A Simple and Convenient Procedure for Lithiation and Side-Chain Substitution of 2-Alkyl-4-(methylthio)quinazolines and 2-Alkyl-4-methoxyquinazolines

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Received 17 May 2005

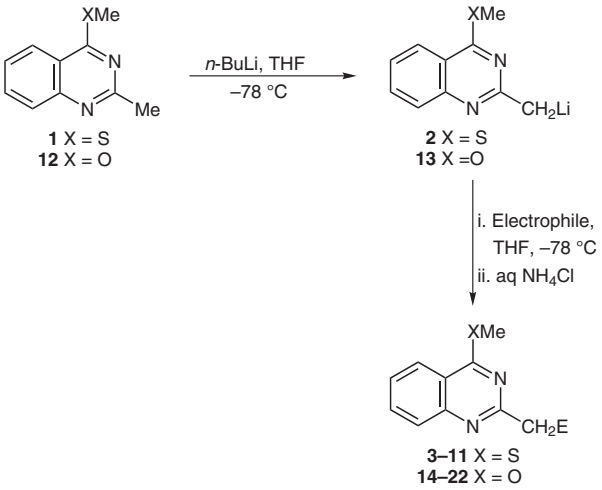
Dedicated to Professor Steven V. Ley on the occasion of his sixtieth birthday

Abstract: 2-Methyl-4-(methylthio)quinazoline has been lithiated, in the 2-methyl group, with *n*-BuLi at –78 °C in THF. The lithium reagent thus obtained reacts with a variety of electrophiles (iodomethane, iodoethane, D_2O, benzaldehyde, 4-anisaldehyde, hexan-2-one, acetophenone, benzophenone, cyclohexanone) to give modified 2-substituted 4-(methylthio)quinazolines in excellent yields. Similarly, lithiation of 4-methoxy-2-methylquinazoline followed by reactions with various electrophiles gave the corresponding modified 2-substituted 4-methoxyquinazolines in excellent yields. Lithiations of 2-ethyl-4-(methylthio)quinazoline, 4-(methylthio)-2-propylquinazoline, 2-ethyl-4-methoxyquinazoline and 4-methoxy-2-propylquinazoline, followed by reactions with a range of electrophiles, behave in a similar manner to give the corresponding modified 2-substituted derivatives in good yields.

Key words: lithiation, side-chain, substitution, 2-alkyl-4-(methylthio)quinazoline, 2-alkyl-4-methoxyquinazoline, electrophiles

Regioselective synthesis of substituted aromatics is one of the classical problems in synthetic chemistry. Simple electrophilic substitution often leads to various isomers and polysubstituted aromatics and usually takes place under forcing conditions in the presence of a catalyst. Lithiation of aromatics followed by electrophilic substitution is one of the most efficient approaches for synthesis of substituted and/or modified derivatives.[2,3] Recently, lithiation of various heterocycles followed by reactions with various electrophiles have been reported to produce complex substituted heterocycles, usually in high yields.[4] However, there are relatively few examples concerning lithiation of 3*H*-quinazolin-4-one derivatives.[5–12] Compounds possessing this ring system are always of interest because of their numerous pharmacological applications.[13] In continuation of our own interest in the use of lithiation reactions for organic synthesis,[14] we have developed several lithiation procedures of various 3*H*-quinazolin-4-ones.[15–22] However, our attempts to bring about lithiation of 4-(methylthio)quinazoline and 4-methoxyquinazoline were unsuccessful, resulting instead in addition of the alkyllithium reagent to the 2-position of the ring.[23] It was therefore of interest to investigate whether the corresponding 4-substituted 2-alkylquinazolines could be lithiated in the side-chain. We now report the successful lithiation and side-chain substitution of 2-alkyl-4-(methylthio)quinazolines and 2-alkyl-4-methoxyquinazolines to produce modified 2-substituted derivatives in high yields.

2-Methyl-4-(methylthio)quinazoline (**1**) was prepared according to the literature procedure.[24] It was hoped that the side-chain lithiation of **1** would take place as for 2-methyl-3*H*-quinazoline-4-thione,[21] so that substitution of the hydrogen at the 2-methyl group could be achieved. Indeed, lithiation of **1** occurred smoothly and rapidly with 1.1 equivalents of *n*-BuLi at –78 °C in anhydrous THF under nitrogen with no nucleophilic attack at either of the imine groups of the quinazoline ring. The lithium reagent **2** was obtained as a purple solution when addition of *n*-BuLi was complete. Reactions of the lithium reagent **2** with a range of electrophiles (iodomethane, iodoethane, D_2O, benzaldehyde, 4-anisaldehyde, hexan-2-one, acetophenone, benzophenone, cyclohexanone) gave the corresponding modified 2-substituted 4-(methylthio)quinazolines **3–11** (Scheme 1; X = S) in excellent yields (Table 1).

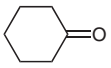


Scheme 1

As indicated in Table 1, the yields of isolated and purified products were excellent in all cases. The spectral characteristics of compounds **3–11** were consistent with the assigned structures (see experimental section for details). The ^{1}H NMR spectra of compounds **6–9** showed that the two hydrogen atoms of the CH_2 group at position 2 occurred as independent, coupled signals, verifying that they

SYNTHESIS 2005, No. 17, pp 2951–2961
Advanced online publication: 23.09.2005
DOI: 10.1055/s-2005-916036; Art ID: Z09505SS

Table 1 Synthesis of Products **3**–**11** According to Scheme 1 (X = S)

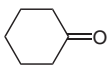
Product	Electrophile	E	Yield (%)[a]
3	MeI	Me	91
4	EtI	Et	88
5	D_2O	D	89
6	PhCHO	PhCH(OH)	83
7	4-$MeOC_6H_4CHO$	4-$MeOC_6H_4CH(OH)$	86
8	MeCOBu	MeC(OH)Bu	84
9	PhCOMe	PhC(OH)Me	85
10	Ph_2CO	$Ph_2C(OH)$	90
11			85

[a] Yield of isolated and purified product.

are diastereotopic. The CH_2 signals resonated as two separated doublets (J = ca 15 Hz) in the cases of compounds **8** and **9**. In the cases of compounds **6** and **7**, the signals were further complicated by coupling to the CHOH group and by having very similar chemical shifts.

Attention was next turned to the lithiation of 4-methoxy-2-methylquinazoline (**12**), which was prepared according to the literature procedure.[25] It was hoped that side-chain lithiation of **12** would take place as for compound **1**. Indeed, use of the same lithiation procedure as was used for compound **1** gave the lithium reagent **13** as a dark pink solution. Reactions of **13** with the same range of electrophiles gave the corresponding modified 2-substituted 4-methoxyquinazolines **14**–**22** (Scheme 1; X = O) in very good yields (Table 2).

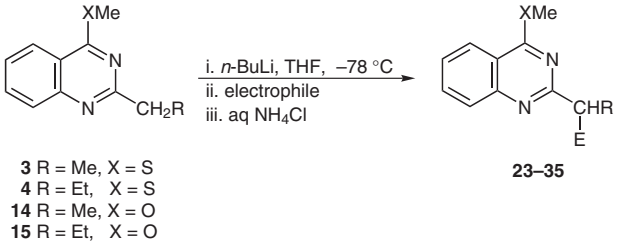
Table 2 Synthesis of Products **14**–**22** According to Scheme 1 (X = O)

Product	Electrophile	E	Yield (%)[a]
14	MeI	Me	90
15	EtI	Et	87
16	D_2O	D	86
17	PhCHO	PhCH(OH)	80
18	4-$MeOC_6H_4CHO$	4-$MeOC_6H_4CH(OH)$	82
19	MeCOBu	MeC(OH)Bu	73
20	PhCOMe	PhC(OH)Me	85
21	Ph_2CO	$Ph_2C(OH)$	81
22			75

[a] Yield of isolated, purified product.

The spectral characteristics of compounds **14**–**20** were very similar to those of compounds **3**–**11** (see experimental section for details).

Attention was next turned to the lithiation of 2-ethyl-4-(methylthio)quinazoline (**3**), 4-(methylthio)-2-propylquinazoline (**4**), 2-ethyl-4-methoxyquinazoline (**14**) and 4-methoxy-2-propylquinazoline (**15**), which had been obtained by alkylation of the lithium reagents **2** and **13** according to Scheme 1 by reactions with MeI and EtI. If successful, this would suggest that the lithiation process was tolerant of a variety of primary alkyl groups at position 2, with either a methylthio or methoxy group at position 4. It was found that successful lithiation was achieved using *n*-BuLi under identical reaction conditions to those used for the lithiation of compounds **1** and **12**, without optimisation of the individual cases. The lithium reagents thus obtained reacted with several electrophiles to give the corresponding modified 2-substituted derivatives **23**–**35** (Scheme 2) in high yields (Table 3).



Scheme 2

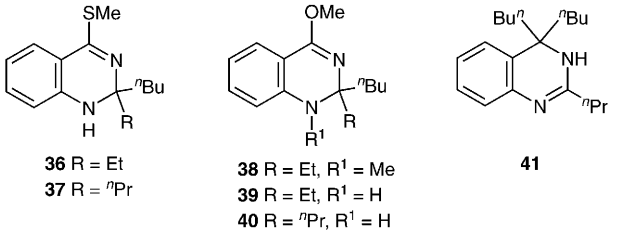
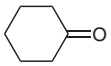
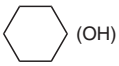


Figure 1

As can been seen from Table 3, the yields of isolated and purified products were good in all cases, though the yields in the 4-(methylthio) series (78–85%) were generally a little better than those in the 4-methoxy series (67–79%). It was also found that following lithiation of **3** and **4**, treatment with an electrophile and then work-up, small quantities of 2-butyl-2-ethyl-4-(methylthio)-1,2-dihydroquinazoline (**36**) and 2-butyl-4-(methylthio)-2-propyl-1,2-dihydroquinazoline (**37**) were obtained as by-products in around 3–7% yields, due to nucleophilic addition of *n*-BuLi at the imine bond at position 2 of the quinazoline ring in compounds **3** and **4**.

