H), 3.21 (q, J = 7.0 Hz, 1H), 2.30 (s, 3H), 1.92−1.35 (m, 10H), 1.32 (d, J = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$): **46a**, δ 170.9, 162.1, 160.3, 145.5, 135.2, 127.3, 127.0, 126.7, 120.3, 72.3, 42.8, 36.9, 35.2, 25.6, 21.9, 21.7, 21.0, 13.5; **46b**, δ 171.0, 162.5, 160.3, 145.9, 135.2, 127.1, 127.0, 126.7, 120.4, 72.7, 42.8, 37.4, 34.8, 25.6, 21.9, 21.7, 21.0, 13.7. HRMS: calcd for $C_{18}H_{24}N_3O_3$ 330.1818, found 330.1818. Anal. Calcd for $C_{18}H_{23}N_3O_3$: C, 65.65; H, 6.99; N, 12.76. Found: C, 65.78; H, 7.02; N, 12.79.

3-(Acetylamino)-2-[1-(1-hydroxycyclopentyl)ethyl]-4(3*H*)-quinazolinone (47): mp 133−135 °C. Compound **47** appears in its NMR spectra as a mixture of two isomers, **a** and **b**, in a ratio of 9:11. ^{1}H NMR (DMSO-d_6): **47a**, δ 10.87 (s, exch, 1H), 8.17 (d, J = 8.0 Hz, 1H), 7.76 (t, J = 8.0 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.46 (t, J = 8.0 Hz, 1H), 5.26 (s, exch, 1H), 3.26 (q, J = 7.0 Hz, 1H), 2.19 (s, 3H), 2.01−1.46 (m, 8H), 1.33 (d, J = 7.0 Hz, 3H); **47b**, δ 10.87 (s, exch, 1H). 8.17 (d, J = 8.0 Hz, 1H), 7.78 (t, J = 8.0 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.46 (t, J = 8.0 Hz, 1H), 5.59 (s, exch, 1H), 2.90 (q, J = 7.0 Hz, 1H), 2.20 (s, 3H), 2.01−1.46 (m, 8H), 1.39 (d, J = 7.0 Hz, 3H). ^{13}C NMR (DMSO-d_6): **47a**, δ 175.1, 167.8, 164.0, 150.4, 139.7, 131.8, 131.7, 131.5, 125.6, 87.9, 48.0, 44.8, 42.7, 28.9, 28.7, 25.7, 20.0; **47b**, δ 175.0, 167.8, 164.0, 150.6, 139.7, 131.8, 131.7, 131.5, 125.7, 87.6, 48.6, 44.9, 43.3, 28.7, 28.9, 25.7, 20.2. HRMS: calcd for $C_{17}H_{22}N_3O_3$ 316.1661, found 316.1661. Anal. Calcd for $C_{17}H_{21}N_3O_3$: C, 61.26; H, 6.91; N, 12.61. Found: C, 61.12; H, 6.91; N, 12.63.

3-(Acetylamino)-2-(2-hydroxy-1-methyl-2-phenylpropyl)-4(3*H*)-quinazolinone (48): mp 130−131 °C. Compound **48** appears in its NMR spectra as a mixture of two isomers, **a** and **b**, in a ratio of 2:3. ^{1}H NMR ($CDCl_3$): **48a**, δ 9.21 (s, exch, 1H), 8.13 (d, J = 8.0 Hz, 1H), 7.76 (t, J = 8.0 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.50−7.24 (m, 6H), 6.03 (s, exch, 1H), 3.57 (q, J = 7.0 Hz, 1H), 2.29 (s, 3H), 1.39 (s, 3H); **48b**, δ 9.24 (s, exch, 1H) 8.13 (d, J = 8.0 Hz, 1H), 7.76 (t, J = 8.0 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.50−7.24 (m, 6H), 6.59 (s, exch, 1H), 3.30 (q, J = 7.0 Hz, 1H), 2.33 (s, 3H), 1.63 (s, 3H), 1.00 (d, J = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$): **48a**, δ 171.1, 161.8, 160.3, 146.2, 145.5, 135.4, 128.2, 127.3, 127.2, 126.9, 126.6, 124.9, 120.4, 75.6, 44.5, 29.9, 21.0; 14.9; **48b**, d 171.0, 162.3, 160.3, 146.2, 145.8, 128.3, 127.1, 126.8, 126.6, 124.8, 120.5, 75.6, 44.6, 29.9, 21.1, 15.3. HRMS: calcd for $C_{20}H_{22}N_3O_3$ 352.1661, found 352.1661. Anal. Calcd for $C_{20}H_{21}N_3O_3$: C, 68.37; H, 5.98; N, 11.92. Found: C, 68.16; H, 6.23; N, 11.62.

