New 2,3-disubstituted quinazolin-4(3*H*)-ones from 2-undecyl-3,1-benzoxazin-4-one

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2-undecyl-4*H*-3,1-benzoxazin-4-one (**2**) was prepared and reacted with primary and secondary amines affording compounds **3–7**, while with hydrazine hydrate it gave the quinazolinone derivative **8**. The reaction of **8** with 3,4,5-trimethoxybenzaldehyde followed by thioglycollic acid yielded **9** and **10**, respectively. Acylation of **8** using cinnamoyl chloride gave **11**. Furthermore, treatment of **2** with hydrazine derivatives provided **12** and **13**. Fusion of **2** with ammonium acetate gave the quinazolinone derivative **14** which upon treatment with ethyl chloroacetate yielded the ester **15**. The hydrazide **17** was obtained from hydrazinolysis of the ester **15**.

Keywords: quinazolinones, 3,1-benzoxazinones

Benzoxazinones temporarily inhibit the catalytic activity of serine proteases by accumulation of a catalytically inactive acyl-enzyme intermediate.[1] In continuation of our program exploring the chemical reactivity of the oxazinone moiety present in 4*H*-3,1-benzoxazin-4-one derivatives with saturated aliphatic substituents at position 2 (the so-called dynamic benzoxazinones),[2-7] and derivatives with bulky substituents involving strong conjugation power (which are so-called static benzoxazinones),[8-16] we report here on the synthesis of a new 2-substituted 3,1-benzoxazin-4-one and the corresponding 2,3-disubstituted 4-quinazolinones.

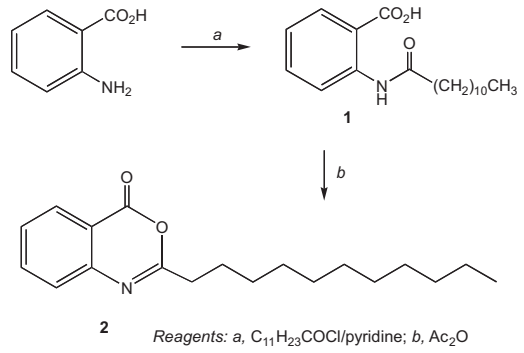
Results and discussion

The title compound 2-undecyl-3,1-benzoxazin-4-one (**2**) was prepared in fairly good yield upon treatment of anthranilic acid with dodecanoyl chloride in the presence of pyridine to give 2-dodecanamidobenzoic acid (**1**) which was cyclised to **2** using freshly distilled acetic anhydride (Scheme 1).

When the lactone **2** reacted with cyclohexylamine in refluxing pyridine it afforded *N*-cyclohexyl-2-dodecanamidobenzamide (**3**), but its reaction with other primary amines such as benzylamine and/or *p*-phenylenediamine yielded the 2,3-disubstituted quinazolin-4(3*H*)-one derivatives **4** and **5**, respectively. Reaction of **2** with secondary amines such as morpholine or thiomorpholine yielded *N*-[2-(morpholine-4-carbonyl)phenyl]dodecanamide **6** and the corresponding thiomorpholine derivative **7**, respectively (Scheme 2).