Similarly, following comparable reactions of **14** and **15**, small quantities of 2-butyl-2-ethyl-4-methoxy-1,2-dihydroquinazoline (**39**) and 2-butyl-4-methoxy-2-propyl-1,2-dihydroquinazoline (**40**) were obtained as by-products in yields of 2–3%. Moreover, in the reaction of the lithium

Table 3 Synthesis of Products **23**–**35** According to Scheme 2

Product	X	R	Electrophile	E	Yield (%)[a]
23	S	Me	MeI	Me	82[b]
24	S	Me	D_2O	D	85[b]
25	S	Me	PhCHO	PhCH(OH)	80[b]
26	S	Me	Ph_2CO	$Ph_2C(OH)$	81[b]
27	S	Et	D_2O	D	82[c]
28	S	Et	4-$MeOC_6H_4CHO$	4-$MeOC_6H_4CH(OH)$	78[c]
29	S	Et			79[c]
30	O	Me	MeI	Me	67[d,e]
31	O	Me	D_2O	D	76[e]
32	O	Me	4-$MeOC_6H_4CHO$	4-$MeOC_6H_4CH(OH)$	71[e]
33	O	Me	Ph_2CO	$Ph_2C(OH)$	73[e]
34	O	Et	D_2O	D	79[f,g]
35	O	Et	Ph_2CO	$Ph_2C(OH)$	71[f,g]

[a] Yield of isolated, purified product.
[b] Compound **36** (Figure 1) was obtained in 3–5% yield.
[c] Compound **37** (Figure 1) was obtained in 4–7% yield.
[d] Compound **38** (Figure 1) was obtained in 3% yield.
[e] Compound **39** (Figure 1) was obtained in 2–3% yield.
[f] Compound **40** (Figure 1) was obtained in 3% yield.
[g] Compound **41** (Figure 1) was obtained in 1–2% yield.

reagent from compound **14** with iodomethane a small quantity of by-product **38** (3%) was obtained due to methylation at N-1. Also, following lithiation of **15** 4,4-dibutyl-2-propyl-1,2-dihydroquinazoline (**41**) was obtained in a yield of 1–2%. Compound **41** was produced as a result of addition of *n*-BuLi at the imine bond at position 4, followed by elimination of the methoxy group and further addition of *n*-BuLi.

The spectral characteristics of compounds **23**–**41** were consistent with the assigned structures (see experimental section for details). The ^1H NMR spectrum of compound **35** showed that the hydrogen atoms of the CH_2 group attached to the newly created asymmetric centre occurred as independent, coupled signals, verifying that they are diastereotopic. Also, the ^{13}C signals of the two sides of the cyclohexane ring in compound **29** appear separately, as do the signals of the two phenyl groups in compound **35**. The NMR spectra of compounds **25**, **28** and **32** showed the expected presence of two racemic diastereoisomers, and in the cases of compounds **25** and **32** these diastereoisomers could be separated by column chromatography.

The first fraction (**25a**) from chromatography of products **25** was an oil, obtained in 48% yield as a single diastereoisomer, and exhibited a ^1H–^1H coupling constant of 2 Hz between the two CH groups of the side-chain at position 2 of the quinazoline. It was identified as the *syn*-isomer, 2-[(1*R**,2*S**)-2-hydroxy-1-methyl-2-phenylethyl]-4-(methylthio)quinazoline. The second fraction (**25b**) was crystalline and obtained in a 32% yield as a single diastereoisomer with a coupling constant of 7 Hz between the corresponding two CH groups. This was firmly identified as the *anti*-isomer, 2-[(1*S**,2*S**)-2-hydroxy-1-methyl-2-phenylethyl]-4-(methylthio)quinazoline by X-ray crystallography (Figure 2). The crystal structure also verified a large dihedral angle between the two central CH groups, which explains why the coupling constant between them is larger than for the other diastereoisomer. Similarly, the components of product **32** were separated into two single diastereoisomers, identified as 2-[(1*R**,2*S**)-2-hydroxy-2-(4-methoxyphenyl)-1-methylethyl]-4-methoxyquinazoline (**32a**, 29%, an oil) by its coupling constant $J_{1,2}$ = 2 Hz, and 2-[(1*R**,2*R**)-2-hydroxy-2-(4-methoxyphenyl)-1-methylethyl]-4-methoxyquinazoline (**32b**, 42%, a solid) with a coupling constant $J_{1,2}$ = 7 Hz.

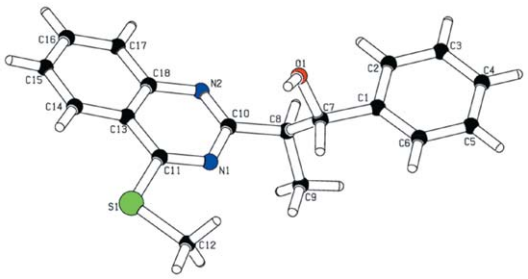


Figure 2 X-ray crystal structure of **25b**

In conclusion, this work describes a simple and convenient method for the side-chain substitution of 4-substituted 2-alkylquinazolines to produce 2-substituted quinazoline derivatives in high yields. These products might have pharmacological activities and would be more difficult to prepare by other means. The procedure applied is general and the results obtained suggest that the lithiation process is tolerant of a variety of primary alkyl groups at position 2.

Melting point determinations were performed by the open capillary method using a Gallenkamp melting point apparatus and are reported uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV400 spectrometer operating at 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR measurements. Chemical shifts are reported relative to TMS and ^{13}C multiplicities are based on DEPT signals. Assignments of signals are based on coupling patterns and expected chemical shift values have not been rigorously confirmed. Signals with similar characteristics might be interchanged. Low-resolution mass spectra were recorded on a Quattro II spectrometer, electron impact (EI) at 70 eV and chemical ionization (CI) at 50 eV by the use of NH_3 as ionization gas. Accurate mass data were obtained on a MAT900 instrument. X-ray analysis was obtained from the EPSRC National Crystallography Service. Column chromatography was carried out using Fisher Scientific silica 60A (35–70 μ). *n*-BuLi was obtained from Aldrich Chemical Company and its concentration was estimated prior to use by the method of Watson and Eastham.[26] THF was distilled from sodium benzophenone ketyl. Other chemicals were obtained from Aldrich Chemical Company and used without further purification. Other solvents were purified by standard procedures.[27,28]

Modified 2-Substituted 4-(Methylthio)quinazolines and 4-Methoxyquinazolines; General Procedure

A solution of *n*-BuLi in hexanes (0.90 mL, 2.5 M, 2.2 mmol) was added to a cold (–78 °C), stirred solution of the appropriate quinazoline **1**, **3**, **4**, **12**, **14** or **15** (2.0 mmol) in anhyd THF (10 mL) under N_2. During the addition a purple or deep pink colour of the new organolithium species appeared, but the mixture was stirred at –78 °C for 1 h to ensure complete formation of the lithium reagent. An electrophile (2.2 mmol), in anhyd THF (8 mL) if solid, otherwise neat, was added. The reaction mixture was stirred for 1 h at –78 °C, then removed from the cooling bath and allowed to warm to r.t., diluted with Et_2O (10 mL) and then quenched with aq sat. NH_4Cl (10 mL). The organic layer was separated, washed with H_2O (2 × 10 mL), dried ($MgSO_4$), and evaporated under reduced pressure. The residue obtained was purified by column chromatography (silica gel; Et_2O–hexane, 1:5) to give the pure product. The yields obtained are recorded in Tables 1– 3.

2-Ethyl-4-(methylthio)quinazoline (3)

Mp 39–40 °C (Lit.[24] 37 °C).

^{1}H NMR ($CDCl_3$): δ = 7.99 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.84 (dd, *J* = 1, 8 Hz, 1 H, H-5), 7.72 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.43 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 3.00 (q, *J* = 7.5 Hz, 2 H, CH_2), 2.66 (s, 3 H, SCH_3), 1.40 (t, *J* = 7.5 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 171.6 (s, C-2), 167.1 (s, C-4), 148.7 (s, C-8a), 133.7 (d, C-7), 128.5 (d, C-8), 126.6 (d, C-5), 124.0 (d, C-6), 122.5 (s, C-4a), 33.4 (t, CH_2), 13.1 (q, CH_3), 12.8 (q, CH_3).

EI–MS: *m*/*z* (%) = 204 (100) [M$^+$], 203 (80), 189 (21), 171 (27), 157 (33), 129 (41), 102 (40), 76 (17), 75 (18), 40 (23).

CI–MS: *m*/*z* (%) = 205 (100) [MH$^+$], 159 (41).

HRMS: *m*/*z* [MH$^+$] calcd for $C_{11}H_{13}N_2S$: 205.0794; found: 205.0794.

2-Propyl-4-(methylthio)quinazoline (4)

Mp 35–36 °C.

^{1}H NMR ($CDCl_3$): δ = 8.03 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.88 (dd, *J* = 1, 8 Hz, 1 H, H-5), 7.77 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.47 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 3.00 (t, *J* = 7.5 Hz, 2 H, CH_2), 2.69 (s, 3 H, SCH_3), 1.95 (app. sextet, *J* = 7.5 Hz, 2 H, CH_2), 1.04 (t, *J* = 7.5 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 171.5 (s, C-2), 166.2 (s, C-4), 148.7 (s, C-8a), 133.7 (d, C-7), 128.5 (d, C-8), 126.6 (d, C-5), 124.0 (d, C-6), 122.5 (s, C-4a), 42.2 (t, CH_2), 22.3 (t, CH_2), 14.4 (q, CH_3), 12.8 (q, CH_3).

EI–MS: *m*/*z* (%) = 218 (30) [M$^+$], 203 (89), 190 (100), 189 (70), 171 (24), 155 (23), 142 (21), 129 (80), 102 (81), 76 (37), 75 (42), 41 (42).

CI–MS: *m*/*z* (%) = 219 (100) [MH$^+$], 206 (24), 198 (42), 173 (90), 160 (27), 153 (31).

HRMS: *m*/*z* [MH$^+$] calcd for $C_{12}H_{15}N_2S$: 219.0950; found: 219.0951.

2-Deuteriomethyl-4-(methylthio)quinazoline (5)

Mp 52–53 °C (mp of undeuteriated analogue 52 °C[24]).

^{1}H NMR ($CDCl_3$): δ = 7.99 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.82 (dd, *J* = 1, 8 Hz, 1 H, H-5), 7.73 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.44 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 2.77 [t (1:1:1), *J* = 2 Hz, 2 H, CH_2D], 2.66 (s, 3 H, SCH_3).

^{13}C NMR ($CDCl_3$): δ = 171.5 (s, C-2), 163.1 (s, C-4), 148.5 (s, C-8a), 133.7 (d, C-7), 128.3 (d, C-8), 126.6 (d, C-5), 123.9 (d, C-6), 122.2 (s, C-4a), 26.7 [t (1:1:1), t, CH_2D], 12.7 (q, SCH_3).

EI–MS: *m*/*z* (%) = 191 (70) [M$^+$], 149 (25), 143 (61), 102 (68), 75 (42), 57 (56), 40 (100).

