Lithiation of 2-Alkyl-3-amino- and 2-Alkyl-3-(methylamino)-4(3*H*)-quinazolinones[1]

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3-Amino-2-methyl-4(3*H*)-quinazolinone has been doubly lithiated, on nitrogen and in the 2-methyl group, with *n*-butyllithium. The lithium reagent thus obtained reacts with a variety of electrophiles (D_2O, benzophenone, cyclohexanone, cyclopentanone, acetophenone, benzaldehyde, tetraisopropylthiuram disulfide (TITD)) to give the corresponding 2-substituted derivatives in very good yields. Reactions of the dilithio reagent with 2 molar equiv of methyl iodide or phenyl isocyanate give disubstituted derivatives. Double lithiation of the 2-ethyl and 2-propyl analogues have been achieved using LDA, and subsequent reactions with most electophiles are then similar. In the reaction of the dianion of the 2-ethyl compound with TITD, deamination from position 3 takes place with the formation of the 2-substituted derivative. In reactions with prochiral ketones, the dianion of the 2-ethyl compound gives very high diastereoselectivity. Lithiation and subsequent reactions of 3-(methylamino) analogues take place in a similar manner, thus providing access to a range of substituted 3-(methylamino)-2-alkyl-4(3*H*)-quinazolinones by a general procedure. Lithiation of 3-(dimethylamino)-2-ethyl-4(3*H*)-quinazolinone did not take place under similar conditions. Lithiation of 3-amino-2-unsubstituted-4(3*H*)-quinazolinone was also unsuccessful.

Introduction

Lithiation of aromatic compounds often occurs proximate to substituents that possess oxygen or nitrogen atoms.[2] Although the precise explanation for the effect is open to question,[3] the synthetic utility of the process is not in doubt.[4−7] The approch can be applied to diaza heterocycles[8] and has been used for the elaboration of 2-methyl-4(3*H*)-quinazolinones[9] and 2-aryl-2-methyl-4(3*H*)-quinazolinones.[10]

As part of our continuing interest in heterocyclic chemistry[11] and in lithiation reactions,[7] we have shown that 3-(acylamino)-2-methyl-4(3*H*)-quinazolinones also undergo double lithiation, at the amido group and in the methyl group at position 2, with *n*-butyllithium,[12] while 2-unsubstituted-, 2-ethyl-, and 2-propyl-3-(acylamino)-4(3*H*)-quinazolinones are similarly lithiated by LDA.[1] The organolithium reagents obtained in such reactions are useful as intermediates for the synthesis of more complex 3-(acylamino)-2-substituted-4(3*H*)-quinazolinones. We have also shown that it is possible to remove the acyl group under hot basic or acidic conditions to give simple 2-alkyl-3-amino-4(3*H*)-quinazolinones.[1,12] However, such forcing conditions for removal of the acylamino group are not always appropriate for some of the more complicated substituents at the 2-position, so it would be extremely useful to be able to effect lithiation proximate to the amino group itself as a means of producing 2-substituted-3-aminoquinazolinones. Attempts at lithiation of aniline and *o*-toluidine, as simple models, were unsuccessful.[13] Nevertheless, we decided to explore the possibility of effecting proximate lithiation of various 3-amino- and 3-(methylamino)-4(3*H*)-quinazolinones. We now report success in this endeavour.

Results and Discussion

2-Alkyl-3-amino-4(3*H*)-quinazolinones **1**−**3** were prepared by the literature procedures.[14−16] 2-Alkyl-3-(meth-

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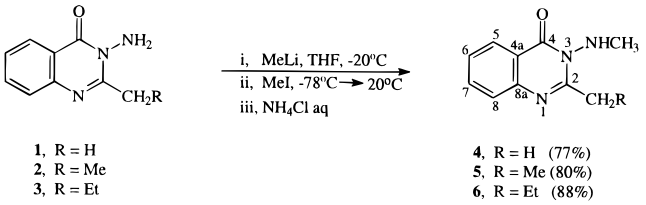
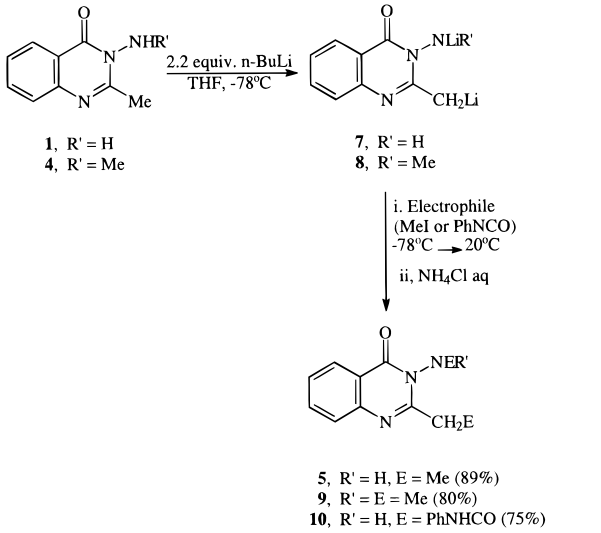
Scheme 1



Scheme 2



ylamino)-4(3*H*)-quinazolinones **4**−**6** were synthesised according to Scheme 1.

Lithiation of **1** and **4** occurred smoothly and rapidly with 2.2 equiv of *n*-BuLi at −78 °C in THF to give dilithio reagents **7** and **8**, respectively, with no nucleophilic attack of *n*-BuLi at either the carbonyl group or the imine group of the quinazolinone ring. Initial addition of the *n*-BuLi provided a yellow solution until approximately 1 molar equiv had been added and then gave a deep red solution as the remaining *n*-BuLi was added. Reactions of the dianions **7** and **8** with 2.2 molar equiv of iodomethane gave rise to the disubstituted products **5** and **9** in 89% and 80% isolated yields, respectively (Scheme 2). Reaction of the dianion **7** with 2.2 molar equiv of phenyl isocyanate similarly gave rise to the disubstituted product **10** in 75% isolated yield. Use of 1.1 molar equiv of PhNCO gave a mixture of **10** and the monosubstituted derivative 3-amino-2-[[(phenylamino)carbonyl]methyl]-4(3*H*)-quinazolinone, which was not isolated.

The ^{1}H NMR signal for the CH_2 group at position 2 of compound **5** appears as a broad signal at room temperature, a simple quartet at 60 °C, and as two overlapping quartets at −20 °C, indicating that there is restricted rotation about the chiral axis of the N−N bond below room temperature. This phenomenon is even more marked for compound **10**, which shows two clear doublets for the CH_2 group at ambient temperature. Similar observations have been made previously for other 3-acylamino derivatives.[1,12]

In order to test the versatility of the dianions of compounds **1** and **4**, they were reacted with a variety of electrophiles (benzophenone, D_2O cyclohexanone, cyclopentanone, acetophenone, benzaldehyde, tetraisopropylthiuram disulfide (TITD), phenyl isocyanate, 2-butanone). The corresponding 2-substituted aminoquinazolinones derivatives **11**−**22** (Scheme 3) were formed in high yields (Table 1). In contrast to the situation with the dianion of compound **1**, reaction of the dianion of compound **4** with 1 equiv of phenyl isocyanate gave rise to the monosubstituted derivative **21** only, with no disubstituted compound formed.

