Synthesis of a Novel Class of 3-(2'-Benzothiazolyl)-2,3-dihydroquinazolin-4(1*H*)-ones under Solvent-free and Catalyst-free Conditions

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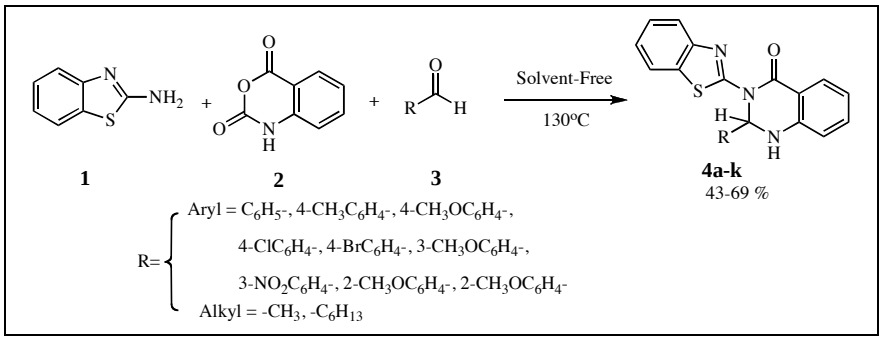

A solvent- and catalyst-free one-pot three-component condensation reaction approach was developed for the synthesis of a new class of 3-(2'-benzothiazolyl)-2,3-dihydroquinazolin-4(1*H*)-ones in relatively good yields.

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INTRODUCTION

2,3-Dihydroquinazolines, an important class of heterocyclic compounds, exhibit a wide spectrum of biological activities and pharmacological properties [1]. Additionally, these compounds can easily be oxidized to their quinazolin-4(3*H*)-ones analogies, which are themselves important biologically active compounds [2,3]. On the other hand, a large variety of substituted benzimidazole or benzothiazole derivatives have been found to posses *in vivo* and *in vitro* growth inhibiting activity against various strains of bacteria, fungi and viruses [4]. Because of this; numerous approaches for their synthesis have been reported in literature [5].

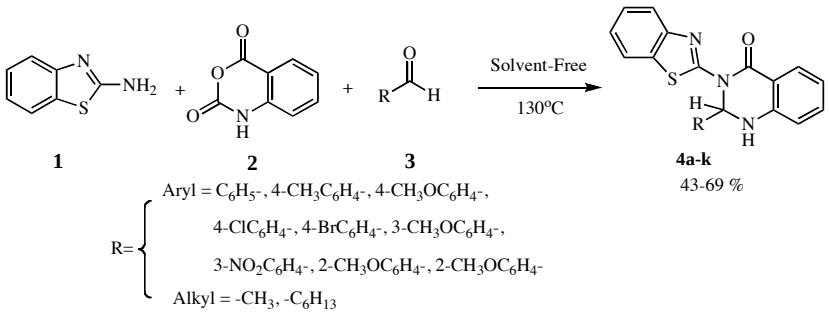
Multi-component reactions (*MCRs*) have recently been discovered to be a powerful method for the synthesis of organic compounds, since the products are formed in a single step and diversity can be achieved by simply varying each compound [6]. In addition solvent-free organic reaction has received considerable progress in reaction times in the reaction of green synthesis [7]. In the view of the principle of green chemistry, a clean synthesis should be a desirable without using any solvent and catalyst [8].

During the course of our studies to synthesis of substituted benzimidazole or benzothiazole heterocyclic compounds [9] and our interest in multi-component reactions [10], we become interested the possibility of synthesising benzimidazo-, triazolo-, or benzothiazo-quinazoline derivates by the one-pot three-component condensation reactions strategy of 2-aminobenzimidazole **1** or 2-aminobenzothiazole or 3-amino-1,2,4-triazole with isatoic anhydride **2** and aldehyde **3** under classical heating conditions without using any catalyst and solvent (Scheme 1).

RESULTS AND DISCUSSION

This solvent-free one-pot method involves the classical heating of a mixture of 2-aminobenzothiazole **1,** isatoic

Scheme 1



anhydride **2** and aldehyde **3** without using any catalyst to give a new family of 3-(2'-benzothiazolyl)-2,3-dihydroquinazolin-4(1*H*)-ones **4** in relatively good yields.

In order to improve the yields, we performed reactions using different quantities of reagents. The best result was obtained with 1:1:1.1 ratios of 2-aminobenzothiazole, isatoic anhydride, and aldehyde.