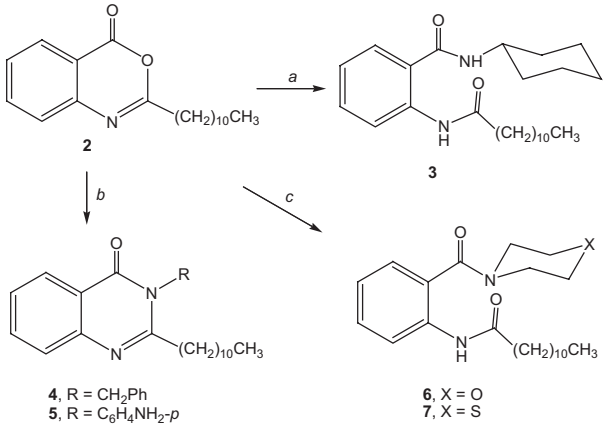
Stirring the 3,1-benzoxazin-4-one **2** with hydrazine hydrate (80%) at room temperature for one hour resulted in the formation of 3-amino-2-undecylquinazolin-4(3*H*)-one (**8**). Treatment of the *N*-aminoquinazolinone **8** with 3,4,5-trimethoxybenzaldehyde in refluxing ethanol yielded the anil **9** which with thioglycollic acid in dry benzene afforded the thiazolidin-4-one **10**. Acylation of **8** by cinnamoyl chloride yielded 3-cinnamoylamino-2-undecylquinazolin-4(3*H*)-one (**11**). The reaction of the lactone **2** with the hydrazine derivatives ethyl carbazate and thiosemicarbazide afforded 3-(ethoxycarbonylamino)-2-undecylquinazolin-4(3*H*)-one (**12**) and 3-(thiocarbamoylamino)-2-undecylquinazolin-4(3*H*)-one (**13**), respectively. An attempt to prepare the hydrazide derivative from **12** failed; with hydrazine hydrate in boiling ethanol the isolated product was identified as 3-amino-2-undecylquinazolin-4-one (**8**) (Scheme 3).

Fusion of **2** with ammonium acetate in oil-bath at 170°C for two hours yielded 2-undecylquinazolin-4(3*H*)-one (**14**) which with ethyl chloroacetate in the presence of anhydrous potassium carbonate in dry acetone afforded the *N*-alkylation product 3-(ethoxycarbonylmethyl)-2-undecylquinazolin-4(3*H*)-one (**15**) rather than the *O*-alkylation product **16**.[17] Hydrazinolysis of the ester **15** in refluxing ethanol formed the hydrazide derivative **17** (Scheme 4).



Reagents: a, $C_{11}H_{23}COCl$/pyridine; *b*, Ac_2O

Scheme 1



Reagents: a, cyclohexylamine / pyridine;
b, RNH_2 ; *c*, morpholine or thiomorpholine / EtOH

Scheme 2

Compounds **2–8**, **10**, **11**, **13**, **15** were found to possess marked activity against *Bacillus subtilis*, *Escherichia coli* and *Candida albicans*.

Experimental

All melting points were measured using a Gallenkamp electric melting point apparatus. IR spectra were recorded on a Pye-Unicam SP1200 spectrophotometer using the KBr wafer technique for solid materials. The ^{1}H NMR and ^{13}C NMR spectra were determined on a Varian Gemini 200 or MHz Bruker AC-200 MHz instrument using TMS as internal standard. Mass spectra were determined using an HP model MS-5988 in EI mode with electron energy 70 eV. Elemental analyses were carried out at the Microanalytical Unit, Faculty of Science, Cairo

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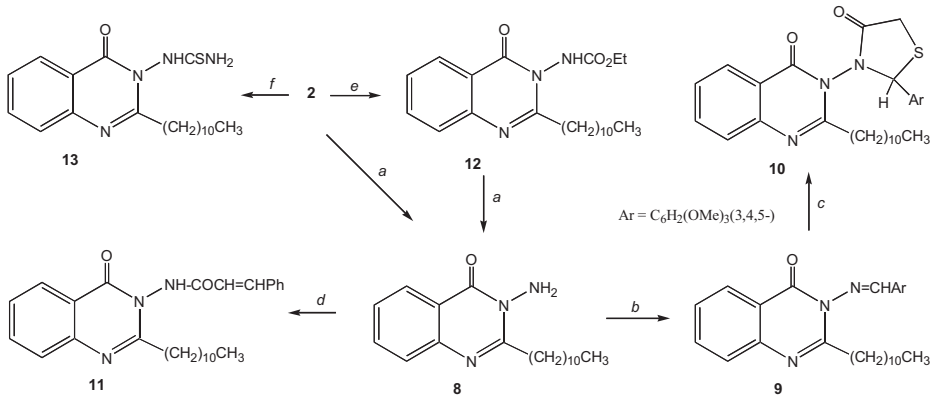
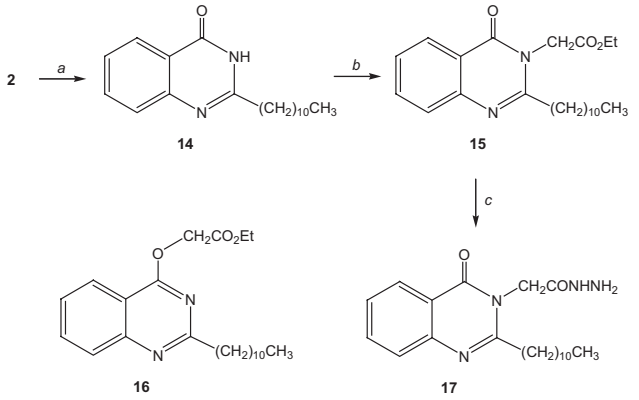