CI–MS: *m*/*z* (%) = 192 (41) [MH$^+$], 191 (100), 145 (40).

HRMS: *m*/*z* [M$^+$] calcd for $C_{10}H_9DN_2S$: 191.0622; found: 191.0621.

2-(2-Hydroxy-2-phenylethyl)-4-(methylthio)quinazoline (6)

Mp 98–99 °C.

^{1}H NMR ($CDCl_3$): δ = 8.07 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.91 (br d, *J* = 8 Hz, 1 H, H-5), 7.84 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.57–7.53 (m, 3 H, H-6, H-2, H-6 of Ph), 7.39 (app. t, *J* = 7.5 Hz, 2 H, H-3, H-5 of Ph), 7.31 (t, *J* = 7.5 Hz, 1 H, H-4 of Ph), 5.84 (br s, exch., 1 H, OH), 5.37 (dd, *J* = 5, 7 Hz, 1 H, CH), 3.5–3.4 (m, 2 H, CH_2), 2.70 (s, 3 H, SCH_3).

^{13}C NMR ($CDCl_3$): δ = 172.5 (s, C-2), 163.9 (s, C-4), 147.8 (s, C-8a), 144.1 (s, C-1 of Ph), 134.4 (d, C-7), 128.8 (d, C-3, C-5 of Ph), 128.5 (d, C-4 of Ph), 127.7 (d, C-8), 127.3 (d, C-5), 126.3 (d, C-2, C-6 of Ph), 124.2 (d, C-6), 122.7 (s, C-4a), 72.6 (d, CH), 47.7 (t, CH_2), 13.1 (q, SCH_3).

EI–MS: *m/z* (%) = 296 (12) [M$^+$], 281 (70), 190 (84), 189 (61), 143 (59), 142 (57), 105 (72), 102 (73), 79 (79), 77 (100), 61 (49), 51 (58).

CI–MS: *m/z* (%) = 297 (100) [MH$^+$], 251 (20), 191 (52), 145 (25).

HRMS: *m/z* [MH$^+$] calcd for $C_{17}H_{17}N_2OS$: 297.1056; found: 297.1054.

2-[2-Hydroxy-2-(4-methoxyphenyl)ethyl]-4-(methylthio)quinazoline (7)
Mp 65–67 °C.

^{1}H NMR ($CDCl_3$): δ = 8.08 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.91 (br d, *J* = 8 Hz, 1 H, H-5), 7.84 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.56 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 7.45 (d, *J* = 8.5 Hz, 2 H, H-2, H-6 of Ar), 6.92 (d, *J* = 8.5 Hz, 2 H, H-3, H-5 of Ar), 5.75 (br s, exch., 1 H, OH), 5.31 (dd, *J* = 5, 7 Hz, 1 H, CH), 3.83 (s, 3 H, OCH_3), 3.5–3.4 (m, 2 H, CH_2), 2.71 (s, 3 H, SCH_3).

^{13}C NMR ($CDCl_3$): δ = 172.5 (s, C-2), 163.9 (s, C-4), 159.3 (s, C-4 of Ar), 147.5 (s, C-8a), 136.3 (s, C-1 of Ar), 134.4 (d, C-7), 128.5 (d, C-8), 127.5 (d, C-2, C-6 of Ar), 127.2 (d, C-5), 124.2 (d, C-6), 122.6 (s, C-4a), 114.2 (d, C-3, C-5 of Ar), 72.2 (d, CH), 55.7 (q, OCH_3), 47.7 (t, CH_2), 13.1 (q, SCH_3).

CI–MS: *m/z* (%) = 327 (94) [MH$^+$], 309 (11), 191 (27), 159 (19), 154 (42), 145 (100), 137 (27), 100 (16).

HRMS: *m/z* [MH$^+$] calcd for $C_{18}H_{19}N_2O_2S$: 327.1162; found: 327.1161.

2-(2-Hydroxy-2-methylhexyl)-4-(methylthio)quinazoline (8)
Oil.

^{1}H NMR ($CDCl_3$): δ = 7.97 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.79 (dd, *J* = 1, 8 Hz, 1 H, H-5), 7.74 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.45 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 5.81 (br s, exch., 1 H, OH), 3.15, 3.06 (2 × d, *J* = 15 Hz, 2 H, CH_2COH), 2.59 (s, 3 H, SCH_3), 1.48–1.44 (m, 2 H, CH_2), 1.40–1.34 (m, 2 H, CH_2), 1.20 (app. sextet, *J* = 7.5 Hz, 2 H, CH_2), 1.55 (s, 3 H, CH_3), 0.80 (t, *J* = 7.5 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 172.0 (s, C-2), 164.1 (s, C-4), 147.9 (s, C-8a), 134.3 (d, C-7), 128.6 (d, C-8), 127.2 (d, C-5), 124.2 (d, C-6), 122.5 (s, C-4a), 72.8 (s, COH), 49.3 (t, CH_2), 42.8 (t, CH_2), 27.3 (q, CH_3), 26.8 (t, CH_2), 23.8 (t, CH_2), 14.5 (q, CH_3), 13.2 (q, CH_3).

EI–MS: *m/z* (%) = 290 (2) [M$^+$], 275 (12), 257 (8), 233 (72), 190 (100), 143 (52), 102 (70), 75 (22), 61 (27), 43 (81).

CI–MS: *m/z* (%) = 291 (100) [MH$^+$], 191 (70).

HRMS: *m/z* [MH$^+$] calcd for $C_{16}H_{23}N_2OS$: 291.1526; found: 291.1523.

2-(2-Hydroxy-2-phenylpropyl)-4-(methylthio)quinazoline (9)
Mp 79–80 °C.

^{1}H NMR ($CDCl_3$): δ = 7.87 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.74 (dd, *J* = 1, 8 Hz, 1 H, H-5), 7.68 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.49 (d, *J* = 7.5 Hz, 2 H, H-2, H-6 of Ph), 7.38 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 7.17 (app. t, *J* = 7.5 Hz, 2 H, H-3, H-5 of Ph), 7.04 (t, *J* = 7.5 Hz, 1 H, H-4 of Ph), 6.71 (br s, exch., 1 H, OH), 3.59, 3.45 (2 × d, *J* = 15.5 Hz, 2 H, CH_2), 2.55 (s, 3 H, SCH_3), 1.53 (s, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 172.1 (s, C-2), 163.4 (s, C-4), 148.5 (s, C-8a), 147.7 (s, C-1 of Ph), 134.3 (d, C-7), 128.5 (d, C-8), 128.4 (d, C-3, C-5 of Ph), 127.3 (d, C-5), 126.7 (d, C-4 of Ph), 125.3 (d, C-2, C-6 of Ph), 124.1 (d, C-6), 122.4 (s, C-4a), 74.6 (s, COH), 50.6 (t, CH_2), 31.8 (q, CH_3), 13.2 (q, SCH_3).

EI–MS: *m/z* (%) = 310 (9) [M$^+$], 295 (66), 253 (12), 190 (89), 143 (63), 121 (40), 105 (76), 102 (78), 77 (92), 61 (42), 51 (57), 43 (100).

CI–MS: *m/z* (%) = 311 (37) [MH$^+$], 191 (100), 175 (8), 145 (9), 138 (11).

HRMS: *m/z* [MH$^+$] calcd for $C_{18}H_{19}N_2OS$: 311.1213; found: 311.1215.

2-(2-Hydroxy-2,2-diphenylethyl)-4-(methylthio)quinazoline (10)
Mp 152–153 °C.

^{1}H NMR (DMSO-d_6): δ = 7.97 (d, *J* = 8 Hz, 1 H, H-8), 7.89–7.84 (m, 2 H, H-5, H-7), 7.62–7.55 (m, 5 H, H-6, H-2, H-6 of 2 × Ph), 7.24 (app. t, *J* = 7.5 Hz, 4 H, H-3, H-5 of 2 × Ph), 7.12 (t, *J* = 7.5 Hz, 2 H, H-4 of 2 × Ph), 6.96 (s, exch., 1 H, OH), 4.00 (s, 2 H, CH_2), 2.48 (s, 3 H, SCH_3).

^{13}C NMR (DMSO-d_6): δ = 171.1 (s, C-2), 162.8 (s, C-4), 148.1 (s, C-8a), 147.1 (s, C-1 of 2 × Ph), 134.9 (d, C-7), 128.2 (d, C-3, C-5 of 2 × Ph), 128.1 (d, C-8), 127.9 (d, C-4 of 2 × Ph), 126.6 (d, C-2, C-6 of 2 × Ph), 126.1 (d, C-5), 123.8 (d, C-6), 121.5 (s, C-4a), 77.5 (s, COH), 49.2 (t, CH_2), 12.4 (q, SCH_3).

EI–MS: *m/z* (%) = 372 (2) [M$^+$], 357 (11), 190 (22), 143 (25), 105 (100), 77 (94), 51 (47).

CI–MS: *m/z* (%) = 373 (100) [MH$^+$], 355 (51), 311 (21).

HRMS: *m/z* [MH$^+$] calcd for $C_{23}H_{21}N_2OS$: 373.1369; found: 373.1371.

2-[(1-Hydroxycyclohexyl)methyl]-4-(methylthio)quinazoline (11)
Oil.

^{1}H NMR ($CDCl_3$): δ = 7.95 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.79 (dd, *J* = 1, 8 Hz, 1 H, H-5), 7.73 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.44 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 5.67 (s, exch., 1 H, OH), 3.12 (s, 2 H, CH_2), 2.59 (s, 3 H, SCH_3), 1.64–1.25 [m, 10 H, $(CH_2)_5$].

^{13}C NMR ($CDCl_3$): δ = 172.0 (s, C-2), 163.8 (s, C-4), 147.9 (s, C-8a), 134.3 (d, C-7), 128.6 (d, C-8), 127.2 (d, C-5), 124.1 (d, C-6), 122.5 (s, C-4a), 71.9 (s, COH), 49.3 (t, CH_2), 38.4 (t, CH_2), 26.2 (t, CH_2), 22.7 (t, CH_2), 13.2 (q, SCH_3).

EI–MS: *m/z* (%) = 288 (4) [M$^+$], 255 (37), 245 (21), 190 (100), 143 (36), 102 (52), 81 (18), 75 (16), 55 (42), 41 (40).

CI–MS: *m/z* (%) = 289 (100) [MH$^+$], 243 (9), 191 (31), 145 (8), 116 (12).

HRMS: *m/z* [MH$^+$] calcd for $C_{16}H_{21}N_2OS$: 289.1369; found: 289.1365.