Scheme 3

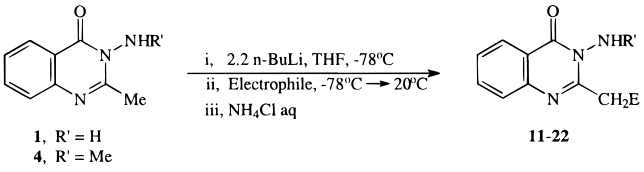
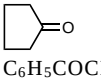
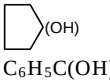


Table 1. Products from the Reaction of the Dilithio Reagents of Compounds 1 and 4 with Electrophiles According to Scheme 3[a]

compd	R′	electrophile	E	yield (%)[b]	mp (°C)
11	H	$(C_6H_5)_2CO$	$(C_6H_5)_2C(OH)$	86	176−8
12	H	D_2O	D	88	153
13	H			84	104−5
14	H			89	158−60
15	H	$C_6H_5COCH_3$	$C_6H_5C(OH)(CH_3)$	86	159−60
16	H	C_6H_5CHO	$C_6H_5CH(OH)$	77	175−6
17	H	$[Pr^i_2NC(S)S]_2$	$Pr^i_2NC(S)S$	75	102−4
18	Me	$(C_6H_5)_2CO$	$(C_6H_5)_2C(OH)$	83	150−1
19	Me	C_6H_5CHO	$C_6H_5CH(OH)$	70	117−8
20	Me	D_2O	D	90	110−11
21	Me	C_6H_5NCO	C_6H_5NHCO	72	222
22	Me	$C_2H_5COCH_3$	$C_2H_5C(OH)(CH_3)$	84	48−50

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

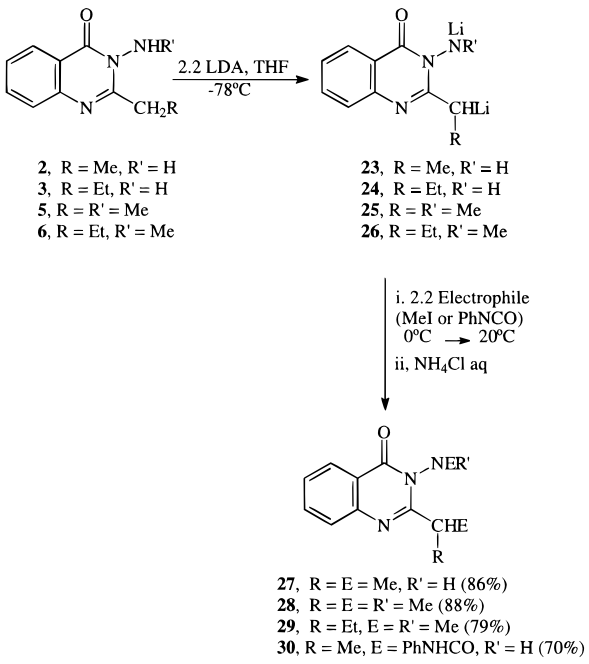
The ^{1}H NMR spectrum of compound **18** shows the CH_2 signal as a broad signal at room temperature and a sharp singlet at 60 °C. For compound **19**, the CH_2 group at position 2 appears as two separated but broad signals at room temperature and as two sharp double doublets at 60 °C.

Our success in lithiating compounds **1** and **4** prompted us to attempt lithiation of 3-amino-2-ethyl-4(3*H*)-quinazolinone (**2**),[15] 3-amino-2-propyl-4(3*H*)-quinazolinone (**3**),[16] 2-ethyl-3-(methylamino)-4(3*H*)-quinazolinone (**5**), and 3-(methylamino)-2-propyl-4(3*H*)-quinazolinone (**6**). Unfortunately, attempted lithiation with *n*-BuLi gave only low yields of the desired products. However, good lithiation was achieved by use of LDA at −78 °C (Scheme 4). Initial addition of LDA provided a yellow solution until approximately 1 equiv had been added and then gave a deep red solid for compound **2** and deep red solutions for compounds **3**, **5**, and **6** as the remaining LDA was added. The dilithio reagents **23**−**26** were allowed to stir at −78 °C for 30 min to ensure complete reaction. Addition of 2.2 molar equiv of iodomethane to **23**, **25**, or **26** followed by slow warming to 0 °C gave rise to products **27**−**29** in 86%, 88%, and 79% isolated yields, respectively (Scheme 4). Reaction of the dianion **23** with 1 equiv of phenyl isocyanate gave a mixture of mono- and disubstituted derivatives as in the case of the methyl derivative **1**. However, reaction of the dianion **23** with 2.2 molar equiv of phenyl isocyanate gave rise to the disubstituted derivative **30** in 70% isolated yield (Scheme 4).

Reactions of the dianions **23**−**26** with a variety of electrophiles at 0 °C gave rise to 2-substituted quinazolinone derivatives **31**−**47** (Scheme 5) in very good yields (Table 2).

The ^{1}H and ^{13}C NMR spectra of compounds **34**, **40**, and **41** show the expected presence of two diastereoisomers. However, for compounds **33** and **35**−**37** the spectra indicate only one diastereoisomer in each case, which is

Scheme 4

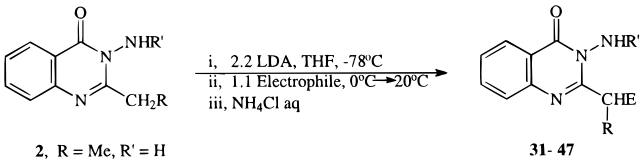


2, R = Me, R' = H
3, R = Et, R' = H
5, R = R' = Me
6, R = Et, R' = Me

23, R = Me, R' = H
24, R = Et, R' = H
25, R = R' = Me
26, R = Et, R' = Me

27, R = E = Me, R' = H (86%)
28, R = E = R' = Me (88%)
29, R = Et, E = R' = Me (79%)
30, R = Me, E = PhNHCO, R' = H (70%)

Scheme 5



2, R = Me, R' = H
3, R = Et, R' = H
5, R = R' = Me
6, R = Et, R' = Me

31- **47**

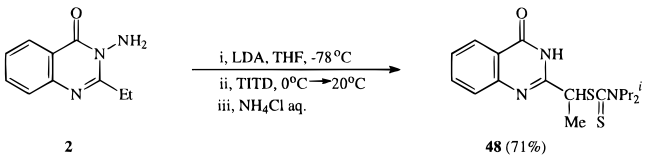
Table 2. Products from the Reaction of the Dilithio Reagents of Compounds 2, 3, 5 and 6 with Electrophiles According to Scheme 5[a]

compd	R	R′	electrophile	E	yield (%)[b]	mp (°C)
31	Me	H			90	175−6
32	Me	H			90	156−8
33	Me	H	$C_6H_5COCH_3$	$C_6H_5C(OH)(CH_3)$	80	172−3
34	Me	H	C_6H_5CHO	$C_6H_5CH(OH)$	80	176
35	Me	H	$C_4H_9COCH_3$	$C_4H_9C(OH)(CH_3)$	71	121−3
36	Me	H	$C_4H_9COC_2H_5$	$C_4H_9C(OH)(C_2H_5)$	83	157−8
37	Me	H	$C_2H_5COCH_3$	$C_2H_5C(OH)(CH_3)$	88	160−1
38	Me	H	$(C_6H_5)_2CO$	$(C_6H_5)_2C(OH)$	84	186−7
39	Me	H	D_2O	D	92	126−8
40	Et	H	$C_6H_5COCH_3$	$C_6H_5C(OH)(CH_3)$	87	59−60
41	Et	H	$C_2H_5COCH_3$	$C_2H_5C(OH)(CH_3)$	92	131
42	Et	H	$(C_6H_5)_2CO$	$(C_6H_5)_2C(OH)$	90	179−80
43	Me	Me	$(C_6H_5)_2CO$	$(C_6H_5)_2C(OH)$	82	181−3
44	Me	Me			80	98−9
45	Me	Me	D_2O	D	82	97−8
46	Me	Me	C_6H_5NCO	C_6H_5NHCO	66	>250
47	Et	Me	$(C_6H_5)_2CO$	$(C_6H_5)_2C(OH)$	80	176−8

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

clearly not expected when two asymmetric centers are introduced during the reaction. The reason for the high diastereoselectivity in those cases is not yet understood. The ambient temperature NMR spectra of compounds **40**−**42** and **47** show diastereotopism for the two hydrogens of the CH_2 group adjacent to the newly created asymmetric center, indicating a significant barrier to rotation around the N−N bond even at room temperature. The ^1H NMR spectrum of compound **43** shows broad NH and CH signals at room temperature, two simple quartets at 60 °C, and the appearance of two diastereoisomers in the ratio of 2:11 at −20 °C.