Reagents and conditions: a, $N_2H_4.H_2O$, *stir, r.t.; b,* ArCHO / EtOH; *c,* $HSCH_2CO_2H$ / dry benzene; *d,* cinnamoyl chloride; *e,* H_2NNHCO_2Et / dry benzene; *f,* $H_2NNHCSNH_2$ / EtOH

Scheme 3



Reagents: a, NH_4OAc, fusion; *b,* $ClCH_2CO_2Et$ / K_2CO_3 / dry acetone; *c,* $N_2H_4.H_2O$ / EtOH

Scheme 4

University using a Perkin-Elmer 2400 CHN Elemental Analyser. The monitoring of the progress of all reactions and the homogeneity of the synthesised compounds were carried out by TLC.

2-Dodecanamidobenzoic acid (**1**): Dodecanoyl chloride (30 ml, 0.15 mol) was added dropwise with stirring at room temperature to a solution of anthranilic acid (14 g, 0.1 mol) in pyridine (50 ml) over a period of 0.5 h. The mixture was then refluxed for 2 h. After cooling, the reaction mixture was diluted with water and acidified with cold dilute hydrochloric acid. The solid product that precipitated was filtered off, washed with cold water, dried, and then recrystallised from petroleum ether (b.p. 80–100°C) to give **1** as colourless crystals (26.8 g., 84%), m.p. 98–99°C. IR: 3335 br (NH, OH), 1680 cm^{-1} (C=O). ^1H NMR ($CDCl_3$): δ 12.5 (s, 1H, COOH, exchangeable with D_2O), 9.7 (s, 1H, NH, exchangeable with D_2O), 8.4–7.4 (m, 4Harom), 2.3 (t, 2H), 1.6 (m, 2H), 1.31–1.2 (m, 16H), 0.9 (t, 3H). MS: *m/z* (%) 320 (M + 1, 2.4), 276 (1.9), 137 (100), 119 (30). Anal. Calcd. for $C_{19}H_{29}NO_3$ (319.45): C, 71.44; H, 9.15; N, 4.38. Found: C, 71.58; H, 8.92; N, 4.13%.

2-Undecyl-4H-3,1-benzoxazin-4-one (**2**): A solution of **1** (3.2 g, 0.01 mol) in freshly distilled acetic anhydride (10 ml) was heated under reflux for 2 h, left to cool, diluted with cold water. The crude white solid that separated out was collected, washed with aqueous sodium carbonate (10%), then with cold water. It was dried and recrystallised from petroleum ether (b.p. 40–60°C) to give **2** as colourless crystals (2.9 g., 90%) m.p. 30–32°C. IR (KBr): 1764 cm^{-1} (lactone C=O). ^1H NMR ($CDCl_3$): δ 8.1–7.4 (m, 4Harom), 2.67 (t, 2H), 1.8 (m, 2H), 1.36–1.2 (m, 16H), 0.82 (t, 3H). MS: *m/z* (%) 301 (M^+, 13), 161 (100), 90 (33). Anal. Calcd. for $C_{19}H_{27}NO_2$ (301.43): C, 75.71; H, 9.02; N, 4.64. Found: C, 75.30; H, 9.25; N, 4.62%.