2-Ethyl-4-methoxyquinazoline (14)
Oil (Lit.[24] bp 107–109 °C/1 Torr).

^{1}H NMR ($CDCl_3$): δ = 8.00 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.80 (br d, *J* = 8 Hz, 1 H, H-5), 7.68 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.36 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 4.08 (s, 3 H, OCH_3), 2.94 (q, *J* = 7.5 Hz, 2 H, CH_2), 1.39 (t, *J* = 7.5 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 168.2 (s, C-4), 167.2 (s, C-2), 151.6 (s, C-8a), 133.5 (d, C-7), 127.4 (d, C-8), 126.2 (d, C-6), 123.6 (d, C-5), 115.0 (s, C-4a), 54.2 (q, OCH_3), 33.3 (t, CH_2), 13.0 (q, CH_3).

EI–MS: *m/z* (%) = 188 (22) [M$^+$], 187 (25), 173 (18), 160 (9), 129 (11), 119 (12), 102 (13), 90 (10), 76 (13), 54 (27), 40 (100).

CI–MS: *m/z* (%) = 189 (100) [MH$^+$], 52 (8).

HRMS: *m/z* [MH$^+$] calcd for $C_{11}H_{13}N_2O$: 189.1022; found: 189.1021.

2-Propyl-4-methoxyquinazoline (15)
Oil.

^{1}H NMR ($CDCl_3$): δ = 7.97 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.82 (dd, *J* = 1, 8 Hz, 1 H, H-5), 7.65 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.33 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 4.06 (s, 3 H, OCH_3), 2.92 (t, *J* = 7.5

Hz, 2 H, CH_2), 1.93 (app. sextet, J = 7.5 Hz, 2 H, CH_2), 1.03 (t, J = 7.5 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 167.0 (s, C-4), 166.9 (s, C-2), 151.5 (s, C-8a), 133.2 (d, C-7), 127.2 (d, C-8), 126.2 (d, C-6), 125.6 (d, C-5), 114.8 (s, C-4a), 53.9 (q, OCH_3), 42.0 (t, CH_2), 20.0 (t, CH_2), 14.2 (q, CH_3).

EI–MS: m/z (%) = 202 (4) [M^+], 187 (35), 174 (100), 160 (7), 145 (16), 117 (10), 102 (15), 90 (12), 68 (11).

CI–MS: m/z (%) = 203 (100) [MH^+], 174 (5).

HRMS: m/z [MH^+] calcd for $C_{12}H_{15}N_2O$: 203.1179; found: 203.1180.

2-Deuteriomethyl-4-methoxyquinazoline (16)
Mp 34–35 °C (mp of undeuteriated analogue 34–35 °C[25]).

^{1}H NMR ($CDCl_3$): δ = 7.99 (dd, J = 1, 8 Hz, 1 H, H-8), 7.76 (br d, J = 8 Hz, 1 H, H-5), 7.67 (app. dt, J = 1, 8 Hz, 1 H, H-7), 7.37 (app. dt, J = 1, 8 Hz, 1 H, H-6), 4.06 (s, 3 H, OCH_3), 2.64 [t (1:1:1), J = 2 Hz, 2 H, CH_2D].

^{13}C NMR ($CDCl_3$): δ = 167.0 (s, C-4), 164.0 (s, C-2), 151.5 (s, C-8a), 133.6 (d, C-7), 127.1 (d, C-8), 126.2 (d, C-5), 123.6 (d, C-6), 114.8 (s, C-4a), 54.3 (q, OCH_3), 26.4 [t (1:1:1), t, CH_2D].

EI–MS: m/z (%) = 175 (97) [M^+], 173 (95), 173 (74), 160 (32), 146 (79), 145 (77), 144 (64), 103 (100), 102 (84), 90 (55), 76 (49), 63 (38).

CI–MS: m/z (%) = 176 (100) [MH^+], 175 (50), 161 (7).

HRMS: m/z [MH^+] calcd for $C_{10}H_{10}DN_2O$: 176.0929; found: 176.0931.

2-(2-Hydroxy-2-phenylethyl)-4-methoxyquinazoline (17)
Mp 94–95 °C.

^{1}H NMR ($CDCl_3$): δ = 8.03 (dd, J = 1, 8 Hz, 1 H, H-8), 7.77 (br d, J = 8 Hz, 1 H, H-5), 7.72 (app. dt, J = 1, 8 Hz, 1 H, H-7), 7.44–7.40 (m, 3 H, H-6, H-2, H-6 of Ph), 7.27 (app. t, J = 7.5 Hz, 2 H, H-3, H-5 of Ph), 7.18 (t, J = 7.5 Hz, 1 H, H-4 of Ph), 5.81 (br s, exch., 1 H, OH), 5.24 (dd, J = 5, 7 Hz, 1 H, CH), 4.06 (s, 3 H, OCH_3), 3.3–3.2 (m, 2 H, CH_2).

^{13}C NMR ($CDCl_3$): δ = 167.3 (s, C-4), 165.0 (s, C-2), 150.9 (s, C-8a), 144.2 (s, C-1 of Ph), 134.3 (d, C-7), 128.7 (d, C-3, C-5 of Ph), 127.7 (d, C-4 of Ph), 127.4 (d, C-8), 127.0 (d, C-5), 126.3 (d, C-2, C-6 of Ph), 123.9 (d, C-6), 115.4 (s, C-4a), 72.5 (d, CH), 54.8 (q, OCH_3), 47.6 (t, CH_2).

EI–MS: m/z (%) = 280 (2) [M^+], 265 (28), 174 (96), 143 (32), 105 (61), 79 (70), 77 (100), 51 (37).

CI–MS: m/z (%) = 281 (100) [MH^+], 175 (13).

HRMS: m/z [MH^+] calcd for $C_{17}H_{17}N_2O_2$: 281.1285; found: 281.1282.

2-[2-Hydroxy-2-(4-methoxyphenyl)ethyl]-4-methoxyquinazoline (18)
Mp 88–89 °C.

^{1}H NMR ($CDCl_3$): δ = 8.05 (br d, J = 8 Hz, 1 H, H-8), 7.79 (br d, J = 8 Hz, 1 H, H-5), 7.73 (app. dt, J = 1, 8 Hz, 1 H, H-7), 7.44 (app. dt, J = 1, 8 Hz, 1 H, H-6), 7.35 (d, J = 8.5 Hz, 2 H, H-2, H-6 of Ar), 6.83 (d, J = 8.5 Hz, 2 H, H-3, H-5 of Ar), 5.73 (br s, exch., 1 H, OH), 5.20 (dd, J = 4.5, 7.5 Hz, 1 H, CH), 4.09 (s, 3 H, OCH_3), 3.73 (s, 3 H, OCH_3), 3.3–3.2 (m, 2 H, CH_2).

^{13}C NMR ($CDCl_3$): δ = 167.3 (s, C-4), 165.0 (s, C-2), 159.2 (s, C-4 of Ar), 150.9 (s, C-8a), 136.4 (s, C-1 of Ar), 134.3 (d, C-7), 127.5 (d, C-2, C-6 of Ar), 127.4 (d, C-8), 127.0 (d, C-5), 123.9 (d, C-6), 115.4 (s, C-4a), 114.1 (d, C-3, C-5 of Ar), 72.1 (d, CH), 55.7 (q, OCH_3), 54.8 (q, OCH_3), 47.6 (t, CH_2).

CI–MS: m/z (%) = 311 (30) [MH^+], 175 (100), 154 (27), 137 (18).

HRMS: m/z [MH^+] calcd for $C_{18}H_{19}N_2O_3$: 311.1390; found: 311.1387.

2-(2-Hydroxy-2-methylhexyl)-4-methoxyquinazoline (19)
Oil.

^{1}H NMR ($CDCl_3$): δ = 8.04 (dd, J = 1, 8 Hz, 1 H, H-8), 7.77 (br d, J = 8 Hz, 1 H, H-5), 7.72 (app. dt, J = 1, 8 Hz, 1 H, H-7), 7.43 (app. dt, J = 1, 8 Hz, 1 H, H-6), 5.84 (br s, exch., 1 H, OH), 4.07 (s, 3 H, OCH_3), 3.08, 2.99 (2 × d, J = 15 Hz, 2 H, CH_2COH), 1.49–1.42 (m, 2 H, CH_2), 1.40–1.31 (m, 2 H, CH_2), 1.20 (app. sextet, J = 7 Hz, 2 H, CH_2), 1.15 (s, 3 H, CH_3), 0.80 (t, J = 7 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 166.9 (s, C-4), 165.0 (s, C-2), 151.0 (s, C-8a), 134.2 (d, C-7), 127.5 (d, C-8), 128.0 (d, C-5), 123.9 (d, C-6), 115.2 (s, C-4a), 72.7 (s, COH), 54.7 (q, OCH_3), 49.7 (t, CH_2), 42.8 (t, CH_2), 27.3 (q, CH_3), 26.7 (t, CH_2), 23.7 (t, CH_2), 14.5 (q, CH_3).

EI–MS: m/z (%) = 274 (2) [M^+], 217 (33), 174 (55), 143 (32), 102 (21), 57 (28), 55 (30), 43 (100).

CI–MS: m/z (%) = 275 (38) [MH^+], 257 (13), 175 (100), 118 (8).

HRMS: m/z [MH^+] calcd for $C_{16}H_{23}N_2O_2$: 275.174; found: 275.1752.

2-(2-Hydroxy-2-phenylpropyl)-4-methoxyquinazoline (20)
Mp 73–74 °C.

^{1}H NMR ($CDCl_3$): δ = 7.96 (dd, J = 1, 8 Hz, 1 H, H-8), 7.73 (dd, J = 1, 8 Hz, 1 H, H-5), 7.68 (app. dt, J = 1, 8 Hz, 1 H, H-7), 7.49 (d, J = 7.5 Hz, 2 H, H-2, H-6 of Ph), 7.37 (app. dt, J = 1, 8 Hz, 1 H, H-6), 7.17 (app. t, J = 7.5 Hz, 2 H, H-3, H-5 of Ph), 7.06 (t, J = 7.5 Hz, 1 H, H-4 of Ph), 6.81 (br s, exch., 1 H, OH), 4.02 (s, 3 H, OCH_3), 352, 3.39 (2 × d, J = 15.5 Hz, 2 H, CH_2), 1.52 (s, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 166.9 (s, C-4), 164.3 (s, C-2), 150.8 (s, C-8a), 148.6 (s, C-1 of Ph), 134.2 (d, C-7), 128.4 (d, C-3, C-5 of Ph), 127.4 (d, C-8), 127.0 (d, C-6), 126.2 (d, C-4 of Ph), 125.3 (d, C-2, C-6 of Ph), 123.9 (d, C-5), 115.2 (s, C-4a), 74.5 (s, COH), 54.8 (q, OCH_3), 50.6 (t, CH_2), 31.7 (q, CH_3).