To explore the scope and limitations of this reaction further, we have extended it to aliphatic and various *ortho*-, *meta*- and *para*-substituted benzaldehydes in the presence of 2-aminobenzothiazole, 2-aminobenzimidazole and 3-amino-1,2,4-triazole. As indicated in Table 1, the reaction proceeds efficiently with benzaldehyde, electron-withdrawing and electron-releasing *ortho*-, *meta*- and *para*-substituted benzaldehydes and aliphatic aldehydes. However the reaction with 3-amino-1,2,4-triazole, and 2-aminobenzoimidazole is completely stopped after heating at 130°C for 3 h. Probably this is a result of the nucleophilicity of NH group of 3-amino-1,2,4-triazole and 2-aminobenzimidazole as comparable to 2-amino-benzothiazole.

The structure of the products **4** was deduced from their IR, ^{1}H nmr, ^{13}C nmr and MS spectra. The mass spectra of these compounds displayed molecular ion peak at appropriate *m/z* values.

The ^{1}H nmr spectrum of **4a** in *DMSO* exhibited a sharp line readily recognized as arising from a methyl group (δ = 2.17) and a multiplet appeared at δ = 6.93-8.30 for aromatic protons and one doublet of doublet (at 7.08 and 7.17, J = 7.7 Hz) for ($CH_3C_6H_4$) and a doublet for methine proton at 7.51, J = 3.01 Hz and a doublet at 8.30, J = 3.20 Hz for NH proton. The ^{1}H spectra of **4b–k** in DMSO are similar to those of **4a**, except for R group, which exhibit characteristic signals with appropriate chemical shifts.

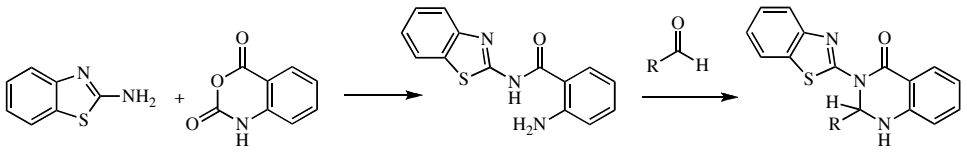
The ^{1}H decoupled ^{13}C nmr spectrum of **4a** showed 20 distinct resonances in agreement with the suggested structures. The ^{1}H and ^{13}C nmr spectra of **4b–k** are similar to those of **4a** except for the R^1 and R^2 groups, which exhibit characteristic signals with appropriate chemical shifts.

We have not established a mechanism for the formation of 2,3-dihydroquinazolin-4(1*H*)-ones ring systems, but a reasonable possibility is indicated in (Scheme 2).

The reaction presumably proceeds in two steps: condensation of 2-aminobenzothiazole **1** and, isatoic anhydride **2** then aldehydes **3** is reacted with compound **5** through a imine synthesis and then cyclisation with addition amid nitrogen in the imine group.

In summary, we have introduced a novel three-component condensation reaction of a 2-aminobenzothiazole, isatoic anhydride and aldehyde for the synthesis of a new class of heterocyclic 2,3-dihydroquinazolin-4(1*H*)-ones ring systems which the one-pot nature and solvent-free protocol in the absence of any catalyst make it an interesting approach.

Scheme 2



1 **2** **5** **6**

Table 1

One-pot synthesis of benzthiazolo-quinazolinone by the condensation reaction of 2-aminobenzothiazole, isatoicanhydrid and aldehyde under solvent- and catalyst-free conditions at 130 °C.