N-Cyclohexyl-2-dodecanamidobenzamide (**3**): The benzoxazinone **2** (1 g, 3.3 mmol) and cyclohexylamine (0.32 ml, 3.3 mmol) in pyridine (10 ml) were heated under reflux for 3 h, then left to cool and acidified with cold dilute hydrochloric acid. The solid product that deposited was collected by filtration, washed with cold water, dried and then recrystallised from petroleum ether (b.p. 60–80°C) to give **3** as colourless crystals (1.21 g., 72%), m.p. 35–37°C. IR (KBr): 3263 br. (NH), 1690, 1676 cm^{-1} (C=O). ^1H NMR ($CDCl_3$): δ 11.02 (s, 1H, Ar-NHCO), 8.69 (d, 1H, N<u>H</u>-C_6H_{11}), 7.3–6.9 (m, 4Harom), 3.9 (br.d, 1H, NH–C<u>H</u>), 2.4 (t, 2H), 2.0 (d,d, 2H), 1.79–1.6 (m, 10H, cyclohexyl protons), 1.4 (m, 16H), 0.9 (t, 3H). MS: *m/z* (%) 401 (M^+ + 1, 22.9), 302 (34.2), 218 (100), 136 (53.9), 120 (73.2), 92 (12.7). Anal. Calcd. for $C_{25}H_{40}N_2O_2$ (400.61): C, 74.95; H, 10.06; N, 6.99. Found: C, 74.71; H, 9.83; N, 6.63%.

3-Benzyl-2-undecylquinazolin-4(3H)-one (**4**): The benzoxazinone **2** (1 g, 3.3 mmol) and benzylamine (0.36 ml, 3.3 mmol) were heated to reflux in ethanol (25 ml) for 3 h. Most of the solvent was distilled off and the reaction mixture was then acidified with cold dilute hydrochloric acid to afford an oily substance (one spot in TLC) which did not solidify even with light-petroleum ether (b.p.40–60°C) to give **4** as a yellow oil (1.03 g, 80%). IR: 1684 cm^{-1} (C=O). ^1H NMR ($CDCl_3$): δ 8.04–7.05 (m, 9Harom), 4.38 (dd, 2H), 1.7–1.2 (m, 20H), 0.86 (t, 3H). MS: *m/z* (%) 390 (M^+, 2.3), 348 (3.5), 207 (12), 181 (0.7), 165 (100), 91 (16).

3-(4-Aminophenyl)-2-undecylquinazolin-4(3H)-one (**5**): The benzoxazinone **2** (1 g, 3.3 mmol) and *p*-phenylenediamine (0.35 g, 3.3 mmol) were refluxed in n-butanol (15 ml) for 10 h. The solid product that separated out after distilling off the excess solvent and cooling was collected by filtration, dried and then recrystallised from petroleum ether (b.p.60–80°C) to give **5** as colourless crystals (0.45 g., 35%) m.p. 96–97°C. IR (KBr): 3419, 3358 (NH_2), 1673 cm^{-1} (C=O). ^1H NMR ($CDCl_3$): δ 8.3–6.75 (m, 8Harom), 3.88 (br.s, 2H, NH_2, exchangeable with D_2O), 2.4 (t, 2H), 1.74 (m, 2H), 1.25 (m, 16H), 0.79 (t, 3H). MS *m/z* (%): 391 (M^+, 12), 264 (21), 251 (100), 106 (20). Anal. Calcd. for $C_{25}H_{33}N_3O$ (391.57): C, 76.68; H, 8.49; N, 10.73. Found: C, 76.69; H, 8.68; N, 10.37%.

N-[2-(Morpholine-4-carbonyl)phenyl]dodecanamide (**6**) *and N-[2-(thiomorpholine-4-carbonyl)phenyl]dodecanamide* (**7**): The benzoxazinone **2** (1 g, 3.3 mmol) and morpholine (0.28 ml, 3.3 mmol) or thiomorpholine (0.35 ml, 3.3 mmol) in ethanol (30 ml) were heated under reflux for 3 h. An oily substance was produced after distillation of the solvent and acidification with cold dilute hydrochloric acid. The oil (one spot on TLC) did not solidify even with light petroleum (b.p.40–60°C) to give **6** and **7**, respectively.