EI–MS: m/z (%) = 294 (2) [M^+], 279 (69), 261 (10), 237 (12), 174 (100), 145 (29), 105 (51), 77 (62), 51 (22), 43 (60).

CI–MS: m/z (%) = 295 (2) [MH^+], 175 (100), 138 (21).

HRMS: m/z [MH^+] calcd for $C_{18}H_{19}N_2O_2$: 295.1441; found: 295.1441.

2-(2-Hydroxy-2,2-diphenylethyl)-4-methoxyquinazoline (21)
Mp 130 °C.

^{1}H NMR ($CDCl_3$): δ = 7.93 (br d, J = 8 Hz, 1 H, H-8), 7.70 (br d, J = 8 Hz, 1 H, H-5), 7.65 (app. dt, J = 1, 8 Hz, 1 H, H-7), 7.53 (s, exch., 1 H, OH), 7.48 (d, J = 7.5 Hz, 4 H, H-2, H-6 of 2 × Ph), 7.35 (app. dt, J = 1, 8 Hz, 1 H, H-6), 7.16 (app. t, J = 7.5 Hz, 4 H, H-3, H-5 of 2 × Ph), 7.04 (t, J = 7.5 Hz, 2 H, H-4 of 2 × Ph), 4.01 (s, 3 H, OCH_3), 3.85 (s, 2 H, CH_2).

^{13}C NMR ($CDCl_3$): δ = 166.9 (s, C-4), 164.3 (s, C-2), 150.7 (s, C-8a), 147.8 (s, C-1 of 2 × Ph), 134.3 (d, C-7), 128.4 (d, C-3, C-5 of 2 × Ph), 127.4 (d, C-8), 127.1 (d, C-6), 126.9 (d, C-5), 126.5 (d, C-2, C-6 of 2 × Ph), 123.9 (d, C-4 of 2 × Ph), 115.2 (s, C-4a), 78.3 (s, COH), 54.9 (q, OCH_3), 49.5 (t, CH_2).

EI–MS: m/z (%) = 356 (3) [M^+], 341 (100), 279 (16), 235 (14).

CI–MS: m/z (%) = 357 (20) [MH^+], 200 (51), 175 (100).

HRMS: m/z [MH^+] calcd for $C_{23}H_{21}N_2O_2$: 357.1598; found: 357.1601.

2-[(1-Hydroxycyclohexyl)methyl]-4-methoxyquinazoline (22)
Oil.

^{1}H NMR ($CDCl_3$): δ = 8.04 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.77 (br d, *J* = 8 Hz, 1 H, H-5), 7.72 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.42 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 5.73 (s, exch., 1 H, OH), 4.07 (s, 3 H, OCH_3), 3.05 (s, 2 H, CH_2), 1.66–1.21 [m, 10 H, $(CH_2)_5$].

^{13}C NMR ($CDCl_3$): δ = 166.9 (s, C-4), 164.7 (s, C-2), 151.0 (s, C-8a), 134.2 (d, C-7), 127.5 (d, C-8), 126.9 (d, C-6), 123.9 (d, C-5), 115.2 (s, C-4a), 71.7 (s, COH), 54.7 (q, OCH_3), 49.3 (t, CH_2), 38.4 (t, CH_2), 26.2 (t, CH_2), 22.7 (t, CH_2).

EI–MS: *m*/*z* (%) = 272 (4) [M^+], 229 (21), 216 (14), 174 (100), 143 (16), 102 (20), 90 (12), 55 (33), 41 (43).

CI–MS: *m*/*z* (%) = 273 (100) [MH^+], 175 (24), 116 (7).

HRMS: *m*/*z* [MH^+] calcd for $C_{16}H_{21}N_2O_2$: 273.1598; found: 273.1595.

2-(1-Methylethyl)-4-(methylthio)quinazoline (23)
Mp 36–37 °C.

^{1}H NMR ($CDCl_3$): δ = 7.92 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.82 (dd, *J* = 1, 8 Hz, 1 H, H-5), 7.69 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.39 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 3.19 (sept, *J* = 7 Hz, 1 H, CH), 2.63 (s, 3 H, SCH_3), 1.34 (d, *J* = 7 Hz, 6 H, 2 × CH_3).

^{13}C NMR ($CDCl_3$): δ = 171.5 (s, C-2), 170.2 (s, C-4), 148.7 (s, C-8a), 133.7 (d, C-7), 128.7 (d, C-8), 126.6 (d, C-5), 124.0 (d, C-6), 122.7 (s, C-4a), 38.5 (d, CH), 22.2 (q, CH_3), 12.8 (q, SCH_3).

EI–MS: *m*/*z* (%) = 218 (18) [M^+], 203 (32), 129 (30), 102 (18), 45 (62), 41 (100).

CI–MS: *m*/*z* (%) = 219 (100) [MH^+], 173 (18), 52 (8).

HRMS: *m*/*z* [MH^+] calcd for $C_{12}H_{15}N_2S$: 219.0950; found: 219.0949.

2-(1-Deuterioethyl)-4-(methylthio)quinazoline (24)
Mp 39–40 °C (identical to that of compound **3**).

^{1}H NMR ($CDCl_3$): δ = 7.98 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.89 (dd, *J* = 1, 8 Hz, 1 H, H-5), 7.73 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.42 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 3.06 (m, 1 H, CHD), 2.68 (s, 3 H, SCH_3), 1.46 (d, *J* = 7.5 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 171.4 (s, C-2), 166.9 (s, C-4), 148.6 (s, C-8a), 133.6 (d, C-7), 128.4 (d, C-8), 126.4 (d, C-5), 123.8 (d, C-6), 122.4 (s, C-4a), 33.0 [t (1:1:1), d, CHD], 13.0 (q, CH_3), 12.6 (q, CH_3).

EI–MS: *m*/*z* (%) = 205 (100) [M^+], 204 (80), 190 (19), 172 (20), 172 (21), 158 (32), 129 (41), 102 (46), 76 (22), 75 (26), 51 (15), 40 (20).

CI–MS: *m*/*z* (%) = 206 (100) [MH^+], 160 (18).

HRMS: *m*/*z* [MH^+] calcd for $C_{11}H_{12}DN_2S$: 206.0857; found: 206.0859.

2-(2-Hydroxy-1-methyl-2-phenylethyl)-4-(methylthio)quinazoline (25)
Product **25** was separated as two compounds **25a** (48%) and **25b** (32%) by column chromatography.

2-[(1*R,2*S**)-2-Hydroxy-1-methyl-2-phenylethyl]-4-(methylthio)quinazoline (25a)**
Oil.

^{1}H NMR ($CDCl_3$): δ = 7.96 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.80 (dd, *J* = 1, 8 Hz, 1 H, H-5), 7.73 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.44 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 7.39 (d, *J* = 7.5 Hz, 2 H, H-2, H-6 of Ph), 7.27 (app. t, *J* = 7.5 Hz, 2 H, H-3, H-5 of Ph), 7.18 (t, *J* = 7.5 Hz, 1 H, H-4 of Ph), 5.69 (br s, exch., 1 H, OH), 5.33 (d, *J* = 2 Hz, 1 H, C*H*OH), 3.36 (dq, *J* = 2, 7 Hz, 1 H, C*H*CH_3), 2.61 (s, 3 H, SCH_3), 1.16 (d, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 172.6 (s, C-2), 168.7 (s, C-4), 147.9 (s, C-8a), 142.8 (s, C-1 of Ph), 134.4 (d, C-7), 128.7 (d, C-8), 128.5 (d, C-3, C-5 of Ph), 127.3 (d, C-5), 127.3 (d, C-6), 126.5 (d, C-2, C-6 of Ph), 124.2 (d, C-4 of Ph), 122.7 (s, C-4a), 74.6 (d, CHOH), 49.1 (d, *C*HCH$_3$), 13.2 (q, CH_3), 13.1 (q, CH_3).

EI–MS: *m*/*z* (%) = 310 (20) [M^+], 295 (100), 280 (18), 267 (10).

CI–MS: *m*/*z* (%) = 311 (100) [MH^+], 205 (73), 52 (25).

HRMS: *m*/*z* [MH^+] calcd for $C_{18}H_{19}N_2OS$: 311.1213; found: 311.1211.

2-[(1*S,2*S**)-2-Hydroxy-1-methyl-2-phenylethyl]-4-(methylthio)quinazoline (25b)**
Mp 105 °C.

^{1}H NMR ($CDCl_3$): δ = 8.07 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.91 (dd, *J* = 1, 8 Hz, 1 H, H-5), 7.83 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.55 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 7.46 (d, *J* = 7.5 Hz, 2 H, H-2, H-6 of Ph), 7.34 (app. t, *J* = 7.5 Hz, 2 H, H-3, H-5 of Ph), 7.27 (t, *J* = 7.5 Hz, 1 H, H-4 of Ph), 5.33 (br s, exch., 1 H, OH), 5.06 (d, *J* = 7 Hz, 1 H, C*H*OH), 3.55 (app. quin, *J* = 7 Hz, 1 H, C*H*CH_3), 2.71 (s, 3 H, SCH_3), 1.39 (d, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 172.4 (s, C-2), 167.5 (s, C-4), 147.9 (s, C-8a), 143.6 (s, C-1 of Ph), 134.2 (d, C-7), 128.7 (d, C-8), 128.6 (d, C-3, C-5 of Ph), 127.7 (d, C-5), 127.2 (d, C-6), 127.1 (d, C-2, C-6 of Ph), 124.1 (d, C-4 of Ph), 122.7 (s, C-4a), 78.1 (d, CHOH), 49.6 (d, *C*HCH$_3$), 18.2 (q, CH_3), 13.1 (q, SCH_3).

EI–MS: *m*/*z* (%) = 310 (3) [M^+], 204 (100), 189 (42), 155 (40), 129 (31), 107 (33), 79 (70), 77 (81), 51 (18).

CI–MS: *m*/*z* (%) = 311 (100) [MH^+], 265 (6), 205 (80), 159 (7), 52 (92).

HRMS: *m*/*z* [MH^+] calcd for $C_{18}H_{19}N_2OS$: 311.1213; found: 311.1211.