Compound	R	Time (hours)	Mp (°C)	Yield (%)[a]	Molecular Formula	Analysis % Calcd./Found			
						C	H	N	S
4a	$4CH_3$-C_6H_4-	2.30	198-199	64	$C_{22}H_{17}N_3OS$	71.14/71.23	4.61/4.64	11.31/11.26	8.63/8.61
4b	C_6H_5-	2.20	233-236	66	$C_{21}H_{15}N_3OS$	70.57/70.69	4.23/4.24	11.76/11.71	8.97/8.93
4c	$4CH_3O$-C_6H_4-	3.15	184-186	69	$C_{22}H_{17}N_3O_2S$	68.20/68.33	4.42/4.44	10.85/10.81	8.28/8.26
4d	4Cl-C_6H_4-	3.20	190-193	53	$C_{21}H_{14}ClN_3OS$	64.36/64.45	3.60/3.63	10.72/10.69	8.18/8.17
4e	4Br-C_6H_4-	4.10	231-234	57	$C_{21}H_{14}BrN_3OS$	57.81/58.01	3.23/3.22	9.63/9.64	7.35/7.34
4f	3Br-C_6H_4-	3.20	183-186	61	$C_{21}H_{14}BrN_3OS$	57.81/58.97	3.23/3.23	9.63/9.61	7.35/7.36
4g	$3NO_2$-C_6H_4-	3.10	251-253	52	$C_{21}H_{14}N_4O_3S$	62.68/62.54	3.51/3.52	13.92/13.95	7.97/7.93
4h	$2CH_3$-C_6H_4-	3.20	198-200	61	$C_{22}H_{17}N_3OS$	71.14/71.29	4.61/4.63	11.31/11.29	8.63/8.65
4i	$2CH_3O$-C_6H_4-	3.15	225-230	57	$C_{22}H_{17}N_3O_2S$	68.20/68.09	4.42/4.43	10.85/10.82	8.28/8.31
4j	CH_3-	5	215-222	61	$C_{16}H_{13}N_3OS$	65.06/64.86	4.44/4.45	14.23/14.20	10.86/10.85
4k	C_6H_{13}-	3.30	148-151	43	$C_{21}H_{23}N_3OS$	69.01/68.92	6.34/6.36	11.50/11.52	8.77/8.73

[a] isolated yield.

EXPERIMENTAL

Melting points were measured on an Electrothermal 9100 apparatus. Mass spectra were recorded on a FINNIGAN-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra were recorded on a Shimadzu IR-470 spectrometer. The elemental analyses were performed with an Elementar Analysensysteme GmbH VarioEL CHNS mode.^{1}H, and ^{13}C nmr spectra were recorded on a BRUKER DRX-300 AVANCE spectrometer at 300.13, and 75.47 MHz. nmr spectra were obtained on solutions in *DMSO-d*$_6$. All the products are new compounds, which were characterized by IR, ^{1}H, and ^{13}C nmr spectral data.

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Typical procedure for the synthesis of 3-(2'-benzothiazolyl)-2,3-dihydro-2-(4-methylphenyl)-4(1*H*)-quinazolinone (4a). A mixture of isatoic anhydride (0.130 g, 1 mmol), *p*-methylbenzaldehyde (0.132 g, 1.1 mmol), and 2-aminobenzthiazole (0.150 g, 1 mmol) was successively added to a screw-capped vial containing a magnetic stirring bar and was heated at 130°C in a preheated oil bath for 2.30 h. Then the reaction mixture was washed with cold water (2×10 ml) and the solid residue was crystallized from acetonitril to yield 0.23 g of 4a as colorless crystals (64%). Colorless crystals. mp 198-199°C; ir (KBr): 3340, 1631, 1609, 1506, 1432, 1254 cm^{-1}; ^{1}H nmr: δ 2.17 (s, CH_3), 6.78 (t, J= 7.29 Hz, CH), 6.93 (d, J= 8.09 Hz, CH), 7.08 (d, J= 7.68 Hz, 2CH), 7.17 (d, J= 7.77 Hz, 2CH), 7.35 (t, J= 7.80 Hz, CH), 7.38 (t, J= 10.16 Hz, CH), 7.45 (t, J= 7.25 Hz, CH), 7.51 (d, J= 3.01 Hz, CH(sp^3)), 7.77 (t, J= 7.03 Hz, CH), 7.79 (d, J= 6.95 Hz, CH), 8.04 (d, ***J***= 7.72 Hz, CH), 8.30 (d, J= 7.72 Hz, CH), 8.30 (d, J= 3.20 Hz, NH) ppm; ^{13}C nmr: δ 20.97, 68.36, 114.09, 116.23, 118.82, 121.37, 122.21, 124.56, 126.16, 126.75, 128.84, 129.54, 133.06, 135.93, 137.02, 138.02, 147.40, 148.14, 151.18, 162.13 ppm; ms: m/z (%) 372 (M+1, 90), 237 (100), 165 (20), 130 (20), 77 (25). *Anal.* Calcd for $C_{22}H_{17}N_3OS$: C, 71.14; H, 4.61; N, 11.31; S, 8.63 %. Found: C, 71.43; H, 4.64; N, 11.26; S, 8.61 %.