Scheme 6



2

48 (71%)

Reaction of the dilithio reagent of **2** with TITD gave rise to compound **48**, in which deamination has taken place (Scheme 6). The ^1H NMR spectrum of compound **48** shows the absence of a NH_2 signal in the region of 6 ppm and presence of a one-proton signal in the region of 12 ppm, which is characteristic for the NH of quinazolinones. It is not clear why lithiated **2** behaves differently than lithiated **1** in this reaction.

Attention was next turned to lithiation of 2-alkyl-3-(dimethylamino)-4(3*H*)-quinazolinones, for which 3-(dimethylamino)-2-ethyl-4(3*H*)-quinazolinone (**10**) was used as the model. It was found that lithiation of **10** did not take place under conditions similar to those used for the lithiation of compounds **1**−**6**. Similarly, attempts to lithiate 3-amino-2-unsubstituted-4(3*H*)-quinazolinone met with failure. No further attempts were made to find conditions under which this lithiation could be effected.

Conclusion

We have demonstrated metalation procedures that allow regiospecific electrophilic substitutions of amino- and (methylamino)quinazolinones to provide efficient syntheses of 3-amino- and 3-(methylamino)-2-substituted-4(3*H*)-quinazolinones. These simple procedures can provide aminoquinazolinone derivatives previously unavailable or available only with difficulty. The present method is particularly useful in that there is no protecting group to be removed in another step from the amino function. In some cases reactions of the dianions with ketones lead to products containing only one of the expected two diastereoisomers, which offers future promise for the development of new stereoselective synthetic methods.

Experimental Section

Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 400 MHz for ^1H 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). *n*-Butyllithium was estimated prior to use by the method of Watson and Eastham.[17] THF was distilled from sodium benzophenone ketyl. Other solvents were purified by standard procedures.[18,19] Other chemicals were used without further purification.

General Procedure for the Synthesis of 2-Alkyl-3-(methylamino)-4(3*H*)-quinazolinones 4−6. A 1.0 M solution of MeLi in THF (4.4 mL, 4.4 mmol) was added dropwise to a stirred solution of **1**−**3** (4.0 mmol) in THF (40 mL) at −20 °C under N_2. The reaction mixture was maintained under these conditions for 30 min and then cooled to −78 °C, after

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which MeI (0.71 g, 5.0 mmol) was added. The resulting colorless solution was stirred for 1 h at −78 °C and then allowed to warm to room temperature. It was 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 obtained were recrystallized, usually from Et_2O.

2-Methyl-3-(methylamino)-4(3*H*)-quinazolinone (4): mp 110−111 °C (lit. mp 108−109 °C).[20]

2-Ethyl-3-(methylamino)-4(3*H*)-quinazolinone (5): mp 97−98 °C (lit. mp 93.0−93.5 °C).[20]

3-(Methylamino)-2-propyl-4(3*H*)-quinazolinone (6): mp 79−80 °C; ^{1}H NMR ($CDCl_3$) δ 8.24 (d, J = 8.0 Hz, 1H), 7.73 (t, J = 8.0 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.44 (t, J = 8.0 Hz, 1H), 5.65 (q, J = 6.0 Hz, exch, 1H), 2.95 (br, 2H), 2.78 (d, J = 6.0 Hz, 3H), 1.88 (sextet, J = 7.5 Hz, 2H), 1.07 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 161.3, 158.3, 147.2, 134.2, 127.1, 126.4, 126.1, 120.7, 38.4, 35.8, 20.7, 14.0; HRMS calcd for $C_{12}H_{15}N_3O$ 217.1215, found 217.1215. Anal. Calcd for $C_{12}H_{15}N_3O$: C, 66.36; H, 6.91; N, 19.35. Found: C, 66.30; H, 7.24; N, 19.03.

General Procedure for the Synthesis of 2-Substituted-4(3*H*)-quinazolinone Derivatives 5 and 9−22. To a cooled (−78 °C), stirred solution of **1** or **4** (2.0 mmol) in THF (20 mL) was added a solution of *n*-BuLi (2.7 mL of 1.6 M, 4.4 mmol). Formation of the dianion was observed as a deep red solution. The mixture was stirred at −78 °C for an additional 45 min, after which an electrophile (4.4 mmol of MeI, 4.4 mmol of PhNCO in the reaction of **1** or 2.2 mmol in the reaction of **4**, 2.2 mmol for other electrophiles) (as a solution in THF for solids) was added. The mixture was stirred for 2 h, allowed to warm to room temperature, diluted with Et_2O (20 mL), and quenched with aqueous saturated NH_4Cl (20 mL) [or dilute HCl (3 M, 10 mL) in the case of compound **17**]. 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 recrystallized from EtOAc or Et_2O.

3-(Dimethylamino)-2-ethyl-4(3*H*)-quinazolinone (9): mp 107−109 °C; ^{1}H NMR ($CDCl_3$) δ 8.22 (d, J = 8.0 Hz, 1H), 7.70 (t, J = 8.0 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.41 (t, J = 8.0 Hz, 1H), 3.08 (s, 6H), 2.95 (q, J = 7.5 Hz, 2H), 1.36 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 162.1, 161.4, 147.0, 134.1, 126.9, 126.2, 126.1, 122.4, 43.6, 28.4, 11.8; HRMS calcd for $C_{10}H_{11}N_3O$ 218.1293, found 218.1293. Anal. Calcd for $C_{12}H_{15}N_3O$: C, 66.36; H, 6.91; N, 19.35. Found: C, 66.18; H, 7.11; N, 19.19.

3-[[(Phenylamino)carbonyl]amino]-2-[[(phenylamino)carbonyl]methyl]-4(3*H*)-quinazolinone (10): mp 256 °C; ^{1}H NMR (DMSO-d_6) δ 10.22 (s, exch, 1H), 9.30 (s, exch, 1H), 9.18 (s, exch, 1H), 8.15 (d, J = 8.0 Hz, 1H), 7.86 (t, J = 8.0 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.65−6.97 (m, 11H), 4.13, 3.84 (2 d, J = 16.0 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 165.6, 159.9, 154.7, 154.5, 146.6, 139.0, 138.9, 134.9, 128.8, 128.7, 127.2, 127.0, 126.4, 123.4, 122.6, 121.0, 119.3, 118.5, 43.0; HRMS calcd for $C_{23}H_{20}N_5O_3$ 414.1566, found 414.1577. Anal. Calcd for $C_{23}H_{19}N_5O_3$: C, 66.82; H, 4.60; N, 16.95. Found: C, 66.71; H, 4.60; N, 16.85.

3-Amino-2-(2-hydroxy-2,2-diphenylethyl)-4(3*H*)-quinazolinone (11): ^{1}H NMR (DMSO-d_6) δ 8.06 (d, J = 8.0 Hz, 1H), 7.71 (t, J = 8.0 Hz, 1H), 7.51−7.12 (m, 13H), 5.97 (s, exch, 2H), 3.99 (s, 2H); ^{13}C NMR (DMSO-d_6) δ 159.7, 156.4, 147.3, 144.8, 134.1, 127.8, 126.3, 126.2, 126.2, 125.8, 125.5, 119.3, 77.0, 41.7; HRMS calcd for $C_{23}H_{20}N_5O_3$ 358.1556, found 358.1556. Anal. Calcd for $C_{22}H_{19}N_3O_2$: C, 73.95; H, 5.32; N, 11.76. Found: C, 73.83; H, 5.24; N, 11.69.

