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ORIGINAL PAPER

Use of dodecanoyl isothiocyanate as building block in synthesis of target benzothiazine, quinazoline, benzothiazole and thiourea derivatives

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Dodecanoyl isothiocyanate (*I*) reacts additively with anthranilic acid to afford derivatives of thiourea *II* and benzothiazine *III* in a one-pot reaction. The cyclisation of thiourea *II* was achieved using acetic anhydride to form quinazoline derivative *IV*. The heating of quinazoline *IV* in acetic anhydride or butan-1-ol gave quinazoline derivatives *V* or *VI*, respectively. Benzothiazine *III* underwent trans-acylation to benzothiazine *VII* in boiling acetic anhydride. The treatment of *IV* with hydrazine hydrate, anthranilic acid or ethyl carbazate afforded derivatives of triazoloquinazoline *VIII*, quinazolinoquinazoline *XI* or thiosemicarbazide *X*, respectively. The reaction of *I* with 2-aminophenol or 2-aminothiophenol afforded thiourea derivative *XIII* or benzothiazole derivative *XIV*, respectively. Most of the synthesised compounds bear a lauroyl (dodecanoyl) group (a hydrocarbon moiety). The structures of the synthesised compounds were confirmed by microanalytical and spectral data.

Keywords: lauroyl isothiocyanate, thiourea, benzothiazine, quinazoline, thiosemicarbazide derivatives

Introduction

Many preparatory methods have been reported for the production of quinazolines (Kidwai et al., 2007; Barluenga et al., 1994; Raffa et al., 2004). Quinazolines and their ring-fused derivatives have attracted considerable attention due to the wide spectrum of their pharmacological activities such as anti-inflammatory (Maggio et al., 2001), antimicrobial (Grover & Kini, 2006) antioxidant (Roopan et al., 2008), anticancer (Chandrika et al., 2008; Khalil et al., 2003), antihypertensive (Alagarsamy & Pathak, 2007) antiviral (Schleiss et al., 2008), diuretic (Hayao et al., 1965; Cohen et al., 1960), antiHIV (Alagarsamy et al., 2007), anticonvulsants (Laddha & Bhatnagar, 2008) and anti-tubercular agents (Mosaad et al., 2004). Moreover, the chemistry of thioxoquinazolines has considerable value and has gained increased interest in both synthetic and biological fields. Accordingly, methods for the syntheses and modification of such ring systems continue to be the focus of research (El-Hiti et al., 2011). Some triazoloquinazolines have exhibited antibacterial activities (Ghorab et al., 2013). Further, 3,1-benzothiazine core moieties possess remarkable potential as anti-radiation agents (Yadav et al., 2009) and bioactive materials (Simerpreet & Cannoo, 2013; Gütschow et al., 2012) in addition to their applications in recording and photographic materials (Obayashi & Okawa, 2001; Canon, 1984). They are used in various organic syntheses and transformations as reaction intermediates (Yadav et al., 2009; Yavari et al., 2010; Ding et al., 2012). A number of effective approaches for their preparation have been reported in the literature (Ding et al., 2013; Gimbert & Vallribera, 2009; Butin et al., 2009). The thiourea backbone also represents a significant structural motif in pharmaceu-

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tical agents (Balzarini et al., 2009; Bukvić Krajačić et al., 2011; Sharma et al., 2010) having antibacterial, antimalarial, antiviral and anti-tumour activities.

In recent years, the potentials of aroyl isothiocyanates (Fahmy et al., 2010; Hemdan, 2010; Hemdan et al., 2010; Hemdan & El-Sayed, 2015) and acyl isothiocyanates (Hemdan et al., 2008, 2012; Hemdan & Abd El-Mawgoude, 2015a, 2015b) have been explored in heterocyclic syntheses. In the present investigation, dodecanoyl isothiocyanate was used as a building block in the synthesis of quinazoline, 3,1-benzothiazine, benzothiazole and thiourea derivatives. Some of the synthesised target compounds were substituted by a lauroyl (dodecanoyl) group (a hydrocarbon moiety) in an attempt to enhance their biological activities.