3-(2'-Benzothiazolyl)-2,3-dihydro-2-(phenyl)-quinazolin-4(1*H*)-one (4b). Colorless crystals. mp 233-236°C; ir (KBr): 3350, 1630, 1612, 1501, 1431, 1389, 1228 cm^{-1}; ^{1}H nmr: δ 6.79 (t, J= 7.43 Hz, CH), 6.97 (d, J= 8.12 Hz, CH), 7.22-7.40 (m, C_6H_5), 7.37 (t, J= 7.03 Hz, CH), 7.42 (t, J= 7.44 Hz, CH), 7.60 (d, J= 3.59 Hz, CH(sp^3)), 7.79 (d, J= 8.13 Hz, CH), 7.82 (t, J= 8.76 Hz, CH), 8.05 (d, J= 7.72 Hz, CH), 8.38 (d, J= 3.63 Hz, NH) ppm; ^{13}C nmr: δ 68.45, 114.09, 116.26, 118.89, 121.40, 122.22, 124.58, 126.25, 126.76, 128.67, 128.91, 129.04, 133.11, 135.97, 140.04, 147.38, 148.15, 158.24, 162.13 ppm; ms: m/z (%) 223 (M-134, 75), 208 (100), 194 (20), 149 (50), 105 (30), 77 (50). *Anal.* Calcd for $C_{21}H_{15}N_3OS$: C, 70.57; H, 4.23; N, 11.76; S, 8.97 %. Found: C, 70.79; H, 4.24; N, 11.71; S, 8.93%.

3-(2'-Benzothiazolyl)-2,3-dihydro-2-(4-methoxyphenyl)-quinazolin-4(1*H*)-one (4c). Colorless crystals. mp 184-186°C; ir (KBr): 3350, 1633, 1608, 1505, 1430, 1304, 1233 cm^{-1}; ^{1}H nmr: δ 3.63 (s, OCH_3), 6.78(t, J= 7.34 Hz, CH), 6.83 (d, J= 7.67 Hz, 2CH), 6.94 (d, J= 8.08 Hz, CH), 7.21(d, J= 7.81 Hz, 2CH), 7.34 (t, J= 7.13 Hz, CH), 7.39 (t, J= 7.12 Hz, CH), 7.44 (t, J= 7.52 Hz, CH), 7.52 (brs, CH(sp^3)), 7.78 (d, J= 7.65 Hz, CH), 7.81 (d, J= 7.61 Hz, CH), 8.04 (d, J= 7.73 Hz, CH), 8.32 (br s, NH) ppm; ^{13}C nmr: δ 55.48, 68.21, 114.06, 114.39, 116.24, 118.79, 121.38, 122.20, 124.55, 126.74, 127.50, 128.85, 131.84, 133.07, 135.94, 147.42, 148.16, 158.19, 159.52, 162.12 ppm; ms: m/z 388(M+1, 50), 253(100), 239(90), 167(20), 77(10). *Anal.* Calcd for $C_{22}H_{17}N_3O_2S$: C, 68.20; H, 4.42; N, 10.85; S, 8.28%. Found: C, 68.33; H, 4.44; N, 10.81; S, 8.26 %.

3-(2'-Benzothiazolyl)-2,3-dihydro-2-(4-cholorophenyl)-quinazolin-4(1*H*)-one (4d). Colorless crystals. mp 190-193°C; ir (KBr): 3335, 1634, 1609, 1506, 1403, 1254 cm^{-1}; ^{1}H nmr: δ 6.81(t, J= 7.35 Hz, 1CH), 6.96 (d, J= 8.20 Hz, 1CH), 7.30 (d, J= 8.53 Hz, 2CH), 7.46(t, J= 7.17 Hz, 1CH), 7.54(d, J= 3.99 Hz, 1CH(sp^3)), 7.78 (d, J= 8.00 Hz, 1CH), 7.79 (d, J= 7.67 Hz, 1CH), 8.06 (d, J= 7.68 Hz, 1CH), 8.34 (d, J= 4.06 Hz, NH) ppm; ^{13}C nmr: δ 64.46, 113.57, 115.77, 118.55, 120.88, 121.61, 124.08, 126.21, 127.62, 128.37, 128.51, 132.58, 132.94, 135.49, 138.53, 146.58, 147.58, 157.59, 161.40 ppm; ms: m/z (%) 271(27), 257(70), 242(100), 178(35), 152(50), 130(25), 108(20). *Anal.* Calcd for $C_{21}H_{14}ClN_3OS$: C, 64.36; H, 3.60; N, 10.72; S, 8.18 %. Found: C, 64.53; H, 3.65; N, 10.69; S, 8.17%.