3-(Acetylamino)-2-(1-iodoethyl)-4(3*H*)-quinazolinone (49): mp 145−146 °C. Compound **49** appears in its NMR spectra as a mixture of two isomers, **a** and **b**, in a ratio of 2:9. ^{1}H NMR (DMSO-d_6): **49a**, δ 10.59 (s, exch, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.80 (t, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.33 (t, J = 8.0 Hz, 1H), 5.40 (q, J = 6.8 Hz, 1H), 3.44 (s, 3H), 2.23 (d, J = 6.8 Hz, 3H); **49b**, δ 10.98 (s, exch, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.80 (t, J = 8.0 Hz, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 5.10 (q, J = 6.8 Hz, 1H), 3.44 (s, 3H), 2.25 (d, J = 6.8 Hz, 3H). ^{13}C NMR (DMSO-d_6): **49a**, δ 168.8, 158.8, 157.3, 146.2, 134.4, 127.4, 126.1, 125.9, 119.5, 25.1, 20.9, 14.2; **49b**, δ 170.8, 159.5, 157.6, 146.2, 134.5, 127.5, 126.9, 126.5, 120.8, 24.2, 20.5, 15.6. HRMS: calcd for $C_{12}H_{12}N_3O_2I$ 356.9974, found 356.9974. Anal. Calcd for $C_{12}H_{11}N_3O_2I$: C, 40.33; H, 3.36. N, 11.76. Found: C, 40.47; H, 3.26; N, 11.71.

2-(2-Hydroxy-2,2-diphenyl-1-methylethyl)-3-[[(hydroxydiphenylmethyl)acetyl]amino]-4(3*H*)-quinazolinone (50): mp 202 °C. Compound **50** appears in its NMR spectra as a mixture of two isomers, **a** and **b**, in a ratio of 3:5. ^{1}H NMR (DMSO-d_6): **50a**, δ 10.99 (s, exch, 1H), 8.06 (d, J = 8.0 Hz, 1H), 7.74−6.88 (m, 24H), 6.29 (s, exch, 1H), 4.19 (q, J = 6.8 Hz, 1H), 3.73, 3.51 (2 d, J = 15.0 Hz, 2H), 1.15 (d, J = 6.8 Hz, 3H); **50b**, δ 11.33 (s, exch, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.74−6.88 (m, 24H), 6.01 (s, exch, 1H), 4.26 (q, J = 6.8 Hz, 1H), 3.79, 3.38 (2 d, J = 15.0 Hz, 2H), 0.70 (d, J = 6.8 Hz, 3H). ^{13}C NMR (DMSO-d_6): **50a**, 171.1, 162.6, 158.4 148.2, 147.5, 146.3, 145.1, 144.8, 134.8, 128.1, 128.0, 126.8, 126.5, 126.4, 125.8, 125.7, 125.3, 125.2, 120.0, 79.2, 76.2, 44.9, 41.4, 14.5; **50b**, δ 171.9, 162.7, 158.4, 148.4, 146.9, 146.1, 145.6, 144.9, 134.9, 128.1, 128.0, 127.8, 127.7, 126.8, 126.0, 125.6, 125.5, 125.4, 120.1, 78.9, 76.2, 44.7, 41.6, 14.0. HRMS: calcd for $C_{38}H_{34}N_3O_4$ 596.2549, found 596.2546. Anal. Calcd for $C_{38}H_{33}N_3O_4$: C, 76.64; H, 5.54; N, 7.06. Found: C, 76.40; H, 5.74; N, 6.99.