3-Amino-2-(monodeuteriomethyl)-4(3*H*)-quinazolinone (12): ^{1}H NMR ($CDCl_3$) δ 8.17 (d, J = 8.0 Hz, 1H), 7.70 (t, J = 8.0 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.41 (t, J = 8.0 Hz, 1H), 4.95 (s, exch, 2H), 2.66 (1:1:1 t, J = 2.1 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 161.5, 155.4, 146.9, 134.2, 126.8, 126.4, 126.2, 119.9, 22.2, 21.9, 21.7; HRMS calcd for $C_9H_8N_3OD$ 176.0808, found 176.0808.

3-Amino-2-[(1-hydroxycyclohexyl)methyl]-4(3*H*)-quinazolinone (13): ^{1}H NMR ($CDCl_3$) δ 8.19 (d, J = 8.0 Hz, 1H), 7.70 (t, J = 8.0 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.43 (t, J = 8.0 Hz, 1H), 5.23 (s, exch, 2H), 4.91 (s, exch, 1H), 3.24 (s, 2H), 1.76−1.34 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 161.1, 155.7, 145.8, 134.2, 126.9, 126.5, 126.4, 119.7, 71.7, 43.0, 38.0, 25.7, 22.1; HRMS calcd for $C_{15}H_{20}N_3O_2$ 274.1556, found 274.1556. Anal. Calcd for $C_{15}H_{19}N_3O_2$: C, 65.93; H, 6.96; N, 15.38. Found: C, 65.81; H, 6.90; N, 15.35.

3-Amino-2-[(1-hydroxycyclopentyl)methyl]-4(3*H*)-quinazolinone (14): ^{1}H NMR ($CDCl_3$) δ 8.17 (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), 5.20 (s, exch, 1H), 5.11 (s, exch, 2H), 3.33 (s, 2H), 1.93−1.67 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 161.1, 156.5, 145.8, 134.3, 126.9, 126.5, 126.3, 119.8, 80.8, 42.5, 40.2, 23.8; HRMS calcd for $C_{14}H_{18}N_3O_2$ 260.1399, found 260.1399. Anal. Calcd for $C_{14}H_{17}N_3O_2$: C, 64.86; H, 6.56; N, 16.21. Found: C, 64.70; H, 6.70; N, 14.48.

3-Amino-2-(2-hydroxy-2-phenylpropyl)-4(3*H*)-quinazolinone (15): ^{1}H NMR (DMSO-d_6) δ 8.14 (d, J = 8.0 Hz, 1H), 7.68 (t, J = 8.0 Hz, 1H), 7.59−7.53 (m, 3H), 7.41 (t, J = 8.0 Hz, 1H), 7.29 (t, J = 7.5 Hz, 2H), 7.18 (t, J = 7.5 Hz, 1H), 6.26 (s, exch, 1H), 5.77 (s, exch, 2H), 3.83, 2.31 (2 d, J = 15.0 Hz, 2H), 1.65 (s, 3H); ^{13}C NMR (DMSO-d_6) δ 159.8, 154.8, 148.0, 145.5, 135.6, 127.7, 126.4, 126.2, 125.9, 125.8, 124.4, 119.4, 73.9, 44.6, 29.7; HRMS calcd for $C_{17}H_{18}N_3O_2$ 296.1399, found 296.1399. Anal. Calcd for $C_{17}H_{17}N_3O_2$: C, 69.15; H, 5.76; N, 14.23. Found: C, 69.06; H, 5.92; N, 14.34.

3-Amino-2-(2-hydroxy-2-phenylethyl)-4(3*H*)-quinazolinone (16): ^{1}H NMR (DMSO-d_6) δ 8.12 (d, J = 8.0 Hz, 1H), 7.77 (t, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.49−7.43 (m, 3H), 7.32 (t, J = 7.7 Hz, 2H), 7.23 (t, J = 7.7 Hz, 1H), 5.82 (s, exch, 2H), 5.54 (d, J = 4.5 Hz, exch,1H), 5.30 (dt, J = 5.0 and 10.0 Hz, 1H), 3.34 (dd, J = 9.6 and 14.4 Hz, 1H), 3.25 (dd, J = 4.8 and 14.4 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 160.1, 155.7, 146.3, 145.1, 133.8, 127.9, 126.8, 126.7, 125.9, 125.8, 125.6, 119.7, 70.4, 43.7; HRMS calcd for $C_{17}H_{18}N_3O_2$ 296.1399, found 296.1399. Anal. Calcd for $C_{17}H_{17}N_3O_2$: C, 69.15; H, 5.76; N, 14.24. Found: C, 68.97; H, 5.73; N, 14.10.

3-Amino-2-[(diisopropyldithiocarbamoyl)methyl]-4(3*H*)-quinazolinone (17): ^{1}H NMR (DMSO-d_6, 100 °C) δ 8.14 (d, J = 8.0 Hz, 1H), 7.77 (t, J = 8.0 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.49 (t, J = 8.0 Hz, 1H), 5.62 (s, exch, 2H), 4.94 (s, 2H), 4.85 (heptet, J = 6.8 Hz, 2H), 1.46 (d, J = 6.8 Hz, 12H); ^{13}C-NMR (DMSO-d_6, 100 °C) δ 194.1, 160.5, 153.7, 146.6, 133.9, 127.0, 126.4, 126.0, 120.3, 53.5, 39.7, 19.9; HRMS calcd for $C_{16}H_{23}N_4OS_2$ 351.1313, found 351.1313. Anal. Calcd for $C_{16}H_{22}N_4OS_2$: C, 54.48; H, 6.28; N, 16.00. Found: C, 54.68; H, 6.49; N, 15.85.

2-(2-Hydroxy-2,2-diphenylethyl)-3-(methylamino)-4(3*H*)-quinazolinone (18): ^{1}H NMR ($CDCl_3$) δ 8.17 (d, J = 8.0 Hz, 1H), 7.70−7.15 (m, 14H), 5.81 (q, J = 6.0 Hz, exch, 1H), 4.0 (br s), 2.74 (d, J = 6.0 Hz, 3H), ^{13}C NMR ($CDCl_3$) δ 160.7, 156.5, 146.9, 145.3, 134.5, 128.2, 126.85, 126.8, 126.7, 126.5, 126.0, 120.4, 77.8, 41.0, 38.5; HRMS calcd for $C_{23}H_{22}N_3O_2$ 372.1712, found 372.1712. Anal. Calcd for $C_{23}H_{21}N_3O_2$: C, 74.39; H, 5.66; N, 11.32. Found: C, 74.23; H, 5.76; N, 11.32.

2-(2-Hydroxy-2-phenylethyl)-3-(methylamino)-4(3*H*)-quinazolinone (19): ^{1}H NMR ($CDCl_3$, 58 °C) δ 8.26 (d, J = 8.0 Hz, 1H), 7.78 (t, J = 8.0 Hz, 1H), 7.70 (t, J = 8.0 Hz, 1H), 7.51−7.47 (m, 3H), 7.40 (t, J = 7.7 Hz, 2H), 7.32 (t, J = 7.7 Hz, 1H), 5.61 (q, J = 5.8 Hz, exch, 1H), 5.34 (dd, J = 2.6 and 9.6 Hz, 1H), 5.22 (s, exch, 1H), 3.49 (dd, J = 2.6 and 17.2 Hz, 1H), 3.27 (dd, J = 9.6 and 17.2 Hz, 1H), 2.72 (d, J = 5.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 160.9, 156.8, 146.1, 143.0, 134.6, 128.5, 127.6, 127.0, 126.8, 126.6, 125.9, 120.7, 70.9, 41.1, 38.1; HRMS calcd for $C_{17}H_{18}N_3O_2$ 296.1399, found 296.1399. Anal. Calcd for $C_{17}H_{17}N_3O_2$: C, 69.15; H, 5.76; N, 14.24. Found: C, 68.97; H, 5.90; N, 14.10.