3-(2'-Benzothiazolyl)-2,3-dihydro-2-(4-bromophenyl)-quinazolin-4(1*H*)-one (4e). Colorless crystals. mp 231-234°C; ir (KBr): 3350, 1630, 1612, 1501, 1431, 1389, 1228 cm^{-1}; ^{1}H nmr: δ 6.81(t, J= 7.47 Hz, 1CH), 6.96 (d, J= 8.18 Hz, 1CH), 7.25 (d, J= 8.25 Hz, 2CH), 7.36(t, J= 7.41 Hz, 1CH), 7.41(t, J= 8.39 Hz, 1CH), 7.45(t, J= 7.71 Hz, 1CH), 7.51 (d, J= 8.60 Hz, 2CH), 7.53 (d, J= 4.20 Hz, 1CH(sp^3)), 7.78 (d, J= 7.64 Hz, 1CH), 7.80 (d, J= 7.42 Hz, 1CH), 8.05 (d, J= 7.79 Hz, 1CH), 8.34(d, J= 3.88 Hz, 1NH) ppm; ^{13}C nmr: δ 68.45, 114.09, 116.26, 118.89, 121.40, 122.22, 124.58, 126.25, 126.76, 128.67, 128.91, 129.04, 133.11, 135.97, 140.04, 147.38, 148.15, 158.24, 162.13 ppm; ms: m/z (%) 223 (75), 208 (100), 194 (20), 149(50), 105(30), 77 (50). *Anal.* Calcd for $C_{21}H_{14}BrN_3OS$: C, 57.81; H, 3.23; N, 9.63; S, 7.35 %. Found: C, 58.01; H, 3.22; N, 9.64; S, 7.34 %.

3-(2'-Benzothiazolyl)-2,3-dihydro-2-(3-boromophenyl)-quinazolin-4(1*H*)-one (4f). Colorless crystals. mp 183-186°C; ir (KBr): 3385, 1644, 1609, 1499, 1435, 1380, 1231 cm^{-1}; ^{1}H nmr: δ 6.85(t, J= 7.33 Hz, 1CH), 6.90 (d, J= 8.25 Hz, 1CH), 7.08-7.44 (m, 6CHarom), 7.68 (s, 1CH), 7.69 (t, J= 8.04 Hz, 1CH), 7.71 (d, J= 4.36 Hz, 1CH), 7.93 (d, J= 7.45 Hz, 1CH), 8.01 (d, J= 7.65 Hz, 1CH), 8.06(d, J= 4.37 Hz, 1NH) ppm; ^{13}C nmr: δ 69.09, 113.40, 116.59, 119.14, 121.55, 122.17, 122.35, 124.67, 126.00, 126.74, 128.53, 128.75, 131.03, 133.03, 134.18, 136.12, 138.72, 145.85, 147.89, 157.28, 162.21 ppm; ms: m/z (%) 436(M+1, 40), 434(M-1, 30), 303(100), 301(98), 288(90), 286(90), 152(35), 77 (35). *Anal.* Calcd for $C_{21}H_{14}BrN_3OS$: C, 57.81; H, 3.23; N, 9.63; S, 7.35 %. Found: C, 58.97; H, 3.23; N, 9.58; S, 7.36 %.

3-(2'-Benzothiazolyl)-2,3-dihydro-2-(3-nitrophenyl)-quinazolin-4(1*H*)-one (4g). Colorless crystals. mp 251-253°C; ir (KBr): 3440, 1637, 1619, 1539, 1524, 1434, 1340 cm^{-1}; ^{1}H nmr: δ 6.82 (t, J= 7.55 Hz, 1CH), 7.01 (d, J= 8.18 Hz, 1CH), 7.35-7.48 (m, 3CH), 7.57-7.64 (m, 2CH), 7.69 (d, J= 4.23 Hz, 1CH(sp^3)), 7.78 (d, J= 9.18 Hz, 1CH), 7.81 (d, J= 9.06 Hz, 1CH), 8.07 (d, J= 8.05 Hz, 1CH), 8.11 (d, J= 8.13 Hz, 1CH), 8.28 (s, 1CH), 8.47 (d, J= 3.95 Hz, 1NH) ppm; ^{13}C nmr: δ 67.30, 113.46, 115.97, 118.89, 120.73, 120.98, 121.83, 123.35, 124.26,

126.35, 128.49, 130.32, 132.05, 132.61, 135.75, 141.89, 146.36, 147.52, 147.98, 157.57, 161.26 ppm; ms: m/z (%) 403 (M+1, 30), 354 (30), 268 (100), 207 (50), 105 (20), 77 (20). *Anal.* Calcd for $C_{21}H_{14}N_4O_3S$: C, 62.68; H, 3.51; N, 13.92; S, 7.97 %. Found: C, 62.54; H, 3.52; N, 13.96; S, 7.93%.