2-[1-(1-Hydroxycyclohexyl)ethyl]-3-[[(1-hydroxycyclohexyl)acetyl]amino]-4(3*H*)-quinazolinone (51): mp 102−104 °C. Compound **51** appears in its NMR spectra as a mixture of two isomers, **a** and **b**, in a ratio of 5:6. ^{1}H NMR ($CDCl_3$): **51a**, δ 9.35 (s, exch, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.61 (t, J = 8.0 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.18 (t, J = 8.0 Hz, 1H), 5.14 (s, exch, 1H), 4.46 (s, exch, 1H), 2.97 (q, J = 7.0 Hz, 1H), 1.96−1.25 (m, 20H), 1.36 (d, J = 7.0 Hz, 3H); **51b**, δ 9.30 (s, exch, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.57 (t, J = 8.0 Hz, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H), 5.68 (s, exch, 1H), 4.28 (s, exch, 1H), 3.23 (q, J = 7.0 Hz, 1H), 1.96−1.25 (m, 20H), 1.28 (d, J = 7.0 Hz, 3H). HRMS: calcd for $C_{24}H_{34}N_3O_4$ 428.2549, found, 428.2549.

2-(1-Methylpropyl)-3-(pivaloylamino)-4(3*H*)-quinazolinone (52): mp 126−128 °C. Compound **52** appears in its NMR spectra as a mixture of two isomers, **a** and **b**, in a ratio of 1:1. ^{1}H NMR ($CDCl_3$): **52a**, δ 8.30 (s, exch, 1H), 8.15 (d, J = 8.0 Hz, 1H), 7.72 (t, J = 8.0 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.40 (t, J = 8.0 Hz, 1H), 2.80 (sextet, J = 6.8 Hz, 1H), 1.94 (d quintet, J = *ca.* 7 and 15 Hz, 1H), 1.58−1.45 (m, 1H), 1.39 (s, 9H), 1.19 (d, J = 6.8 Hz, 3H), 0.92 (t, J = 6.8 Hz, 3H); **52b**, δ 8.30 (s, exch, 1H), 8.15 (d, J = 8.0 Hz, 1H), 7.72 (t, J = 8.0 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.40 (t, J = 8.0 Hz, 1H), 2.89 (sextet, J = 6.6 Hz, 1H), 1.73 (d quintet, J = *ca.* 7 and 15 Hz, 1H), 1.58−1.45 (m, 1H), 1.40 (s, 9H), 1.29 (d, J = 6.6 Hz, 3H), 0.86 (t, J = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$): **52a**, δ 179.1, 161.4, 160.7, 147.2, 134.6, 127.3, 126.6, 126.4, 120.4, 40.0, 37.9, 27.2, 27.1, 18.7, 11.9; **52b**, δ 179.2, 161.4, 160.7, 147.2, 134.7, 127.6, 126.6, 126.4, 120.5, 39.0, 37.6, 28.7, 27.2, 17.6, 12.0. HRMS: calcd for $C_{17}H_{24}N_3O_2$ 302.1869, found 302.1869. Anal. Calcd for $C_{17}H_{23}N_3O_2$: C, 67.77; H, 7.64; N, 13.95. Found: C, 67.55; H, 7.75; N, 13.99.