2-(2-Hydroxy-1-methyl-2,2-diphenylethyl)-4-(methylthio)quinazoline (26)
Mp 103–105 °C.

^{1}H NMR ($CDCl_3$): δ = 7.82 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.72 (br d, *J* = 8 Hz, 1 H, H-5), 7.64 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.66–6.85 (m, 12 H, H-6, OH, 2 × Ph), 3.38 (q, *J* = 7 Hz, 1 H, CH), 2.57 (s, 3 H, SCH_3), 1.25 (d, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 172.3 (s, C-2), 168.6 (s, C-4), 149.0 (s, C-8a), 146.5 (s, C-1 of 2 × Ph), 134.3 (d, C-7), 128.5 (d, C-3, C-5 of 2 × Ph), 128.3 (d, C-8), 126.6 (d, C-5), 126.5 (d, C-2, C-6 of 2 × Ph), 125.9 (d, C-4 of 2 × Ph), 124.2 (d, C-6), 122.3 (s, C-4a), 79.9 (s, COH), 45.0 (d, CH), 16.9 (q, CH_3), 12.4 (q, SCH_3).

EI–MS: *m*/*z* (%) = 386 (8) [M^+], 371 (31), 204 (64), 182 (35), 157 (17), 129 (20), 105 (100), 77 (88), 51 (29).

CI–MS: *m*/*z* (%) = 387 (100) [MH^+], 371 (18).

HRMS: *m*/*z* [MH^+] calcd for $C_{24}H_{23}N_2OS$: 387.1526; found: 387.1528.

2-(1-Deuteriopropyl)-4-(methylthio)quinazoline (27)
Mp 35–36 °C (identical to that of compound **4**).

^{1}H NMR ($CDCl_3$): δ = 8.01 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.88 (dd, *J* = 1, 8 Hz, 1 H, H-5), 7.77 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.47 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 2.97 (m, 1 H, CHD), 2.69 (s, 3 H, SCH_3), 1.93 (app. quin, *J* = 7.5 Hz, 2 H, CH_2), 1.03 (t, *J* = 7.5 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 171.5 (s, C-2), 166.2 (s, C-4), 148.7 (s, C-8a), 133.7 (d, C-7), 128.6 (d, C-8), 126.6 (d, C-5), 124.0 (d, C-6), 122.5 (s, C-4a), 41.8 [t (1:1:1), d, CHD], 22.3 (t, CH_2), 14.4 (q, CH_3), 12.8 (q, CH_3).

EI–MS: *m*/*z* (%) = 219 (30) [M$^+$], 204 (90), 191 (100), 172 (22), 146 (28), 143 (30), 129 (95), 102 (93), 76 (40), 75 (42), 51 (39), 42 (53).

CI–MS: *m*/*z* (%) = 220 (100) [MH$^+$], 174 (8).

HRMS: *m*/*z* [MH$^+$] calcd for $C_{12}H_{14}DN_2S$: 220.1013; found: 220.1014.

2-[1-Ethyl-2-hydroxy-2-(4-methoxyphenyl)ethyl]-4-(methylthio)quinazoline (28)

Mp 118–120 °C. The product was a mixture of diastereoisomers, which were not separated; however, many individual NMR signals could be identified; **28a**/**28b** = 5:6 (by ^{1}H NMR).

EI–MS: *m*/*z* (%) = 354 (1) [M$^+$], 339 (8), 218 (39), 203 (100), 190 (74), 169 (21), 155 (29), 135 (80), 109 (22), 102 (63), 77 (72), 63 (33), 51 (32).

CI–MS: *m*/*z* (%) = 355 (19) [MH$^+$], 219 (100), 173 (11), 154 (53), 138 (45), 121 (63).

HRMS: *m*/*z* [MH$^+$] calcd for $C_{20}H_{23}N_2O_2S$: 355.1475; found: 355.1481.

Compound 28a

^{1}H NMR ($CDCl_3$): δ = 7.99 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.84 (br d, *J* = 8 Hz, 1 H, H-5), 7.77–7.69 (m, 1 H, H-7), 7.49–7.41 (m, 1 H, H-6), 7.20 (d, *J* = 8.5 Hz, 2 H, H-2, H-6 of Ar), 6.70 (d, *J* = 8.5 Hz, 2 H, H-3, H-5 of Ar), 5.45 (s, exch., 1 H, OH), 5.18 (d, *J* = 3 Hz, 1 H, C*H*OH), 3.72 (s, 3 H, OCH_3), 3.25 (m, 1 H, C*H*CH_2), 2.62 (s, 3 H, SCH_3), 1.93–1.61 (m, 2 H, CH_2), 0.81 (t, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 172.2 (s, C-2), 167.3 (s, C-4), 159.0 (s, C-4 of Ar), 147.8 (s, C-8a), 135.0 (s, C-1 of Ar), 134.3 (d, C-7), 129.0 (d, C-8), 127.8 (d, C-2, C-6 of Ar), 127.3 (d, C-5), 124.2 (d, C-6), 122.6 (s, C-4a), 113.8 (d, C-3, C-5 of Ar), 74.9 (d, CHOH), 65.3 (d, *C*HCH$_2$), 55.6 (q, OCH_3), 21.0 (t, CH_2), 13.1 (q, CH_3), 12.4 (q, CH_3).

Compound 28b

^{1}H NMR ($CDCl_3$): δ = 7.94 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.80 (br d, *J* = 8 Hz, 1 H, H-5), 7.77–7.69 (m, 1 H, H-7), 7.49–7.41 (m, 1 H, H-6), 7.29 (d, *J* = 8.5 Hz, 2 H, H-2, H-6 of Ar), 6.81 (d, *J* = 8.5 Hz, 2 H, H-3, H-5 of Ar), 5.00 (d, *J* = 6 Hz, 1 H, C*H*OH), 4.90 (s, exch., 1 H, OH), 3.71 (s, 3 H, OCH_3), 3.13 (m, 1 H, C*H*CH_2), 2.60 (s, 3 H, SCH_3), 1.93–1.61 (m, 2 H, CH_2), 0.64 (t, *J* = 7.5 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 172.1 (s, C-2), 166.6 (s, C-4), 158.9 (s, C-4 of Ar), 148.0 (s, C-8a), 136.3 (s, C-1 of Ar), 134.1 (d, C-7), 128.7 (d, C-8), 127.6 (d, C-2, C-6 of Ar), 127.2 (d, C-5), 124.1 (d, C-6), 122.7 (s, C-4a), 114.3 (d, C-3, C-5 of Ar), 75.8 (d, CHOH), 65.3 (d, *C*HCH$_2$), 56.7 (q, OCH_3), 25.9 (t, CH_2), 13.2 (q, CH_3), 12.6 (q, CH_3).

2-[1-(1-Hydroxycyclohexyl)propyl]-4-(methylthio)quinazoline (29)

Mp 82–83 °C.

^{1}H NMR ($CDCl_3$): δ = 7.98 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.83 (dd, *J* = 1, 8 Hz, 1 H, H-5), 7.74 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.44 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 5.07 (br s, exch., 1 H, OH), 2.90 (dd, *J* = 6, 9 Hz, 1 H, CH), 2.59 (s, 3 H, SCH_3), 1.96–1.20 [m, 12 H, CH_2, $(CH_2)_5$], 0.65 (t, *J* = 7.5 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 171.9 (s, C-2), 167.3 (s, C-4), 147.9 (s, C-8a), 134.3 (d, C-7), 128.8 (d, C-8), 127.2 (d, C-5), 124.2 (d, C-6), 122.6 (s, C-4a), 73.2 (s, COH), 58.1 (d, CH), 39.0 (t, CH_2), 35.8 (t, CH_2), 26.3 (t, CH_2), 22.6 (t, CH_2), 22.5 (t, CH_2), 21.9 (t, CH_2), 13.2 (q, CH_3), 12.9 (q, CH_3).

EI–MS: *m*/*z* (%) = 316 (4) [M$^+$], 273 (9), 218 (32), 203 (100), 169 (33), 155 (53), 129 (31), 102 (38), 99 (41), 81 (85), 55 (92), 41 (90).

CI–MS: *m*/*z* (%) = 317 (100) [MH$^+$], 299 (10).

HRMS: *m*/*z* [MH$^+$] calcd for $C_{18}H_{25}N_2OS$: 317.1682; found: 317.1683.

2-(1-Methylethyl)-4-methoxyquinazoline (30)

Oil.

^{1}H NMR ($CDCl_3$): δ = 7.98 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.77 (dd, *J* = 1, 8 Hz, 1 H, H-5), 7.67 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.36 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 4.06 (s, 3 H, OCH_3), 3.12 (sept, *J* = 7 Hz, 1 H, CH), 1.30 (d, *J* = 7 Hz, 6 H, 2 × CH_3).

^{13}C NMR ($CDCl_3$): δ = 171.5 (s, C-4), 167.4 (s, C-2), 151.7 (s, C-8a), 133.5 (d, C-7), 127.6 (d, C-8), 126.3 (d, C-6), 123.8 (d, C-5), 115.4 (s, C-4a), 54.2 (q, OCH_3), 38.3 (d, CH), 22.0 (q, CH_3).

EI–MS: *m*/*z* (%) = 202 (30) [M$^+$], 187 (100), 174 (21), 160 (11), 144 (9), 129 (14), 119 (16), 102 (15), 90 (17), 76 (18), 68 (38).

CI–MS: *m*/*z* (%) = 203 (100) [MH$^+$], 187 (5).

HRMS: *m*/*z* [MH$^+$] calcd for $C_{12}H_{15}N_2O$: 203.1179; found: 203.1181.

2-(1-Deuterioethyl)-4-methoxyquinazoline (31)

Oil.

^{1}H NMR ($CDCl_3$): δ = 7.99 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.79 (dd, *J* = 1, 8 Hz, 1 H, H-5), 7.67 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.36 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 4.04 (s, 3 H, OCH_3), 2.90 (m, 1 H, CHD), 1.38 (d, *J* = 7.5 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 168.2 (s, C-4), 167.2 (s, C-2), 151.6 (s, C-8a), 133.5 (d, C-7), 128.9 (d, C-8), 126.6 (d, C-6), 124.9 (d, C-5), 115.1 (s, C-4a), 54.2 (q, OCH_3), 32.0 [t (1:1:1), d, CHD], 12.9 (q, CH_3).

EI–MS: *m*/*z* (%) = 189 (48) [M$^+$], 188 (51), 174 (62), 160 (16), 129 (15), 119 (42), 102 (24), 90 (46), 76 (30), 63 (37), 55 (100), 42 (52).