3-(2'-Benzothiazolyl)-2,3-dihydro-2-(2-methylphenyl)-quinazolin-4(1*H*)-one (4h). Colorless crystals. mp 198-200°C; ir (KBr): 3330, 1631, 1609, 1501, 1452, 1389, 1231 cm^{-1}; ^1H nmr: δ 2.72 (s, CH_3), 6.81 (d, J= 7.83 Hz, 1CH), 6.82 (t, J= 7.58 Hz, 1CH), 6.96-7.44 (m, 7CHarom), 7.59 (d, J= 4.09 Hz, 1CH), 7.71 (d, J= 7.96 Hz, 1CH), 7.91-8.01 (m, 2CHarom), 7.95 (d, J= 4.48 Hz, NH) ppm; ^{13}C nmr: δ 19.67, 66.92, 113.39, 116.21, 118.70, 121.48, 122.12, 124.00, 124.55, 126.53, 126.68, 128.74, 128.88, 131.67, 133.00, 135.85, 136.00, 138.61, 146.28, 147.99, 157.48, 162.40 ppm; ms: m/z (%) 372 (M+1, 90), 237 (100), 193 (30), 165 (20), 105 (20), 77 (30). *Anal.* Calcd for $C_{22}H_{17}N_3OS$: C, 71.14; H, 4.61; N, 11.31; S, 8.63%. Found: C, 71.29; H, 4.63; N, 11.19; S, 8.65%.

3-(2'-Benzothiazolyl)-2,3-dihydro-2-(2-methoxyphenyl)-quinazolin-4(1*H*)-one (4i). Colorless crystals. mp 225-230°C; ir (KBr): 3346, 1647, 1614, 1511, 1460, 1440 cm^{-1}; ^1H nmr: δ 3.94 (s, OCH_3), 6.71-6.89 (m, 4CH), 7.07 (d, J= 8.13 Hz, 1CH), 7.19-7.43 (m, 4CH), 7.67 (d, J= 3.45 Hz, 1CH), 7.73 (d, J= 7.86 Hz, 1CH), 7.77 (d, J= 3.48 Hz, 1NH), 7.87 (d, J= 7.77 Hz, 1CH), 8.01 (d, J= 7.77 Hz, 1CH) ppm; ^{13}C nmr: δ 56.25, 65.71, 112.14, 113.05, 116.01, 118.49, 120.35, 121.46, 122.11, 124.54, 125.50, 126.68, 127.15, 128.68, 130.29, 133.04, 135.85, 147.15, 148.01, 157.08, 157.56, 162.65 ppm; ms: m/z (%) 388 (60), 253 (100), 238 (50), 167 (20), 132 (25), 77 (20). *Anal.* Calcd for $C_{22}H_{17}N_3O_2S$: C, 68.20; H, 4.42; N, 10.85; S, 8.28%. Found: C, 68.09; H, 4.43; N, 10.79; S, 8.31 %.

3-(2'-Benzothiazolyl)-2,3-dihydro-2-methyl-quinazolin-4(1*H*)-one (4j). Colorless crystals. mp 215-222°C; ir (KBr): 3307, 1645, 1614, 1508, 1440 cm^{-1}; ^1H nmr: δ 1.62 (d, J= 6.04 Hz, CH_3), 4.80 (brs, NH), 6.72 (q, J= 5.89 Hz, 1CH), 6.80 (d, J= 8.08 Hz, 1CH), 6.95 (t, J= 7.48 Hz, 1CH), 7.31 (t, J= 7.26 Hz, 1CH), 7.43 (t, J= 8.20 Hz, 1CH), 7.45 (t, J= 7.79 Hz, 1CH), 7.84 (d, J= 7.82 Hz, 1CH), 7.58 (d, J= 7.58 Hz, 1CH), 8.07 (d, J= 7.80 Hz, 1CH) ppm; ^{13}C nmr: δ 19.68, 65.12, 113.06, 116.23, 118.47, 121.35, 122.02, 124.37, 126.60, 128.89, 133.01, 135.83, 147.38, 148.28, 127.45, 161.35 ppm; MS: m/z (%) 296 (M+1, 40), 280 (100), 161 (25), 77 (10). *Anal.* Calcd for $C_{16}H_{13}N_3OS$: C, 65.06; H, 4.44; N, 14.23; S, 10.86 %. Found: C, 64.86; H, 4.45; N, 14.20; S, 10.85%.