3-(Methylamino)-2-(monodeuteriomethyl)-4(3*H*)-quinazolinone (20): ^{1}H NMR ($CDCl_3$) δ 8.24 (d, J = 8.0 Hz, 1H), 7.73 (t, J = 8.0 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.44 (t, J = 8.0 Hz, 1H), 5.73 (q, J = 6.0 Hz, exch, 1H), 2.78 (d, J = 6.0 Hz, 3H), 2.68 (1:1:1 t, J = 2.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 161.1, 155.6, 147.1, 134.3, 126.9, 126.5, 126.2, 120.7, 38.0, 21.5, 21.3, 21.1; HRMS calcd for $C_{10}H_{11}N_3OD$ 191.1043, found 191.1043.

3-(Methylamino)-2-[[(phenylamino)carbonyl]methyl]-4(3*H*)-quinazolinone (21): ^{1}H NMR (DMSO-d_6) δ 10.22 (s, exch, 1H), 8.14 (d, J = 8.0 Hz, 1H), 7.81 (t, J = 8.0 Hz, 1H), 7.65−7.54 (m, 3H), 7.51 (t, J = 8.0 Hz, 1H), 7.29 (t, J = 7.5

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Hz, 2H), 7.04 (t, J = 7.5 Hz, 1H), 6.36 (q, J = 5.6 Hz, exch, 1H), 4.04 (s, 2H), 2.67 (d, J = 5.6 Hz, 3H); ^{13}C NMR (DMSO-d_6) δ 166.1, 160.3, 154.6, 146.5, 139.0, 134.2, 128.5, 126.8, 126.4, 125.9, 123.0, 121.1, 119.0, 43.2, 36.4; HRMS calcd for $C_{17}H_{16}N_4O_2$ 308.1273, found 308.1273. Anal. Calcd for $C_{17}H_{16}N_4O_2$: C, 66.23; H, 5.19; N, 18.18. Found: C, 66.18; H, 5.20; N, 18.38.

2-(2-Hydroxy-2-methylbutyl)-3-(methylamino)-4(3*H*)-quinazolinone (22): ^{1}H NMR ($CDCl_3$) δ 8.23 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.45 (t, J = 8.0 Hz, 1H), 6.01 (s, exch, 1H), 5.88 (q, J = 5.9 Hz, exch, 1H), 3.21 (br, 2H), 2.78 (d, J = 5.9 Hz, 3H), 1.67 (q, J = 7.5 Hz, 2H), 1.30 (s, 3H), 0.99 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 160.8, 156.9, 145.8, 134.5, 126.9, 126.6, 126.5, 120.5, 72.2, 41.1, 38.2, 35.1, 26.4, 8.4; 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, 64.37; H, 7.28; N, 16.09. Found: C, 64.25; H, 7.42; N, 16.01.

General Procedures for the Synthesis of 2-Substituted-4(3*H*)-quinazolinones 27−48. A solution of LDA in heptane (2.7 mL of 1.6 M, 4.4 mmol) was added dropwise under N_2 to a stirred solution of the appropriate 2-alkylquinazolinone derivatives **3**, **4**, **5**, or **6** (2.0 mmol) in dry THF (20 mL) at −78 °C. The mixture was stirred at −78 °C for 15 min, and then the temperature was slowly allowed to rise to 0 °C. The electrophile (4.4 mmol of MeI, 4.4 mmol of PhNCO in the case of synthesis of **30** or 2.2 mmol for synthesis of **46**, 2.2 mmol in the case of other electrophiles) (as a solution in THF for solids) was added. The mixture was stirred for 30 min, then allowed to warm to room temperature, diluted with EtOAc (20 mL), and quenched with aqueous saturated NH_4Cl (20 mL) [or 3 M HCl (10 mL) in the case of compound **48**]. The organic layer was washed with H_2O (2 × 20 mL), dried ($MgSO_4$), and evaporated. The products obtained were recrystallized, usually from EtOAc.

3-(Methylamino)-2-(1-methylethyl)-4(3*H*)-quinazolinone (27): mp 50−51 °C; ^{1}H NMR ($CDCl_3$) δ 8.23 (d, J = 8.0 Hz, 1H), 7.74−7.66 (m, 2H), 7.42 (t, J = 8.0 Hz, 1H), 5.63 (q, J = 6.0 Hz, exch, 1H), 3.64 (septet, J = 6.8 Hz, 1H), 2.90 (d, J = 6.0 Hz, 3H), 1.36 (d, J = 6.8 Hz, 6H); ^{13}C NMR ($CDCl_3$) δ 162.4, 161.5, 147.3, 134.1, 127.4, 126.4, 126.1, 120.6, 38.8, 30.6, 21.1; HRMS calcd for $C_{12}H_{15}N_3O$ 217.1215, found 217.1215. Anal. Calcd for $C_{12}H_{15}N_3O$: C, 66.36; H, 6.91; N, 19.35. Found: C, 66.46; H, 6.93; N, 19.21.

3-(Dimethylamino)-2-(1-methylethyl)-4(3*H*)-quinazolinone (28): mp 65−66 °C; ^{1}H NMR ($CDCl_3$) δ 8.21 (d, J = 8.0 Hz, 1H), 7.69 (t, J = 8.0 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.40 (t, J = 8.0 Hz, 1H), 3.65 (septet, J = 6.8 Hz, 1H), 3.08 (s, 6H), 1.33 (d, J = 6.8 Hz, 6H); ^{13}C NMR ($CDCl_3$) δ 164.3, 162.3, 147.0, 134.0, 127.1, 126.1, 126.0, 122.2, 48.8, 31.1, 21.2; HRMS calcd for $C_{13}H_{18}N_3O$ 232.1450, found 232.1450. Anal. Calcd for $C_{13}H_{17}N_3O$: C, 67.53; H, 7.36; N, 18.18. Found: C, 67.70; H, 7.57; N, 18.18.

3-(Dimethylamino)-2-(1-methylpropyl)-4(3*H*)-quinazolinone (29): mp 60−61 °C; ^{1}H NMR ($CDCl_3$) δ 8.21 (d, J = 8.0 Hz, 1H), 7.69 (t, J = 8.0 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.40 (t, J = 8.0 Hz, 1H), 3.51 (sextet, J = 6.9 Hz, 1H), 3.08, 3.07 (2 s, 6H), 1.92 (d quintet, J = 7.4 and 13.4 Hz, 1H), 1.62 (d quintet, J = 7.4 Hz, 14.1 Hz, 1H), 1.30 (d, J = 6.9 Hz, 3H), 0.94 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 163.9, 162.3, 147.1, 134.0, 127.1, 126.0, 125.9, 122.2, 43.8, 43.7, 37.7, 28.3, 19.3, 12.3; HRMS calcd for $C_{14}H_{20}N_3O$ 246.1606, found 246.1606. Anal. Calcd for $C_{14}H_{19}N_3O$: C, 68.57; H, 7.75; N, 17.14. Found: C, 68.78; H, 7.95; N, 16.94.