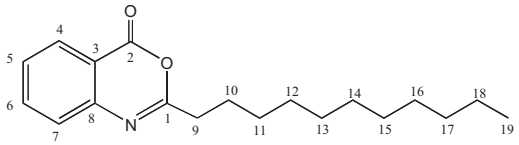


Table 1 ^{13}C NMR of compound **2**, in $CDCl_3$

Atom no.	δ (ppm)	Atom no.	δ (ppm)	Atom no.	δ (ppm)
C-1	163.8	C-6	130.7	C-10	20.6
C-2	161.7	C-7	127.1	C-11–C-17	29.6
C-3	110.6	C-8	143.3	C-18	21.9
C-4	128.2	C-9	30.9	C-19	14.7
C-5	126.1				

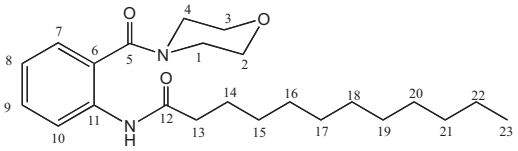


Table 2 ^{13}C NMR of compound **6**, in $CDCl_3$

Atom no.	δ (ppm)	Atom no.	δ (ppm)	Atom no.	δ (ppm)
C-1, C-4	43.9	C-10	126.4	C-16, C-17	29.3
C-2, C-3	65.7	C-11	135.2	C-18, C-19	29.4
C-5	170.1	C-12	172.4	C-20	29.7
C-6	133.9	C-13	36.9	C-21	30.7
C-7	128.1	C-14	26.3	C-22	22.6
C-8	125.3	C-15	28.1	C-23	14.3
C-9	130.2				

Morpholide (**6**): Yellow oil (0.69 g., 54%). IR: 3308 cm^{-1} (NH), 1732, 1687 cm^{-1} (C=O). ^1H NMR ($CDCl_3$): δ 9.9 (s, 1H, NH, exchangeable with D_2O), 7.87–7.3 (m, 4Harom), 3.61 (m, 4H, CH_2OCH_2), 3.54 (m, 4H, CH_2NCH_2), 2.59 (t, 2H), 1.66 (t, 2H), 1.4–1.2 (m, 16H), 0.9 (t, 3H). MS *m/z* (%): 388 ($M^{+\cdot}$, 1.2), 302 (61), 206 (17), 137 (61), 120 (100), 92 (25).

Thiomorpholide (**7**): Yellow oil (0.60 g., 45%). IR: 3265 (NH), 1732, 1686 cm^{-1} (C=O). ^1H NMR ($CDCl_3$): δ 9.1 (s, 1H, NHCO, exchangeable with D_2O), 7.81–7.3 (m, 4Harom), 3.51 (m, 4H, CH_2NCH_2), 2.57 (m, 4H, CH_2SCH_2), 2.51 (t, 2H), 1.66 (t, 2H), 1.3–1.2 (m, 16H), 0.9 (t, 3H). MS: *m/z* (%) 404 (M^+, 14), 302 (100), 222 (5.6), 136 (30), 120 (62), 92 (26).

3-Amino-2-undecylquinazolin-4(3H)-one (**8**): The benzoxazinone **2** (1 g., 3.3 mmol) and hydrazine hydrate 80% (0.5 ml, 0.01 mol) in ethanol (15 ml) were stirred at room temperature for 1 h. The solid that precipitated was filtered off, washed with light petroleum (b.p. 60–80°C), dried, and then recrystallised from light petroleum (b.p.80–100°C) to give **8** as colourless crystals (0.67 g., 64%), m.p. 97–99°C. IR: 3322, 3261 (NH_2), 1652 cm^{-1} (C=O). ^1H NMR ($CDCl_3$):δ 8.1–7.6 (m, 4Harom), 5.32 (br.s, 2H, NH_2, exchangeable with D_2O), 1.3–1.2 (m, 20H), 0.89 (t, 3H). MS: *m/z* (%) 315 ($M^{+\cdot}$, 6.4), 175 (100), 146 (27), 118 (4.9), 77 (8.5). Anal. Calcd. for $C_{19}H_{29}N_3O$ (315.46): C, 72.34; H, 9.26; N, 13.32. Found: C, 71.92; H, 9.80; N, 13.08%.