3-(2'-Benzothiazolyl)-2,3-dihydro-2-hexyl-quinazolin-4(1*H*)-one (4k). Colorless crystals. mp 148-151°C; ir (KBr): 3370, 2926, 1633, 1513, 1435 cm^{-1}; ^1H nmr: δ 0.80 (t, J= 6.83 Hz, CH_3), 1.27-1.29 (m, $3CH_2$), 1.31 (m, CH_2), 1.66 (m, CH_2), 1.89 (m, CH_2), 6.37 (ddd, J= 7.53 Hz, J= 6.37 Hz, J= 3.70 Hz, CH), 6.81 (t, J= 7.58 Hz, CH), 6.90 (d, J= 8.12 Hz, CH), 7.34 (t, J= 7.49 Hz, CH), 7.42 (t, J= 7.91 Hz, CH), 7.46 (t, J= 7.32 Hz, CH), 7.67 (d, J= 3.60 Hz, NH), 7.81 (d, J= 7.99 Hz, CH), 7.82 (d, J= 7.61 Hz, CH), 8.00 (d, J= 7.78 Hz, CH) ppm; ^{13}C nmr: δ 14.35, 22.44, 24.97, 28.40, 31.48, 32.48, 68.06, 113.49, 116.06, 118.35, 121.27, 122.05, 124.35, 126.62, 128.86, 132.98, 135.83, 147.18, 148.22, 157.68, 161.53 ppm; ms: m/z (%) 380 (M+15, 10), 280 (100), 245 (30). *Anal.* Calcd for $C_{21}H_{23}N_3OS$: C, 69.01; H, 6.34; N, 11.50; S, 8.77 %. Found: C, 68.92; H, 6.37; N, 11.52; S, 8.73%.

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REFERENCES

[1] (a) Martin, T. A.; Wheller, A. G.; Majewski, R. F.; Corrigan, J. R. *J. Med. Chem.* **1964**, *7*, 812. (b) Jen, T.; Dienel, B.; Dowalo, F.; Hoeven, H. V.; Bender, P.; Love, B. *J. Med. Chem.* **1973**, *16*, 633. (c) Bigge, C. F.; Wu, J.-P.; Malone, T. C.; Taylor, C. P.; Vartanian, M. G. *Bioorg. Med. Chem. Lett.* **1993,** *1*, 39. (d) Liverton, N. J.; Armstrong, D. J.; Claremon, D. A.; Remy, D. C.; Baldwin, J. J.; Lynch, R. J.; Zhang, G.; Gould, R. *Bioorg. Med. Chem. Lett.* **1998,** *8*, 483. (e) Kobayashi, S.; Ueno, M.; Suzuki, R.; Ishitani, H. *Tetrahedron Lett.* **1999,** *40*, 2175. (f) Cao, S.-L.; Feng, Y.-P.; Jiang, Y.-Y.; Liu, S.-Y.; Ding, G.-Y.; Li, R.-T. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1915.

[2] (a) Lopez, S. E.; Rosales, M. E.; Urdaneta, N.; Godoy, M. V.; Charris, J. E. *J. Chem. Research(S)* **2000**, 258. (b) Abdel-Jalil, R. J.; Volter, W.; Saeed, M. *Tetrahedron Lett.* **2004**, *45*, 3475.

[3] (a) Gravier, D.; Dupin, J. P.; Casadebaig, F.; Hou, G.; Boisseau, M.; Bernard, H. *Pharmazie* **1992**, *47*, 91. (b) Baker, B. R.; Schaub, R. E.; Joseph, J. P.; McEvoy, F. J.; Williams, J. H. *J. Org. Chem.* 1953, *18*, 133. (c) Wolfe, J. F.; Rathman, T. L.; Sleevi, M. C.; Campbell, J. A.; Greenwood, T. D. *J. Med. Chem.* **1990**, *33*, 161.