2-[1-(Hydroxydiphenylmethyl)propyl]-3-(pivaloylamino)-4(3*H*)-quinazolinone (53): mp 175 °C. Compound **53** appears in its NMR spectra as a mixture of two isomers, **a** and **b**, in a ratio of 1:6. ^{1}H NMR ($CDCl_3$): **53a** δ 8.13 (d, J = 8.0 Hz, 1H), 7.83−7.08 (m, 13H), 6.79 (s, exch, 1H), 6.38 (s, exch, 1H), 4.11 (br, 1H), 1.98, 1.80 (two m, 2H), 1.33 (s, 9H), 0.74 (br, 3H); **53b**, δ 8.13 (d, J = 8.0 Hz, 1H), 7.83−7.08 (m, 13H), 4.17 (dd, J = 3 and 10 Hz, 1H), 2.18 (ddq, J = 10, 15 and 7 Hz, 1H), 1.92 (ddq, J = 3, 15 and 10 Hz, 1H), 1.43 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 177.9, 160.3, 159.0, 147.1, 145.5, 144.2, 135.1, 128.4, 127.9, 127.2, 127.1, 125.8, 125.1, 120.5, 79.6, 50.4, 38.9, 27.36, 23.4, 12.8. HMRS: calcd for $C_{29}H_{32}N_3O_3$ 470.2444, found 470.2444. Anal. Calcd for $C_{29}H_{31}N_3O_3$: C, 74.20; H, 6.61; N, 8.95. Found: C, 73.97; H, 6.71; N, 8.98.

2-[1-(1-Hydroxycyclohexyl)propyl]-3-(pivaloylamino)-4(3*H*)-quinazolinone (54): mp 80 °C. Compound **54** appears in its NMR spectra as a mixture of two isomers, **a** and **b**, in a ratio of 10:11. ^{1}H NMR ($CDCl_3$): **54a**, δ 8.16 (d, J = 8.0 Hz, 1H), 8.04 (s, exch, 1H), 7.74 (t, J = 8.0 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.42 (t, J = 8.0 Hz, 1H), 4.16 (s, exch, 1H), 2.91 (dd, J = 4.4 and 9.6 Hz, 1H), 2.16−1.16 (complex overlapping

signals, 12H), 1.42 (s, 9H), 0.87 (t, J = 7.5 Hz, 3H); **54b**, δ 8.26 (s, exch, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.76 (t, J = 8.0 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.46 (t, J = 8.0 Hz, 1H), 5.58 (s, exch, 1H), 3.01 (dd, J = 3.3 and 9.7 Hz, 1H), 2.16−1.16 (complex overlapping signals, 12H), 0.83 (t, J = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$): **54a**, δ 178.8, 162.1, 160.0, 145.6, 134.8, 127.2, 126.9, 126.8, 120.6, 72.9, 49.7, 39.0, 37.6, 35.8, 28.3, 27.2, 25.8, 22.7, 20.6, 12.5; **54b**, δ 177.9, 160.4, 159.8, 146.1, 135.1, 127.4, 127.0, 126.7, 120.4, 73.8, 51.5, 38.9, 37.6, 34.4, 27.3, 27.0, 25.6, 21.9, 21.6, 13.2. HRMS: calcd for $C_{22}H_{32}N_3O_3$ 386.2444, found 386.2444. Anal. Calcdfor $C_{22}H_{31}N_3O_3$: C, 68.57; H, 8.05; N, 10.91. Found: C, 68.65; H, 8.17; N, 10.73.

3-(Acetylamino)-2-(1-methylpropyl)-4(3*H*)-quinazolinone (55): mp 102−104 °C. Compound **55** appears in its NMR spectra as a mixture of two isomers, **a** and **b**, in a ratio of 1:1. ^{1}H NMR ($CDCl_3$): **55a**, δ 9.47 (s, exch, 1H), 8.17 (d, J = 8.0 Hz, 1H), 7.73 (t, J = 8.0 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 2.92 (sextet, J = 7.0 Hz, 1H), 2.26 (s, 3H), 1.99 (d quintet, J = *ca.* 7 and 15 Hz, 1H), 1.62−1.51 (m, 1H), 1.23 (d, J = 7.0 Hz, 3H), 0.93 (t, J = 7.5 Hz, 3H); **55b**, δ 9.47 (s, exch, 1H), 8.17 (d, J = 8.0 Hz, 1H), 7.73 (t, J = 8.0 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 3.04 (sextet, J = 7.0 Hz, 1H), 2.27 (s, 3H), 1.81 (d quintet, J = *ca.* 7 and 15 Hz, 1H), 1.62−1.51 (m, 1H), 1.30 (d, J = 7.0 Hz, 3H), 0.87 (t, J = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$): **55a**, δ 170.7, 161.6, 161.2, 147.3, 134.9, 127.6, 126.6, 126.5, 120.3, 37.9, 28.8, 21.0, 18.0, 12.0; **55b**, δ 170.8, 161.5, 161.1, 147.3, 134.9, 127.6, 126.6, 126.5, 120.4, 37.5, 27.1, 19.2, 17.9, 11.8. HRMS: calcd for $C_{14}H_{17}N_3O_2$ 259.1321, found 259.1321. Anal. Calcd for $C_{14}H_{17}N_3O_2\ H_2O$: C, 60.66; H, 6.86; N, 15.16. Found: C, 60.71; H, 7.58; N, 15.15.