3-(3,4,5-Trimethoxybenzylideneamino)-2-undecylquinazolin-4(3H)-one (**9**): The aminoquinazolinone **8** (0.5 g, 1.58 mmol) and 3,4,5-trimethoxybenzaldehyde (0.3 g, 1.58 mmol) were heated in refluxing ethanol (10 ml) for 3 h. Most of the solvent was then distilled off. Cooling the resulting solution gave a solid which was collected by filtration, dried and then recrystallised from petroleum ether (b.p.80–100°C) to give **9** as pale yellow crystals (0.43 g, 55%), m.p. 78–80°C. IR: 1664 cm^{-1} (C=O). ^1H NMR (DMSO-d_6): δ 8.89 (s, 1H, CH=N), 8.1–7.3 (m, 6Harom), 3.94 (s, 6H, 2OMe), 3.8 (s, 3H, OMe), 1.39–1.21 (m, 20H), 0.86 (t, 3H). MS: *m/z* (%) 494 (M^+ + 1, 28), 300 (5.2), 193 (100), 160 (42). Anal. Calcd. for $C_{29}H_{39}N_3O_4$ (493.66): C, 70.56; H, 7.96; N, 8.51. Found: C, 70.31; H, 8.27; N, 8.63%.

3-[4-Oxo-2-(3,4,5-trimethoxyphenyl)thiazolidin-3-yl]-2-undecylquinazolin-4(3H)-one (**10**): The imine **9** (0.5 g, 1 mmol) and thioglycollic acid (0.1 ml, 1 mmol) in dry benzene (15 ml) was heated under reflux for 12 h. Most of the solvent was distilled off to give an oily substance which on trituration with boiling light-petroleum ether (b.p.40–60°C) gave a pale yellow solid which recrystallised from petroleum ether (b.p.80–100°C) to give **10** as pale yellow crystals (0.37 g, 66%), m.p. 40–42°C. IR: 1718, 1661 cm^{-1} (C=O). ^1H NMR ($CDCl_3$): δ 8.1–7.07 (m, 6Harom), 6.1 (s, 1H, NCHS), 3.95 (d,d, 2H, SCH_2CO), 3.83 (s, 9H, 3OMe), 1.3–1.2 (m, 20H), 0.9 (t, 3H). MS *m/z* (%): 495 ($M^{+\cdot}$ – CH_2S–CO + 2H·, 51), 298 (40), 194 (36), 54 (100). Anal. Calcd. for $C_{31}H_{41}N_3O_5S$ (567.76): C, 65.58; H, 7.27; N, 7.4; S, 5.64. Found: C, 66.01; H, 7.55; N, 7.31; S, 5.92%.

3-Cinnamoylamino-2-undecylquinazolin-4(3H)-one (**11**): The aminoquinazolinone **8** (0.5 g, 1.58 mmol) was refluxed with cinnamoyl chloride (0.26 g, 1.58 mmol) in pyridine (15 ml) for 8 h. The reaction mixture was acidified with cold dilute hydrochloric acid. The solid that precipitated was filtered off, washed with cold water, dried and then recrystallised from benzene to give **11** as colourless crystals (0.60 g, 86%), m.p 107–108°C. IR: 3344 (NH), 1696, 1671 cm^{-1} (C=O). ^1H NMR ($CDCl_3$): δ 8.9 (s, 1H, NH, exchangeable with D_2O), 8.1–7.3 (m, 9Harom), 7.0 (s, 1H), 7.3 (s, 1H), 1.3–1.2 (m, 20H), 0.92 (t, 3H). MS: *m/z* (%) 445 (M^+, 13.9), 305 (35.7), 131 (100), 103 (37.9), 77 (19.9). Anal. Calcd. for $C_{28}H_{35}N_3O_2$ (445.61): C, 75.47; H, 7.91; N, 9.42. Found: C, 75.57; H, 8.16; N, 9.32%.