2-[1-[(Phenylamino)carbonyl]ethyl]-3-[[(phenylamino)-carbonyl]amino]-4(3*H*)-quinazolinone (30): mp >300 °C. The ^{1}H NMR spectra of compound **30** shows a mixture of two isomers, **a** and **b**, in a ratio of 1:8. ^{1}H NMR (DMSO-d_6): **30a**, δ 10.21 (s, exch, 1H), 9.21 (s, exch, 1H), 8.94 (s, exch, 1H), 8.14 (d, J = 8.0 Hz, 1H), 7.86 (t, J = 8.0 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.72−7.14 (m, 11H), 4.40 (q, J = 6.4 Hz, 1H), 1.55 (d, J = 6.4 Hz, 3H); **30b**, δ 10.21 (s, exch, 1H), 9.71 (s, exch, 1H), 9.50 (s, exch, 1H), 8.14 (d, J = 8.0 Hz, 1H), 7.86 (t, J = 8.0 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.72−7.16 (m, 11H), 4.18 (q, J = 7.1 Hz, 1H), 1.61 (d, J = 7.1 Hz, 3H). ^{13}C NMR (DMSO-d_6): δ 170.1, 159.8, 156.9, 154.4, 146.3, 139.2, 138.7, 134.6, 128.6, 128.4, 127.5, 126.7, 126.2, 123.4, 122.4, 120.8, 119.4, 118.3, 45.1, 15.7. HRMS: calcd for $C_{24}H_{22}N_5O_3$ 428.1723, found 428.1720. Anal. Calcd for $C_{24}H_{21}N_5O_3$: C, 67.45; H, 4.92; N, 16.39. Found: C, 67.33; H, 4.89; N, 13.30.

3-Amino-2-[1-(1-hydroxycyclohexyl)ethyl]-4(3*H*)-quinazolinone (31): ^{1}H NMR ($CDCl_3$) δ 8.22 (d, J = 8.0 Hz, 1H), 7.73 (t, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.45 (t, J = 8.0 Hz, 1H), 5.49 (s, exch, 1H), 4.93 (s, exch, 2H), 3.91 (q, J = 7.0 Hz, 1H), 1.89−1.25 (m, 10H), 1.36 (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 162.0, 161.6, 145.7, 134.5, 127.0, 126.6, 126.4, 119.7, 75.5, 41.7, 37.6, 34.9, 25.8, 22.1, 21.8, 13.6; 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, 67.07; H, 7.49; N, 14.89.

3-Amino-2-[1-(1-hydroxycyclopentyl)ethyl]-4(3*H*)-quinazolinone (32): ^{1}H NMR ($CDCl_3$) δ 8.22 (d, J = 8.0 Hz, 1H), 7.73 (t, J = 8.0 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.45 (t, J = 8.0 Hz, 1H), 5.60 (s, exch, 1H), 4.91 (s, exch, 2H), 3.74 (q, J = 7.0 Hz, 1H), 1.94−1.47 (m, 8H), 1.44 (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 162.3, 161.7, 145.8, 134.5, 126.9, 126.6, 126.5, 119.9, 83.2, 40.7, 38.4, 24.1, 24.0, 15.3; HRMS calcd for $C_{15}H_{20}N_3O_2$ 274.1555, found 274.1555. Anal. Calcd for $C_{15}H_{19}N_3O_2$: C, 65.93; H, 6.96; N, 15.38. Found C, 66.11; H, 7.12; N, 15.59.

3-Amino-2-(2-hydroxy-1-methyl-2-phenylpropyl)-4(3*H*)-quinazolinone (33): ^{1}H NMR ($CDCl_3$) δ 8.27 (d, J = 8.0 Hz, 1H), 7.78 (t, J = 8.0 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.58 (d, J = 8.3 Hz, 2H), 7.49 (t, J = 8.0 Hz, 1H), 7.39 (t, J = 8.3 Hz, 2H), 7.27 (t, J = 8.3 Hz, 1H), 6.44 (s, exch, 1H), 4.90 (s, exch, 2H), 4.26 (q, J = 7.0 Hz, 1H), 1.54 (s, 3H), 1.08 (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 162.0, 161.7, 146.3, 145.6, 134.7, 128.1, 127.0, 126.8, 126.6, 126.5, 125.0, 119.9, 75.6, 43.7, 30.3, 15.0; HRMS calcd for $C_{18}H_{20}N_3O_2$ 310.1556, found 310.1556. Anal. Calcd for $C_{18}H_{19}N_3O_2$: C, 69.90; H, 6.15; N, 13.59. Found: C, 69.94; H, 6.30; N, 13.82.

3-Amino-2-(2-hydroxy-1-methyl-2-phenylethyl)-4(3*H*)-quinazolinone (34): The NMR spectra of compound **34** show a mixture of two isomers, **a** and **b**, in a ratio of 3:7. ^{1}H NMR (DMSO-d_6): **34a**, δ 8.15 (d, J = 8.0 Hz, 1H), 7.75 (t, J = 8.0 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.48−7.10 (m, 6H), 5.67 (d, J = 3 Hz, exch, 1H), 5.39 (s, exch, 2H), 5.23 (dd, J = 3 and 7 Hz, 1H), 3.99 (dq, J = 3 and 7 Hz, 1H), 1.23 (d, J = 7 Hz, 3H); **34b**, δ 8.17 (d, J = 8.0 Hz, 1H), 7.75 (t, J = 8.0 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.48−7.21 (m, 6H), 5.84 (s, exch, 2H), 5.53 (d, J = 4.3 Hz, exch, 1H), 4.74 (dd, J = 4.3 and 9.3 Hz, 1H), 4.13 (dq, J = 7.0 and 9.3 Hz, 1H), 1.11 (d, J = 7.0 Hz, 3H). ^{13}C NMR (DMSO-d_6): **34a**, δ 160.6, 159.2, 145.9, 142.6, 133.6, 127.5, 127.3, 126.8, 126.6, 125.9, 125.5, 119.7, 73.7, 41.9, 11.9; **34b**, δ 160.8, 159.8, 146.5, 143.5, 133.3, 127.9, 126.8, 126.7, 126.6, 125.9, 125.8, 119.5, 78.6, 42.4, 15.4. HRMS: calcd for $C_{16}H_{16}N_3O_2$ 282.1243, found 282.1243. Anal. Calcd for $C_{16}H_{15}N_3O_2$: C, 68.33; H, 5.34; N, 14.94. Found: C, 68.15; H, 5.51; N, 14.74.

3-Amino-2-(1,2-dimethyl-2-hydroxyhexyl)-4(3*H*)-quinazolinone (35): ^{1}H NMR ($CDCl_3$) δ 8.23 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.46 (t, J = 8.0 Hz, 1H), 5.73 (s, exch, 1H), 4.91 (s, exch, 2H), 3.88 (q, J = 7.0 Hz, 1H), 1.64−1.37 (m, 6H), 1.35 (d, J = 7.0 Hz, 3H), 1.19 (s, 3H), 0.96 (t, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 162.1, 161.6, 145.7, 134.7, 127.0, 126.6, 126.5, 119.8, 73.5, 41.2, 39.1, 25.9, 23.3, 26.5, 14.1, 14.0; HRMS calcd for $C_{16}H_{24}N_3O_2$ 290.1869, found 290.1869. Anal. Calcd for $C_{16}H_{23}N_3O_2$: C, 66.43; H, 7.96; N, 14.53. Found: C, 66.55; H, 7.86; N, 14.53.