CI–MS: *m*/*z* (%) = 190 (100) [MH$^+$], 189 (25), 175 (19).

HRMS: *m*/*z* [MH$^+$] calcd for $C_{11}H_{12}DN_2O$: 190.1085; found: 190.1085.

2-[2-Hydroxy-2-(4-methoxyphenyl)-1-methylethyl]-4-methoxyquinazoline (32)

Product **32** was separated as two compounds **32a** (29%) and **32b** (42%) by column chromatography.

2-[(1*R,2*S**)-2-Hydroxy-2-(4-methoxyphenyl)-1-methylethyl]-4-methoxyquinazoline (32a)**

Oil.

^{1}H NMR ($CDCl_3$): δ = 8.07 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.80 (br d, *J* = 8 Hz, 1 H, H-5), 7.75 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.46 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 7.30 (d, *J* = 8.5 Hz, 2 H, H-2, H-6 of Ar), 6.82 (d, *J* = 8.5 Hz, 2 H, H-3, H-5 of Ar), 5.72 (br s, exch., 1 H, OH), 5.28 (d, *J* = 2 Hz, 1 H, C*H*OH), 4.11 (s, 3 H, OCH_3), 3.74 (s, 3 H, OCH_3), 3.26 (dq, *J* = 2, 7 Hz, 1 H, C*H*CH_3), 1.15 (d, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 169.9 (s, C-4), 167.5 (s, C-2), 158.9 (s, C-4 of Ar), 150.9 (s, C-8a), 134.9 (s, C-1 of Ar), 134.3 (d, C-7), 129.0 (d, C-8), 127.6 (d, C-2, C-6 of Ar), 127.1 (d, C-6), 123.9 (d, C-5), 115.4 (s, C-4a), 113.8 (d, C-3, C-5 of Ar), 74.3 (d, CHOH), 55.7 (q, OCH_3), 54.8 (q, OCH_3), 49.1 (d, *C*HCH$_3$), 13.1 (q, CH_3).

EI–MS: *m*/*z* (%) = 324 (1) [M$^+$], 309 (10), 188 (90), 187 (78), 173 (50), 160 (16), 137 (18), 136 (51), 135 (100), 119 (24), 102 (18), 92 (32), 77 (52), 68 (34), 51 (21), 39 (35).

CI–MS: *m*/*z* (%) = 325 (100) [MH$^+$], 309 (14), 307 (38).

HRMS: *m*/*z* [MH$^+$] calcd for $C_{19}H_{21}N_2O_3$: 325.1547; found: 325.1549.

2-[(1*R,2*R**)-2-Hydroxy-2-(4-methoxyphenyl)-1-methylethyl]-4-methoxyquinazoline (32b)**
Mp 116 °C.

^{1}H NMR ($CDCl_3$): δ = 8.03 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.79 (br d, *J* = 8 Hz, 1 H, H-5), 7.71 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.42 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 7.28 (d, *J* = 8.5 Hz, 2 H, H-2, H-6 of Ar), 6.76 (d, *J* = 8.5 Hz, 2 H, H-3, H-5 of Ar), 5.17 (br s, exch., 1 H, OH), 4.89 (d, *J* = 7 Hz, 1 H, C*H*OH), 4.08 (s, 3 H, OCH_3), 3.69 (s, 3 H, OCH_3), 3.34 (app. quin, *J* = 7 Hz, 1 H, C*H*CH_3), 1.24 (d, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 168.8 (s, C-4), 167.5 (s, C-2), 159.2 (s, C-4 of Ar), 150.9 (s, C-8a), 135.9 (s, C-1 of Ar), 134.1 (d, C-7), 128.3 (d, C-8), 127.3 (d, C-2, C-6 of Ar), 126.9 (d, C-6), 123.9 (d, C-5), 115.4 (s, C-4a), 114.0 (d, C-3, C-5 of Ar), 77.6 (d, CHOH), 55.6 (q, OCH_3), 54.7 (q, OCH_3), 49.6 (d, *C*HCH_3), 18.0 (q, CH_3).

EI–MS: *m*/*z* (%) = 324 (1) [M$^+$], 309 (11), 188 (100), 187 (88), 173 (80), 160 (26), 155 (20), 137 (52), 136 (65), 135 (86), 119 (41), 102 (33), 92 (51), 77 (78), 68 (66), 51 (34), 39 (38).

CI–MS: *m*/*z* (%) = 325 (30) [MH$^+$], 307 (11), 189 (100), 175 (8), 154 (58), 137 (57).

HRMS: *m*/*z* [MH$^+$] calcd for $C_{19}H_{21}N_2O_3$: 325.1547; found: 325.1550.

2-(2-Hydroxy-1-methyl-2,2-diphenylethyl)-4-methoxyquinazoline (33)
Mp 91–93 °C.

^{1}H NMR ($CDCl_3$): δ = 8.04 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.82 (br d, *J* = 8 Hz, 1 H, H-5), 7.75 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.68 (d, *J* = 7.5 Hz, 4 H, H-2, H-6 of 2 × Ph), 7.45 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 7.36 (app. t, *J* = 7.5 Hz, 2 H, H-3, H-5 of Ph), 7.28 (s, exch., 1 H, NH), 7.22 (t, *J* = 7.5 Hz, 1 H, H-4 of Ph), 7.13 (t, *J* = 7.5 Hz, 2 H, H-3, H-5 of Ph), 6.99 (t, *J* = 7.5 Hz, 1 H, H-4 of Ph), 4.60 (q, *J* = 7 Hz, 1 H, CH), 4.15 (s, 3 H, OCH_3), 1.37 (d, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 169.6 (s, C-4), 167.1 (s, C-2), 150.9 (s, C-8a), 149.2, 146.6 (2 × s, C-1 of 2 × Ph), 134.2 (d, C-7), 128.5, 128.2 (2 × d, C-3, C-5 of 2 × Ph), 127.4 (d, C-8), 126.6 (d, C-4 of 2 × Ph), 126.5 (d, C-6), 126.4, 125.6 (2 × d, C-2, C-6 of 2 × Ph), 123.9 (d, C-5), 115.0 (s, C-4a), 79.9 (s, COH), 54.8 (q, OCH_3), 49.8 (d, CH), 16.8 (q, CH_3).

EI–MS: *m*/*z* (%) = 370 (1) [M$^+$], 188 (29), 173 (23), 105 (100), 77 (81), 51 (25).

CI–MS: *m*/*z* (%) = 371 (100) [MH$^+$], 353 (12).

HRMS: *m*/*z* [MH$^+$] calcd for $C_{24}H_{23}N_2O_2$: 371.1754; found: 371.1757.

2-(1-Deuteriopropyl)-4-methoxyquinazoline (34)
Oil.

^{1}H NMR ($CDCl_3$): δ = 8.00 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.81 (br d, *J* = 8 Hz, 1 H, H-5), 7.68 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 7.36 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 4.08 (s, 3 H, OCH_3), 2.99 (m, 1 H, CHD), 1.88 (app. quin, *J* = 7.5 Hz, 2 H, CH_2), 1.00 (t, *J* = 7.5 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 167.2 (s, C-4), 167.1 (s, C-2), 151.6 (s, C-8a), 133.5 (d, C-7), 127.4 (d, C-8), 126.2 (d, C-6), 123.6 (d, C-5), 115.0 (s, C-4a), 54.2 (q, OCH_3), 41.8 [t (1:1:1), d, CHD], 22.1 (t, CH_2), 14.3 (q, CH_3).

EI–MS: *m*/*z* (%) = 203 (5) [M$^+$], 188 (40), 175 (100), 161 (18), 146 (22), 129 (12), 119 (20), 102 (31), 90 (22), 76 (21), 42 (29).

CI–MS: *m*/*z* (%) = 204 (100) [MH$^+$], 175 (8).

HRMS: *m*/*z* [MH$^+$] calcd for $C_{12}H_{14}DN_2O$: 204.1242; found: 204.1243.

2-(2-Hydroxy-1-ethyl-2,2-diphenylethyl)-4-methoxyquinazoline (35)
Mp 139–140 °C.

^{1}H NMR ($CDCl_3$): δ = 7.91 (dd, *J* = 1, 8 Hz, 1 H, H-8), 7.72 (br d, *J* = 8 Hz, 1 H, H-5), 7.65–7.54 (m, 5 H, H-7, H-2, H-6 of 2 × Ph), 7.32 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 7.23 (app. t, *J* = 7.5 Hz, 2 H, H-3, H-5 of Ph), 7.09–7.05 (m, 2 H, OH, H-4 of Ph), 6.96 (app. t, *J* = 7.5 Hz, 2 H, H-3, H-5 of Ph), 6.81 (t, *J* = 7.5 Hz, 1 H, H-4 of Ph), 4.02 (br s, 4 H, CH, OCH_3), 1.90 (m, 1 H, C*H*H), 1.69 (m, 1 H, CH*H*), 0.68 (d, *J* = 7.5 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 168.0 (s, C-4), 166.7 (s, C-2), 150.7 (s, C-8a), 149.0, 146.8 (2 × s, C-1 of 2 × Ph), 134.1 (d, C-7), 128.5, 128.1 (2 × d, C-3, C-5 of 2 × Ph), 127.5 (d, C-4 of 2 × Ph), 126.9 (d, C-8), 126.5 (d, C-6), 126.3, 125.8 (2 × d, C-2, C-6 of 2 × Ph), 123.8 (d, C-5), 115.0 (s, C-4a), 80.3 (s, COH), 57.1 (d, CH), 54.8 (q, OCH_3), 24.2 (t, CH_2), 12.8 (q, CH_3).

EI–MS: *m*/*z* (%) = 384 (1) [M$^+$], 369 (11), 229 (90), 187 (63), 174 (28), 158 (30), 158 (31), 105 (100), 77 (94), 68 (23), 51 (63), 41 (65).

CI–MS: *m*/*z* (%) = 385 (21) [MH$^+$], 287 (7), 204 (29), 203 (100), 200 (72), 183 (73), 174 (12), 105 (9).

HRMS: *m*/*z* [MH$^+$] calcd for $C_{25}H_{25}N_2O_2$: 385.1911; found: 385.1911.

2-Butyl-2-ethyl-4-(methylthio)-1,2-dihydroquinazoline (36)
Oil.