3-Ethoxycarbonylamino-2-undecylquinazolin-4(3H)-one (**12**): The benzoxazinone **2** (1 g, 3.3 mmol) and ethyl carbazate (0.35 g, 3.3 mmol) in dry benzene (15 ml) were heated under reflux for 6 h. An oily substance (one spot in TLC) was produced after distillation of the solvent which we could not solidify even by light-petroleum ether (b.p. 40–60°C) to give **12** as a yellow oil (0.96 g, 75%). IR: 3255 (NH), 1756, 1701 cm^{-1} (C=O). ^1H NMR (DMSO-d_6): δ 10.4 (s, 1H, NH, exchangeable with D_2O), 8.1–7.4 (m, 4Harom), 4.2–4.04 (q, 2H), 1.7–1.2 (m, 20H), 0.9–0.84 (m, 6H). MS: *m/z* (%) 387 (M^+, 3.1), 247 (54), 175 (22), 104 (65), 77 (10.5), 57 (100).

Treatment of **12** *with hydrazine hydrate* Compound **12** (1 g, 2.6 mmol) was stirred in ethanol (25 ml) while hydrazine hydrate (80%, 0.5 ml, 0.01 mol) was added dropwise over 30 min at room temperature. The solid that deposited was recrystallised and identified as the amine **8**.

3-Thiocarbamoylamino-2-undecylquinazolin-4(3H)-one (**13**): The benzoxazinone **2** (1 g, 3.3 mmol) and thiosemicarbazide (0.3 g, 3.3 mmol) was refluxed in ethanol (25 ml) for 3 h. After removal of most of the solvent the residue was collected by filtration, dried and recrystallised from petroleum ether (b.p.80–100°C) to give **13** as colourless crystals (0.85 g, 69%), m.p: 101–102°C. IR: 3473, 3367, 3274, 3155 (NH, NH_2), 1687 (C=O), 1170 cm^{-1} (C=S). ^1H NMR ($CDCl_3$): δ 10.1 (br.s, 2H, NH_2, exchangeable with D_2O), 8.5 (br.s, 1H, NH, exchangeable with D_2O), 8.1–7.6 (m, 4Harom), 1.4–1.19 (m, 20H), 0.9 (t, 3H). MS: *m/z* (%) 341 ($M^+ – H_2S$, 17.8), 173 (41), 160 (100), 120 (13). Anal. Calcd. for $C_{20}H_{30}N_4OS$ (374.55): C, 64.13; H, 8.07; N, 14.95; S, 8.56%. Found: C, 63.82; H, 7.78; N, 5.16; S, 8.24%.

2-Undecylquinazolin-4(3H)-one (**14**): The benzoxazinone **2** (1 g, 3.3 mmol) and ammonium acetate (3 g) was fused in an oil-bath at 170°C for 2 h. After cooling, the reaction mixture was poured into water then the solid that was deposited was collected by filtration, dried and then recrystallised from petroleum ether (b.p. 60–80°C) to give **14** as colourless crystals (0.95 g, 94%), m.p. 94–95°C. IR: 3358, 3172 (NH, OH), 1674 cm^{-1} (C=O). ^1H NMR ($CDCl_3$): δ 11.08 (s, 1H, NH, exchangeable with D_2O), 8.1–7.6 (m, 4Harom), 1.46–1.2 (m, 20H), 0.96 (t, 3H). MS: *m/z* (%) 300 (M^+, 4.5), 257 (3.4), 215 (6.5), 173 (34), 160 (100). Anal. Calcd. for $C_{19}H_{28}N_2O$ (300.45): C, 75.95; H, 9.39; N, 9.32. Found: C, 75.78; H, 9.37; N, 9.06%.

Ethyl (3,4-dihydro-4-oxo-2-undecylquinazolin-3-yl)acetate (**15**): The quinazolinone **14** (0.5 g, 1.6 mmol), ethyl chloroacetate (0.6 ml, 4.8 mmol) and anhydrous potassium carbonate (1 g) was refluxed in dry acetone (25 ml) on water bath for 30 h. Most of the solvent was distilled off and the reaction mixture was then diluted with water to afford a solid product that was collected by filtration and recrystallised from benzene to give **15** as pale yellow crystals (0.44 g, 71%), m.p. 80–81°C. IR (KBr): 1732, 1670 cm^{-1} (C=O). ^1H NMR (DMSO-d_6): δ 8.1–6.75 (m, 4Harom), 4.9 (s, 2H, N-CH_2CO), 4.2 (q, 2H), 2.79 (t, 2H), 2.03 (t, 3H), 1.68 (t, 2H), 1.4–1.2 (m, 16H), 0.85 (m, 3H). MS: *m/z* (%) 357 ($M^+ – C_2H_4$- H·, 8.2), 174 (100), 146 (19). Anal. Calcd. for $C_{23}H_{34}N_2O_3$ (386.54): C, 71.47; H, 8.86; N, 7.24. Found: C, 71.25; H, 9.18; N, 7.62%.