3-Amino-2-(2-ethyl-2-hydroxy-1-methylhexyl)-4(3*H*)-quinazolinone (36): ^{1}H NMR ($CDCl_3$) δ 8.23 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 8.0 Hz, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.46 (t, J = 8.0 Hz, 1H), 5.58 (s, exch, 1H), 4.90 (s, exch, 2H), 3.96 (q, J = 7.0 Hz, 1H), 1.71−1.24 (m, 8H), 1.35 (d, J = 7.0 Hz, 3H), 0.96 (t, J = 7.0 Hz, 3H), 0.84 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 162.2, 161.6, 145.7, 134.5, 127.0, 126.6, 126.5, 119.7, 75.8, 39.4, 34.0, 30.4, 25.4, 23.2, 14.1, 14.0, 8.1; 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, 67.27; H, 8.25; N, 13.86. Found: C, 67.19; H, 8.51; N, 13.78.

3-Amino-2-(1,2-dimethyl-2-hydroxybutyl)-4(3*H*)-quinazolinone (37): ^{1}H NMR ($CDCl_3$) δ 8.22 (d, J = 8.0 Hz, 1H), 7.73 (t, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.45 (t, J = 8.0 Hz, 1H), 5.13 (s, exch, 1H), 5.06 (s, exch, 2H), 3.90 (q, J = 7.0 Hz, 1H), 1.56 (m, 2H), 1.39 (d, J = 7.0 Hz, 3H), 1.25

(s, 3H), 0.90 (t, J = 7.7 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 161.44, 161.36, 145.8, 134.3, 127.0, 126.6, 126.4, 119.7, 74.6, 40.9, 34.7, 23.2, 14.4, 8.5; HRMS calcd for $C_{16}H_{24}N_3O_2$ 290.1869, found 290.1869. Anal. Calcd for $C_{16}H_{23}N_3O_2$: C, 66.43; H, 7.96; N, 14.53. Found: C, 66.55; H, 8.66; N, 14.53.

3-Amino-2-(2,2-diphenyl-2-hydroxy-1-methylethyl)-4(3*H*)-quinazolinone (38): ^{1}H NMR ($CDCl_3$) δ 8.12 (d, J = 8.0 Hz, 1H), 7.66−7.01 (m, 14H), 5.06 (q, J = 6.9 Hz, 1H), 4.92 (s, exch, 2H), 1.30 (d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 162.0, 161.6, 148.4, 145.4, 145.3, 134.5, 128.2, 126.7, 126.5, 126.4, 125.5, 125.3, 119.6, 79.6, 41.4, 14.9; HRMS calcd for $C_{23}H_{22}N_3O_2$ 372.1712, found 372.1712. Anal. Calcd for $C_{23}H_{21}N_3O_2$: C, 74.39; H, 5.66; N, 11.32. Found: C, 74.30; H, 5.85; N, 11.18.

3-Amino-2-(1-monodeuterioethyl)-4(3*H*)-quinazolinone (39): ^{1}H NMR ($CDCl_3$) δ 8.20 (d, J = 8.0 Hz, 1H), 7.70 (t, J = 8.0 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.41 (t, J = 8.0 Hz, 1H), 4.90 (s, exch, 2H), 3.04−3.00 (m, 1H), 1.38 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 161.8, 159.0, 147.0, 134.2, 127.1, 126.3, 126.2, 119.9, 27.8, 27.6, 27.4, 11.2; HRMS calcd for $C_{10}H_{11}N_3OD$ 191.1043, found 191.1043.

3-Amino-2-(1-ethyl-2-hydroxy-2-phenylpropyl)-4(3*H*)-quinazolinone (40): The NMR spectra of compound **40** show a mixture of two isomers, **a** and **b**, in a ratio of 2:9. ^{1}H-NMR ($CDCl_3$): **40a**, δ 8.08 (d, J = 8.0 Hz, 1H), 7.94−7.03 (m, 8H), 6.18 (s, exch, 1H), 4.52 (s, exch, 2H), 4.38 (dd, J = 3.9 and 9.6 Hz, 1H), 2.17−2.03 (overlapping m, 2H), 1.42 (s, 3H), 0.87 (t, J = 7.5 Hz, 3H); **40b**, δ 8.27 (d, J = 8.0 Hz, 1H), 7.94−7.03 (m, 8H), 6.08 (s, exch, 1H), 4.94 (s, exch, 2H), 4.38 (dd, J = 3.9 and 9.6 Hz, 1H), 1.97−1.90 (overlapping m, 2H), 1.42 (s, 3H), 0.67 (t, J = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$): **40a**, δ 161.1, 160.8, 148.6, 145.6, 134.4, 128.7, 128.6, 128.2, 126.8, 126.4, 124.5, 119.4, 76.2, 50.3, 29.7, 23.0, 12.0; **40b**, δ 161.7, 161.5, 146.6, 145.9, 134.7, 128.3, 127.9, 127.1, 126.9, 126.4, 125.0, 119.8, 75.9, 50.1, 30.5, 23.6, 11.9. HRMS: calcd for $C_{19}H_{22}N_3O_2$ 324.1712, found, 324.1712. Anal. Calcd for $C_{19}H_{21}N_3O_2$: C, 70.59; H, 6.50; N,13.00. Found: C, 70.49; H, 6.43; N, 12.72.

3-Amino-2-(1-ethyl-2-hydroxy-2-methylbutyl)-4(3*H*)-quinazolinone (41): The NMR spectra of compound **41** show a mixture of two isomers, **a** and **b**, in a ratio of 1:1. ^{1}H NMR ($CDCl_3$): **41a**, δ 8.14 (d, J = 8.0 Hz, 1H), 7.77 (t, J = 8.0 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.48 (t, J = 8.0 Hz, 1H), 4.96 (s, exch, 2H), 4.70 (s, exch, 1H), 3.96 (dd, J = 3.5 and 11.0 Hz, 1H), 2.14−2.00 (m, 1H), 2.00−1.87 (m, 1H), 1.72 (q, J = 7.0 Hz, 2H), 1.28 (s, 3H), 0.91 (t, J = 7.0 Hz, 3H), 0.83 (t, J = 7.0 Hz, 3H); **41b**, δ 8.14 (d, J = 8.0 Hz, 1H), 7.77 (t, J = 8.0 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.48 (t, J = 8.0 Hz, 1H), 5.26 (s, exch, 1H), 5.07 (s, exch, 2H), 3.91 (dd, J = 3.5 and 11.0 Hz, 1H), 2.14−2.00 (m, 1H), 2.00−1.87 (m, 1H), 1.45 (q, J = 7.0 Hz, 2H), 1.07 (s, 3H), 0.97 (t, J = 7.0 Hz, 3H), 0.85 (t, J = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$): **41a**, δ 161.6, 161.5, 146.0, 134.3, 127.2, 126.6, 126.5, 119.7, 74.4, 48.4, 31.9, 23.4, 22.3, 12.1, 8.2; **41b**, δ 161.4, 160.5, 145.9, 134.5, 127.1, 126.6, 126.5, 119.7, 75.1, 47.8, 35.1, 26.2, 22.8, 12.2, 8.2. HRMS: calcd for $C_{15}H_{22}N_3O_2$ 276.1712, found 276.1712. Anal. Calcd for $C_{15}H_{21}N_3O_2$: C, 65.45; H, 7.64; N, 15.27. Found: C, 65.47; H, 7.66; N, 15.23.