^{1}H NMR ($CDCl_3$): δ = 7.28 (dd, *J* = 1, 8 Hz, 1 H, H-5), 7.03 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 6.49 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 6.34 (dd, *J* = 1, 8 Hz, 1 H, H-8), 3.66 (br s, exch., 1 H, NH), 2.30 (s, 3 H, SCH_3), 1.70–1.48 (m, 4 H, 2 × CH_2), 1.35–1.18 (m, 4 H, 2 × CH_2), 0.82 (t, *J* = 7.5 Hz, 3 H, CH_3), 0.80 (t, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 159.6 (s, C-4), 144.4 (s, C-8a), 132.9 (d, C-7), 125.4 (d, C-5), 117.0 (d, C-6), 116.3 (s, C-4a), 113.7 (d, C-8), 76.0 (s, C-2), 41.1 (t, CH_2), 34.3 (t, CH_2), 26.3 (t, CH_2), 23.8 (t, CH_2), 14.6 (q, CH_3), 12.5 (q, CH_3), 8.5 (q, CH_3).

EI–MS: *m*/*z* (%) = 262 (3) [M$^+$], 233 (91), 205 (100), 189 (32), 172 (26), 158 (28), 129 (19), 117 (16), 102 (40).

CI–MS: *m*/*z* (%) = 263 (100) [MH$^+$], 217 (26).

HRMS: *m*/*z* [MH$^+$] calcd for $C_{15}H_{23}N_2S$: 263.1576; found: 263.1575.

2-Butyl-4-(methylthio)-2-propyl-1,2-dihydroquinazoline (37)
Mp 35–36 °C.

^{1}H NMR ($CDCl_3$): δ = 7.28 (dd, *J* = 1, 8 Hz, 1 H, H-5), 7.03 (app. dt, *J* = 1, 8 Hz, 1 H, H-7), 6.49 (app. dt, *J* = 1, 8 Hz, 1 H, H-6), 6.33 (br d, *J* = 8 Hz, 1 H, H-8), 3.68 (br s, exch., 1 H, NH), 2.31 (s, 3 H, SCH_3), 1.68–1.61 (m, 2 H, CH_2), 1.53–1.45 (m, 2 H, CH_2), 1.41–1.13 (m, 6 H, 3 × CH_2), 0.82, 0.80 (2 × overlap. t, *J* = 7.5 Hz, 6 H, 2 × CH_3).

^{13}C NMR ($CDCl_3$): δ = 159.4 (s, C-4), 144.4 (s, C-8a), 132.9 (d, C-7), 125.4 (d, C-5), 117.0 (d, C-6), 116.2 (s, C-4a), 113.6 (d, C-8), 75.8 (s, C-2), 44.2 (t, CH_2), 41.5 (t, CH_2), 26.3 (t, CH_2), 23.4 (t, CH_2), 17.4 (t, CH_2), 14.9 (q, CH_3), 14.6 (q, CH_3), 12.5 (q, CH_3).

EI–MS: *m*/*z* (%) = 276 (5) [M$^+$], 233 (100), 219 (93), 203 (19), 190 (24), 189 (44), 176 (40), 158 (55), 143 (18), 129 (20), 117 (15), 102 (17), 41 (69).

CI–MS: *m*/*z* (%) = 277 (100) [MH$^+$], 231 (5), 219 (4).

HRMS: *m*/*z* [MH$^+$] calcd for $C_{16}H_{25}N_2S$: 277.1733; found: 277.1733.

2-Butyl-2-ethyl-4-methoxy-1-methyl-1,2-dihydroquinazoline (38)
Oil.

^{1}H NMR ($CDCl_3$): δ = 7.33 (d, *J* = 8 Hz, 1 H, H-5), 7.12 (app. t, *J* = 8 Hz, 1 H, H-7), 6.43 (app. t, *J* = 8 Hz, 1 H, H-6), 6.32 (d, *J* = 8 Hz, 1 H, H-8), 3.71 (s, 3 H, OCH_3), 2.65 (s, 3 H, NCH_3), 1.83–1.72 (m, 2 H, CH_2), 1.54–1.50 (m, 2 H, CH_2), 1.33–1.12 (m, 4 H, 2 × CH_2), 0.78 (app. t, *J* = 7 Hz, 6 H, 2 × CH_3).

^{13}C NMR ($CDCl_3$): δ = 158.3 (s, C-4), 149.6 (s, C-8a), 133.4 (d, C-7), 124.7 (d, C-5), 114.7 (d, C-6), 110.2 (s, C-4a), 108.9 (d, C-8), 80.4 (s, C-2), 52.6 (q, OCH_3), 41.3 (t, CH_2), 34.4 (q, NCH_3), 31.2 (t, CH_2), 26.2 (t, CH_2), 23.3 (t, CH_2), 14.6 (q, CH_3), 8.5 (q, CH_3).

EI–MS: *m*/*z* (%) = 260 (10) [M^+], 231 (22), 203 (33), 149 (6), 132 (5), 104 (7), 70 (24), 57 (26), 41 (100).

CI–MS: *m*/*z* (%) = 261 (100) [MH^+], 231 (6), 231 (9), 203 (15).

HRMS: *m*/*z* [MH^+] calcd for $C_{16}H_{25}N_2O$: 261.1961; found: 261.1965.

2-Butyl-2-ethyl-4-methoxy-1,2-dihydroquinazoline (39)
Oil.

^{1}H NMR ($CDCl_3$): δ = 7.33 (d, *J* = 8 Hz, 1 H, H-5), 7.04 (app. t, *J* = 8 Hz, 1 H, H-7), 6.48 (app. t, *J* = 8 Hz, 1 H, H-6), 6.35 (d, *J* = 8 Hz, 1 H, H-8), 3.73 (s, 3 H, OCH_3), 3.62 (br s, exch., 1 H, NH), 1.63–1.47 (m, 4 H, 2 × CH_2), 1.37–1.18 (m, 4 H, 2 × CH_2), 0.82 (t, *J* = 7.5 Hz, 3 H, CH_3), 0.80 (t, *J* = 7.5 Hz, 3 H, CH_3).

^{13}C NMR ($CDCl_3$): δ = 157.5 (s, C-4), 147.1 (s, C-8a), 132.9 (d, C-7), 125.2 (d, C-5), 116.7 (d, C-6), 112.9 (d, C-8), 110.7 (s, C-4a), 74.8 (s, C-2), 52.8 (q, OCH_3), 42.5 (t, CH_2), 35.6 (t, CH_2), 26.3 (t, CH_2), 23.4 (t, CH_2), 14.6 (q, CH_3), 8.5 (q, CH_3).

EI–MS: *m*/*z* (%) = 246 (1) [M^+], 217 (31), 189 (40), 105 (22), 84 (24), 77 (30), 51 (40), 49 (69), 41 (100).

CI–MS: *m*/*z* (%) = 247 (100) [MH^+], 217 (12), 189 (14).

HRMS: *m*/*z* [MH^+] calcd for $C_{15}H_{23}N_2O$: 247.1805; found: 247.1806.

2-Butyl-4-methoxy-2-propyl-1,2-dihydroquinazoline (40)
Oil.

^{1}H NMR ($CDCl_3$): δ = 7.33 (d, *J* = 8 Hz, 1 H, H-5), 7.05 (app. t, *J* = 8 Hz, 1 H, H-7), 6.48 (app. t, *J* = 8 Hz, 1 H, H-6), 6.34 (d, *J* = 8 Hz, 1 H, H-8), 3.74 (br s, 4 H, NH, OCH_3), 1.71–1.58 (m, 2 H, CH_2), 1.52–1.40 (m, 2 H, CH_2), 1.38–1.17 (m, 6 H, 3 × CH_2), 0.82, 0.80 (2 × overlap. t, *J* = 7 Hz, 6 H, 2 × CH_3).

^{13}C NMR ($CDCl_3$): δ = 157.4 (s, C-4), 147.0 (s, C-8a), 133.0 (d, C-7), 125.3 (d, C-5), 116.7 (d, C-6), 113.0 (d, C-8), 111.1 (s, C-4a), 74.7 (s, C-2), 52.8 (q, OCH_3), 45.5 (t, CH_2), 42.8 (t, CH_2), 26.3 (t, CH_2), 23.4 (t, CH_2), 17.4 (t, CH_2), 14.8 (q, CH_3), 14.6 (q, CH_3).

EI–MS: *m*/*z* (%) = 260 (1) [M^+], 217 (72), 203 (100), 189 (30), 174 (16), 160 (19), 146 (12), 120 (13), 98 (23), 84 (39), 41 (100).

CI–MS: *m*/*z* (%) = 261 (100) [MH^+], 247 (5), 229 (3), 217 (12), 203 (16).

HRMS: *m*/*z* [MH^+] calcd for $C_{16}H_{25}N_2O$: 261.1961; found: 261.1963.

4,4-Dibutyl-2-propyl-1,2-dihydroquinazoline (41)
Mp 58 °C.

^{1}H NMR ($CDCl_3$): δ = 6.91–6.73 (m, 4 H, H-5, H-6, H-7, H-8), 4.94 (br s, exch., 1 H, NH), 2.09 (t, *J* = 7.5 Hz, 2 H, CH_2), 1.64–1.49 (m, 4 H, 2 × CH_2), 1.36–0.83 (complex m, 10 H, 5 × CH_2), 0.78 (t, *J* = 7.5 Hz, 3 H, CH_3), 0.59 (t, *J* = 7 Hz, 6 H, 2 × CH_3).

^{13}C NMR ($CDCl_3$): δ = 158.9 (s, C-2), 147.5 (s, C-8a), 128.1 (d, C-5), 128.0 (d, C-7), 126.3 (s, C-4a), 124.5 (d, C-6), 124.5 (d, C-8), 59.9 (s, C-4), 45.3 (t, CH_2), 38.6 (t, CH_2), 26.6 (t, CH_2), 23.3 (t, CH_2), 21.5 (t, CH_2), 14.4 (q, CH_3), 14.2 (q, CH_3).

EI–MS: *m*/*z* (%) = 286 (1) [M^+], 229 (55), 171 (8), 158 (12), 57 (28), 41 (100).

CI–MS: *m*/*z* (%) = 287 (100) [MH^+], 229 (28).

HRMS: *m*/*z* [MH^+] calcd for $C_{19}H_{31}N_2$: 287.2482; found: 287.2486.

Acknowledgment

We thank the University of Wales Swansea for financial support, the EPSRC Mass Spectrometry Service, University of Wales Swansea, for recording the mass spectra and the EPSRC National Crystallography Service for the crystal structure. We also thank the EPSRC, the Higher Education Funding Council for Wales (ELWa-HEFCW) and the University of Wales Swansea for grants that enabled the purchase and upgrading of NMR equipment used in the course of this work. G. A. El-Hiti thanks the Royal Society of Chemistry for an international author grant.

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