[4] (a) Paget, C. J.; Chamberlin, J. W.; Wikel, J. H. British Patent 1,568,542, 1982; *Chem. Abstr.***1983**, *91,* 30754. (b) Paget, C. J.; Kisner, K.; Stone, R. L.; Delong, D. C. *J. Med. Chem.* **1969**, *12*, 1010. (c) Tamm, J. *In The Strategy in Chemotherapy,* Cowan, S. T.; Rowatt, E. Ed, Cambridge University Press, Cambridge, 1958.

[5] (a) Sharma, S. D.; Kaur, V. *Synthesis* **1989**, 677. (b) Kung, P. P.; Casper, M. D.; Cook, K. L.; Willson-Lin-gardo, L. *J. Med. Chem.* **1999**, *42*, 4705. (c) Corbett, J. W.; Ko, S. S.; Rodgers, J. D.; Gearhart, L. A.; Magnus, N. A.; Bachheler, L. T.; Diamond, S.; Jeffey, S.; Trainor, G. L.; Anderson, P. S.; Erickson-Vitanen, K. *J. Med. Chem.* **2000**, *43*, 2019. (d) Liu, J. F.; Lee, J.; Dalton, A. M.; Bi, G.; Yu, L.; Baldino, C. M.; McElory, E.; Brown, M. *Tetrahedron Lett.* **2005**, *46*, 1241. (e) Moore, J. A.; Sutherland, G. J.; Sowerby, R.; Kelly, E. G.; Palermo, S.; Webster, W. *J. Org. Chem.***1969**, *34*, 887. (f) Shi, D.; Rong, L.; Wang, J.; Zhuang, Q.; Wang, X.; Hu, H. *Tetrahedron Lett.* **2003**, *44*, 3199. (g) Sadanandam, Y. S.; Reddy, K. R. M.; Rao, A. B. *Eur. J. Org. Chem.* **1987**, *22*, 169. (h) Salehi, P.; Dabiri, M.; Zolfigol, M. A.; Baghbanzadeh, M. *Synlett* **2005**, 1155. (i) Dabiri, M.; Salehi, P.; Otokesh, S.; Baghbanzadeh, M.; Kozehgary, G.; Mohammadi, A. A. *Tetrahedron Lett.* **2005**, *46*, 6123. (j) Baghbanzadeh, M.; Salehi, P.; Dabiri, M.; Kozehgary, G. *Synthesis* **2006**, 344.

[6] (a) Kappe, C. O. *Curr. Opin. Chem. Biol.* **2002**, *6*, 314. (b) Domling, A.; Ugi, I. *Angew. Chem. In. Ed.* **2000**, *39*, 3168. (c) *Multicomponent Reactions*, Zhu, J.; Bienayme, H. Ed. Wiley-VCH: Weinheim, 2005.

[7] (a) Cave, G. W. V.; Raston, G. L.; Scott, J. L. *Chem. Commun.* 2001, 2159. (b) Tanaka, K.; Toda, F. *Chem. Rev.* **2000**, *100*, 1025. (c) Metzger, J. O. *Angew. Chem. Int. Ed.* **1998**, *37*, 2975.

[8] Anastas, P. T.; Warner, J. C. *Green Chemistry—Theory and Practice*, Oxford University Press, New York, 1998.

[9] (a) Shaabani, A.; Rahmati, A.; Naderi, S. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 5553. (b) Shaabani, A.; Safaei, H. R.; Bijanzadeh, H. R.; *Synth. Commun.* **2001**, *31*, 2639.

[10] (a) Shaabani, A.; Teimouri, M. B.; Arab-Ameri, S. *Tetrahedron Lett.* **2004**, *45,* 8409. (b) Shaabani, A.; Teimouri, M. B.; Bijanzadeh, H. R. *Tetrahedron Lett.* **2002**, *43*, 9151. (c) Shaabani, A.; Yavari, I.; Teimouri, M. B.; Bazgir, A.; Bijanzadeh, H. R. *Tetrahedron* **2001**, *57*, 1375. (d) Shaabani, A.; Bazgir, A. *Tetrahedron Lett.* **2004**, *45*, 2575. (e) Shaabani, A.; Bazgir, A.; Teimouri, F. *Tetrahedron Lett.* **2003**, *44*, 857. (f) Shaabani, A.; Bazgir, A.; Bijanzadeh, H. R. *Mol. Divers.* **2004**, *8*, 141. (g) Shaabani, A.; Rahmati, A. *Catal. Lett.* **2005**, *100,* 177.