3-Amino-2-[1-(hydroxydiphenylmethyl)propyl]-4(3*H*)-quinazolinone (42): ^{1}H NMR (DMSO-d_6) δ 8.04 (d, J = 8.0 Hz, 1H), 7.74−7.14 (m, 14H), 5.92 (s, exch, 2H), 5.15 (dd, J = 3.9 and 9.7 Hz, 1H), 1.89 (ddq, J = 4.0, 7.0 and 14.0 Hz, 1H), 1.60 (ddq, J = 7.0, 10.0 and 14.0 Hz, 1H), 0.76 (t, J = 7.6 Hz, 3H); ^{13}C NMR (DMSO-d_6) δ 162.8, 160.6, 148.8, 146.0, 145.0, 134.4, 128.1, 128.0, 126.5, 126.3, 126.2, 126.1, 126.0, 125.1, 119.5, 79.8, 47.0, 23.6, 11.7; HRMS calcd for $C_{24}H_{24}N_3O_2$ 386.1869, found 386.1869 Anal. Calcd for $C_{24}H_{23}N_3O_2$: C, 74.80; H, 5.97; N, 10.91. Found: C, 74.61; H, 6.00; N, 10.85.

2-(2,2-Diphenyl-2-hydroxy-1-methylethyl)-3-(methylamino)-4(3*H*)-quinazolinone (43): ^{1}H-NMR ($CDCl_3$, 58 °C) δ 8.13 (d, J = 8.0 Hz, 1H), 7.65−6.92 (m, 14H), 5.65 (q, J = 5.9 Hz, exch, 1H), 4.92 (t, J = 6.8 Hz, 1H), 2.87 (d, J = 5.9 Hz, 3H), 1.36 (d, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 58 °C) δ 162.8, 161.0, 148.6, 145.8, 145.8, 134.5, 128.2, 128.1, 126.8, 126.7, 126.6, 126.56, 126.5, 125.8, 125.7, 120.6, 80.1, 41.6, 38.9, 15.8; HRMS calcd for $C_{24}H_{24}N_3O_2$ 386.1869, found 386.1869. Anal. Calcd for $C_{24}H_{23}N_3O_2$: C, 74.80; H, 5.97; N, 10.91. Found: C, 74.65; H, 6.15; N, 10.76.

2-[1-(1-Hydroxycyclopentyl)ethyl]-3-(methylamino)-4(3*H*)-quinazolinone (44): ^{1}H NMR ($CDCl_3$) δ 8.25 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.47 (t, J = 8.0 Hz, 1H), 5.80 (br s, exch, 1H), 5.68 (q, J = 5.9 Hz, exch, 1H), 3.49 (q, J = 6.8 Hz, 1H), 2.80 (d, J = 5.9 Hz, 3H), 1.92−1.60 (m, 8H), 1.47 (d, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 162.7, 160.9, 145.9, 134.5, 126.94, 126.93, 126.5, 120.5, 83.1, 40.7, 38.8, 38.5, 38.4, 24.1, 24.0, 15.9; 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, 66.75; H, 7.46; N, 14.40.

3-(Methylamino)-2-(1-monodeuterioethyl)-4(3*H*)-quinazolinone (45): ^{1}H NMR ($CDCl_3$) δ 8.24 (d, J = 8.0 Hz, 1H), 7.73 (t, J = 8.0 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.44 (t, J = 8.0 Hz, 1H), 5.65 (q, J = 6.0 Hz, exch, 1H), 3.00 (br s, 1H), 2.79 (d, J = 6.0 Hz, 3H), 1.39 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 161.3, 159.2, 147.2, 134.2, 127.2, 126.4, 126.2, 120.7, 38.4, 27.1, 26.9, 26.7, 11.4; HRMS calcd for $C_{11}H_{12}N_3$-OD 204.1121, found 204.1121.

3-(Methylamino)-2-[1-[(phenylamino)carbonyl]ethyl]-4(3*H*)-quinazolinone (46): ^{1}H NMR (DMSO-d_6) δ 10.16 (s, exch, 1H), 8.14 (d, J = 8.0 Hz, 1H), 7.81 (t, J = 8.0 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.58 (d, J = 7.7 Hz, 2H), 7.51 (t, J = 8.0 Hz, 1H), 7.27 (t, J = 7.7 Hz, 2H), 7.01 (t, J = 7.7 Hz, 1H), 6.24 (q, J = 5.5 Hz, exch, 1H), 4.02 (q, J = 7.1 Hz, 1H), 2.63 (d, J = 5.5 Hz, 3H), 1.57 (d, J = 7.1 Hz, 3H); ^{13}C NMR (DMSO-d_6) δ 170.5, 160.4, 157.0, 146.4, 139.3, 134.1, 128.4, 127.2, 126.3, 125.8, 122.9, 121.7, 119.1, 45.3, 34.1, 15.8; HRMS calcd for $C_{18}H_{19}N_4O_2$ 323.1508, found 323.1508 Anal. Calcd for $C_{18}H_{18}N_4O_2$: C, 67.08; H, 5.59; N, 17.39. Found: C, 67.22; H, 5.60; N, 17.42.

2-[1-(Diphenylhydroxymethyl)propyl]-3-(methylamino)-4(3*H*)-quinazolinone (47). The NMR spectra of compound **47** show a mixture of two isomers, **a** and **b**, in a ratio of 1:3. ^{1}H NMR ($CDCl_3$, 58 °C); **47a**, δ 8.14 (d, J = 8.0 Hz, 1H), 7.74−6.94 (m, 14H), 5.25 (q, J = 5.9 Hz, exch, 1H), 5.07 (dd, J = 3.6 and 10.9 Hz, 1H), 2.68 (d, J = 5.9 Hz, 3H), 1.97, 1.82 (2 m, 2H), 0 .82 (t, J = 7.6 Hz, 3H); **47b**, δ 8.14 (d, J = 8.0 Hz, 1H), 7.74−6.94 (m, 14H), 5.25 (q, J = 5.9 Hz, exch, 1H), 4.91 (dd, J = 4.2 and 9.5 Hz, 1H), 2.68 (d, J = 5.9 Hz, 3H), 2.10, 1.98 (2 m, 2H), 0.82 (t, J = 7.6 Hz, 3H). ^{13}C NMR ($CDCl_3$): **47a**, δ 161.44, 161.38, 147.6, 145.49, 145.48, 134.6, 128.07, 128.1, 126.8, 126.7, 126.63, 126.6, 126.5, 125.5, 125.1, 119.8, 80.0, 48.3, 38.2, 24.3, 12.9; **47b**, δ 161.9, 160.9, 148.2, 145.42, 145.36, 134.6, 128.2, 127.8, 126.8, 126.7, 126.6, 126.5, 126.46, 125.6, 125.5, 120.4, 80.0, 48.2, 38.2, 24.3, 12.0. HRMS: calcd for $C_{25}H_{25}N_3O_2$ 400.2025, found 400.2025. Anal. Calcd for $C_{25}H_{26}N_3O_2$: C, 75.19; H, 6.26; N, 10.53. Found: C, 75.32; H, 6.31; N, 10.46.

2-[1-(Diisopropyldithiocarbamoyl)ethyl]-4(3*H*)-quinazolinone (48): mp 180−182 °C; ^{1}H NMR (DMSO-d_6, 100 °C) δ 12.35 (s, exch, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.76 (t, J = 8.0 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.46 (t, J = 8.0 Hz, 1H), 5.25 (q, J = 7.1 Hz, 1H), 4.80 (septet, J = 6.8 Hz, 2H), 1.75 (d, J = 7.1 Hz, 3H), 1.43 (d, J = 6.8 Hz, 12H); ^{13}C NMR (DMSO-d_6, 100 °C) δ 193.3, 161.5, 157.2, 148.5, 134.1, 127.0, 126.3, 125.8, 121.4, 53.6, 48.6, 19.9, 19.8, 18.9; HRMS calcd for $C_{17}H_{24}N_3OS_2$ 350.1361, found 350.1380. Anal. Calcd for $C_{17}H_{23}N_3OS_2$: C, 58.28; H, 6.57; N, 12.00. Found: C, 58.08; H, 6.63; N, 11.783.

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Supporting Information Available: Compound characterization data, complete with NMR peak assignments (14 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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