3-(Acetylamino)-2-[1-(hydroxydiphenylmethyl)propyl]-4(3*H*)-quinazolinone (56): mp 177−178 °C. Compound **56** appears in its NMR spectra as a mixture of two isomers, **a** and **b**, in a ratio of 1:2. ^{1}H NMR (DMSO-d_6): **56a**, δ 10.88 (s, exch, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.78−6.99 (m, 14H), 4.15 (t, J = 5.5 Hz, 1H), 2.28 (s, 3H), 1.93−1.78 (overlapping m, 1H), 1.74−1.63 (overlapping m, 1H), 0.64 (t, J = 7.6 Hz, 3H); **56b**, δ 11.20 (s, exch, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.79−6.99 (m, 14H), 4.28 (t, J = 5.5 Hz, 1H), 2.23 (s, 3H), 1.93−1.78 (overlapping m, 1H), 1.74−1.63 (overlapping m, 1H), 0.51 (t, J = 7.6 Hz, 3H). ^{13}C NMR (DMSO-d_6): **56a**, 170.3, 161.8, 158.2, 148.4, 145.8, 144.4, 135.0, 127.9, 127.8, 127.0, 126.3, 125.8, 125.5, 120.0, 79.1, 47.3, 22.9, 20.8, 12.4; **56b**, δ 170.0, 162.1, 158.1, 148.3, 145.3, 144.6, 135.0, 128.1, 127.7, 126.5, 126.3, 125.6, 125.2, 119.9, 79.5, 48.1, 25.5, 20.7, 12.7. HRMS: calcd for $C_{26}H_{26}N_3O_3$ 428.1974, found 428.1974. Anal. Calcd for $C_{26}H_{25}N_3O_3$: C, 73.07; H, 5.85; N, 9.84. Found: C, 73.16; H, 5.99; N, 9.59.

3-(Acetylamino)-2-[1-(1-hydroxycyclohexyl)propyl]-4(3*H*)-quinazolinone (57): mp 78−80 °C. Compound **57** appears in its NMR spectra as a mixture of two isomers, **a** and **b**, in a ratio of 1:1. ^{1}H NMR ($CDCl_3$): **57a**, δ 8.99 (s, exch, 1H), 8.17 (d, J = 8.0 Hz, 1H), 7.76 (t, J = 8.0 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.43 (t, J = 8.0 Hz, 1H), 4.49 (s, exch, 1H), 3.04 (dd, J = 4.4 and 10.0 Hz, 1H), 2.30 (s, 3H), 2.07−1.11 (complex overlapping signals, 12H), 0.81 (t, J = 7.5 Hz, 3H); **57b**, δ 8.93 (s, exch, 1H), 8.17 (d, J = 8.0 Hz, 1H), 7.77 (t, J = 8.0 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.45 (t, J = 8.0 Hz, 1H), 5.52 (s, exch, 1H), 3.10 (dd, J = 3.9 and 9.9 Hz, 1H), 2.31 (s, 3H), 2.07−2.11 (complex overlapping signals, 12H), 0.83 (t, J = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$): **57a**, δ 170.7, 162.0, 160.4, 145.7, 135.3, 127.3, 127.1, 126.9, 120.4, 72.9, 50.1, 37.5, 34.8, 25.8, 22.6, 21.8, 21.5, 21.1, 13.0; **57b**, δ 170.2, 160.8, 160.3, 146.1, 135.1, 127.5, 126.94, 126.90, 120.2, 63.5, 51.6, 37.7, 35.7, 25.7, 22.0, 21.9, 21.5, 21.0, 12.2. HRMS: calcd for $C_{19}H_{26}N_3O_3$ 344.1974, found 344.1974. Anal. Calcd for $C_{19}H_{25}N_3O_3$: C, 66.47; H, 7.29; N, 12.24. Found: C, 66.29; H, 7.51; N, 12.19.