2-(3,4-Dihydro-4-oxo-2-undecylquinazolin-3-yl)acetohydrazide (**17**): The ester **15** (0.5 g, 1.3 mmol) and hydrazine hydrate 80% (0.3 ml, 6 mmol) in ethanol (25 ml) was refluxed for 2 h. After distillation of most of the solvent, a colourless solid was formed which was collected by filtration and recrystallised from benzene to give **17** as colourless crystals (0.42 g, 87%), m.p. 165–166°C. IR: 3333 br. (NH, NH_2), 1681, 1655 cm^{-1} (C=O). MS: *m/z* (%) 372 (M^+, 2.6), 342 (91), 341 (100), 314 (42), 313 (45). Anal. Calcd. for $C_{21}H_{32}N_4O_2$ (372.52): C, 67.71; H, 8.65; N, 15.03. Found: C, 67.49; H, 8.51; N, 14.97%.

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References

1 U. Neumann, N. Schechter and M. Gütschow, *Bioorg. Med. Chem.*, 2001, **9**, 947.
2 A. Sammour, A. Rabi, M.A. El-Hashash and M.A. Sayed, *J. Chem. UAR*, 1976, **19**, 571.
3 A.M. Fahmy, M.A. El-Hashash, M.A. Habishy and S. Nassar, *Rev. Roumaine Chim.*, 1978, **23**, 11.
4 M.A. El-Hashash, M.A. Hassan and M.A. Sayed, *Pakistan J. Sci. Ind. Res.*, 1977, **20**, 336.
5 M.M. Mohamed, M.A. El-Hashash, A.M. El-Gendy and M.M. Hamed, *Indian J. Chem.*, 1982, **21B**, 593.

6 M.A. El-Hashash, M.A. Kaddah, M. El-Kady and M.M. Amer, *Pakistan J. Sci. Ind. Res.*, 1982, **25**, 104.
7 M.S.Y. Khan, M. Akhter and A. Husain, *Indian J. Chem.*, 2006, **45B**, 1020.
8 M.M. Gineinah, M.A. El-Sherbeny, M.N. Nasr and A.R. Maarouf, *Arch. Pharm. Med. Chem.*, 2002, **335**, 556.
9 D.R. Huron, M.E. Gorre, A.J. Kraker, C.L. Sawyers, N. Rosen and M.M. Moasser, *Clin. Cancer Res.*, 2003, **9**, 1267.
10 M.M. Mohamed, M.A. El-Hashash, A.M. El-Gendy, I. Mohamed and O.A. Sayed, *J. Chem. Soc. Pakistan,* 1986, **8**, 37.
11 M.A. El-Hashash, S.A. Shiba, F.A. El-Bassiouny and I.M. El-Deen, *Pakistan J. Chem. Soc.*, 1991, **13**, 274.
12 M.S. Amine, M.A. El-Hashash and I.A. Attia, *Indian J. Chem.*, 1993, **32B**, 577.
13 M.A. El-Hashash, F.M.A. Soliman, L. Souka and N. Abdel-Ghaffar, *Rev Roumaine Chim.*, 1995, **40**, 59.
14 E.A. Kassab, M.A. El-Hashash, F.M.A. Soliman and R.S. Ali, *Egypt. J. Chem.*, 2001, **44**, 169.
15 M.M. Gineinah, M.N. Nasr, A.M. Abdela, A.A. El-Emam and S.A. Said, *Med. Chem. Res.*, 2000, **10**, 243.
16 J.V. Partin, I.E. Anglin and N.B. Kyprianou, *J. Cancer*, 2003, **88**, 1615.
17 S.S. El-Saka, M.A. El-Hashash, I.I. Abd El-Gawad and G.E. Ahmed, *Egypt. J. Chem.*, **20**05, **48**, 773.