2-[1-(1-Hydroxycyclohexyl)propyl]-3-[[(1-hydroxycyclohexyl)acetyl]amino]-4(3*H*)-quinazolinone (58): mp 72−73 °C. Compound **58** appears in its NMR spectra as a mixture of two isomers, **a** and **b**, in a ratio of 10:11. ^{1}H NMR ($CDCl_3$): **58a**, δ 9.02 (s, exch, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.73−7.61 (m, 2H), 7.26 (t, J = 8.0 Hz, 1H), 5.44 (s, exch, 1H), 4.25 (s, exch, 1H), 2.16 (dd, J = 4.0 and 10.0 Hz, 1H), 2.63−1.05 (complex overlapping signals, 22H), 0.84 (t, J = 7.5 Hz, 3H); **58b**, δ 8.90 (s, exch, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.73−7.61 (m, 2H), 7.26 (t, J = 8.0 Hz, 1H), 5.44 (s, exch, 1H), 4.25 (s, exch, 1H), 3.07 (dd, J = 4.4 and 9.6 Hz, 1H), 2.63−1.05 (complex overlapping signals, 22H), 0.98 (t, J = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$): **58a**, δ 171.6, 162.06, 160.5, 146.0, 135.0, 127.3, 126.9, 126.8, 120.0, 73.5, 71.0, 50.2, 47.2, 42.0, 37.5, 36.1, 34.8, 25.49, 25.47, 25.4, 22.6, 22.1, 21.7, 21.6, 12.3; **58b**, δ 171.1, 160.8, 160.4, 145.6, 135.2, 127.0, 126.9, 126.8, 120.2, 73.0, 71.0, 51.6, 46.9, 38.6, 37.6, 36.7, 35.7, 25.8, 25.47, 25.46, 22.6, 22.0, 21.8, 21.6, 12.9. HRMS: calcd for $C_{25}H_{35}N_3O_4$ 441.2628, found 441.2628. Anal. Calcd for $C_{25}H_{35}N_3O_4$: C, 68.03; H, 7.94; N, 9.52. Found: C, 67.92; H, 8.06; N, 9.36.

Hydrolysis Reactions. 3-Amino-2-methyl-4(3*H*)-quinazolinone (32). A mixture of compound **15** or **23** (0.80 mmol), MeOH (10 mL), and aqueous NaOH (20%, 7 mL) was heated under reflux for 1 h. The solvent was removed in vacuo, and the residue was extracted with EtOAc (15 mL). The extract was washed with H_2O (2 × 10 mL), dried ($MgSO_4$), and evaporated to give **32** (0.11 g, 0.6 mmol): mp 152 °C (lit. mp 152 °C).[20]

3-Amino-2-(1-methylethyl)-4(3*H*)-quinazolinone-(34c). A mixture of compound **17** or **25** (0.70 mmol), MeOH (10 mL), and aqueous NaOH (20%, 5 mL) or hydrochloric acid (1 M, 5 mL) was heated under reflux for 1 h. In the acidic reaction the mixture was then neutralized with aqueous NaOH. The solvent was removed in vacuo, and the residue was extracted with EtOAc (15 mL). The extract was washed with H_2O (2 × 10 mL), dried ($MgSO_4$), and evaporated to give **34c** (*ca.* 0.011 g, 0.52 mmol; 75%), which was recrystallized from light petroleum ether (bp 100−120 °C): mp 81 °C (lit. mp 80).[21]

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Supporting Information Available: Compound characterization data, complete with NMR peak assignments (21 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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