Experimental

General

All reagents and solvents were purchased from Merck-Schuchardt (Germany) and used as received; commercially available solvents (Adwek-Egypt) were used for crystallisations. Melting points were determined in open capillary tubes on a Gallenkemp melting point apparatus and are uncorrected. Elemental analyses were carried out using a PerkinElmer 2400 CHN elemental analyser. FTIR spectra were recorded on a PerkinElmer Spectrum RXIFT-IR systems using the KBr disc technique. ^{1}H NMR spectra were measured in DMSO-d_6 on a Varian Gemini 300 MHz instrument with TMS as internal standard. Mass spectra were recorded on a Shimadzu GC-MS, QP 1000 EX instrument operating at 70 eV. The reactions and purity of the products were monitored by thin-layer chromatography using ethyl acetate/hexane ($\varphi_r = 2:1$) as the eluent. Merck 60 F254 silica gel TLC plates (0.2 mm; Darmstadt, Germany) and visualisation by UV irradiation (254 nm) were used. Dodecanoyl isothiocyanate (*I*) was prepared following the published method (El-Bordany, 2012).

Preparation of 2-(3-dodecanoylthioureido) benzoic acid (II) and N-(4-oxo-4H-3,1-benzothiazin-2-yl)dodecanamide (III)

Anthranilic acid (3 mmol) was added to a solution of isothiocyanate *I* (3 mmol) in acetonitrile (30 mL) and the reaction mixture was refluxed for 1 h followed by cooling to ambient temperature to afford a mixture of *II* and *III* as a solid precipitate. This mixture was suspended in boiling ethanol (2 × 20 mL). The combined filtrates were cooled to give *III* as yellow crystals (0.41 g, 38 %). The residue (0.69 g) was dissolved in 50 mL of boiling petroleum ether (80–100 °C) to give, upon cooling, colourless crystals of *II* (0.62 g, 55 %).

Preparation of 3-dodecanoyl-2-thioxo-2,3-dihydroquinazolin-4(1H)-one (IV), 3-acetyl-2-thioxo-2,3-dihydroquinazolin-4(1H)-one (V) and N-(4-oxo-4H-benzo[d][1,3]thiazin-2-yl)acetamide (VII)

Compound *II* (1 g) was refluxed in acetic anhydride (Ac_2O; 10 mL) for 1 h then the solid product was filtered and re-crystallised from EtOH to give colourless crystals of *IV* (0.83 g). Similarly, the refluxing of *III* or *IV* (0.5 g) in Ac_2O (10 mL) for 3 h afforded *VII* or *V*, respectively. The crystallisation of crude products from hot EtOH gave yellow crystals of *VII* (0.23 g) and colourless crystals of *V* (0.23 g).

Preparation of 2-thioxo-2,3-dihydroquinazolin-4(1H)-one (VI), 3-undecyl-[1,2,4]triazolo[3,4-b]quinazolin-5(10H)-one (VIII), dodecanehydrazide (IX), 4-dodecanoyl-1-ethoxycarbonylthiosemicarbazide (X), 6H-quinazolino[3,2-a]quinazoline-5,12-dione (XI), 1-dodecanoyl-3-(2-hydroxyphenyl)thiourea (XIII) and N-(benzo[d]thiazol-2-yl) dodecanamide (XIV)

Compound *IV* (1 g) in 10 mL of butan-1-ol was heated under reflux in the presence of a few drops of triethylamine for 6 h. The reaction mixture was concentrated to half its original volume, then cooled to ambient temperature and the solid product was filtered and re-crystallised from EtOH to afford *VI* as pale yellow crystals (0.37 g). A similar procedure, with the addition of hydrazine hydrate (3 mmol) or ethyl carbazate (IUPAC nomenclature: ethoxycarbohydrazide) (3 mmol) or anthranilic acid (3 mmol) or 2-aminophenol (3 mmol) or 2-aminothiophenol (3 mmol) and reaction time of 6–9 h (monitored by TLC) afforded compounds *VIII–XIV*, respectively. The following solvents were used for crystallisation: petroleum ether (60–80 °C) for *VIII* and *X* (colourless crystals); petroleum ether (40–60 °C) for *IX* (colourless crystals); petroleum ether (80–100 °C) for *XIII* (colourless crystals) and *XIV* (pale yellow crystals); EtOH for *XI* (colourless crystals).

Results and discussion

In the present study, the reactions of dodecanoyl isothiocyanate (*I*) with different nucleophiles were investigated to obtain the target annulated heterocycles of known biological activity. Hence, the interaction of equimolar quantities of *I* with anthranilic acid in a dry acetonitrile afforded a mixture of 2-(3-dodecanoylthioureido)benzoic acid (*II*) and *N*-(4-oxo-4*H*-3,1-benzothiazin-2-yl)dodecanamide (*III*). Heating of the thiourea derivative *II* in Ac_2O afforded 3-dodecanoyl-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (*IV*) (Fig. 1). Further heating of compound *IV* in

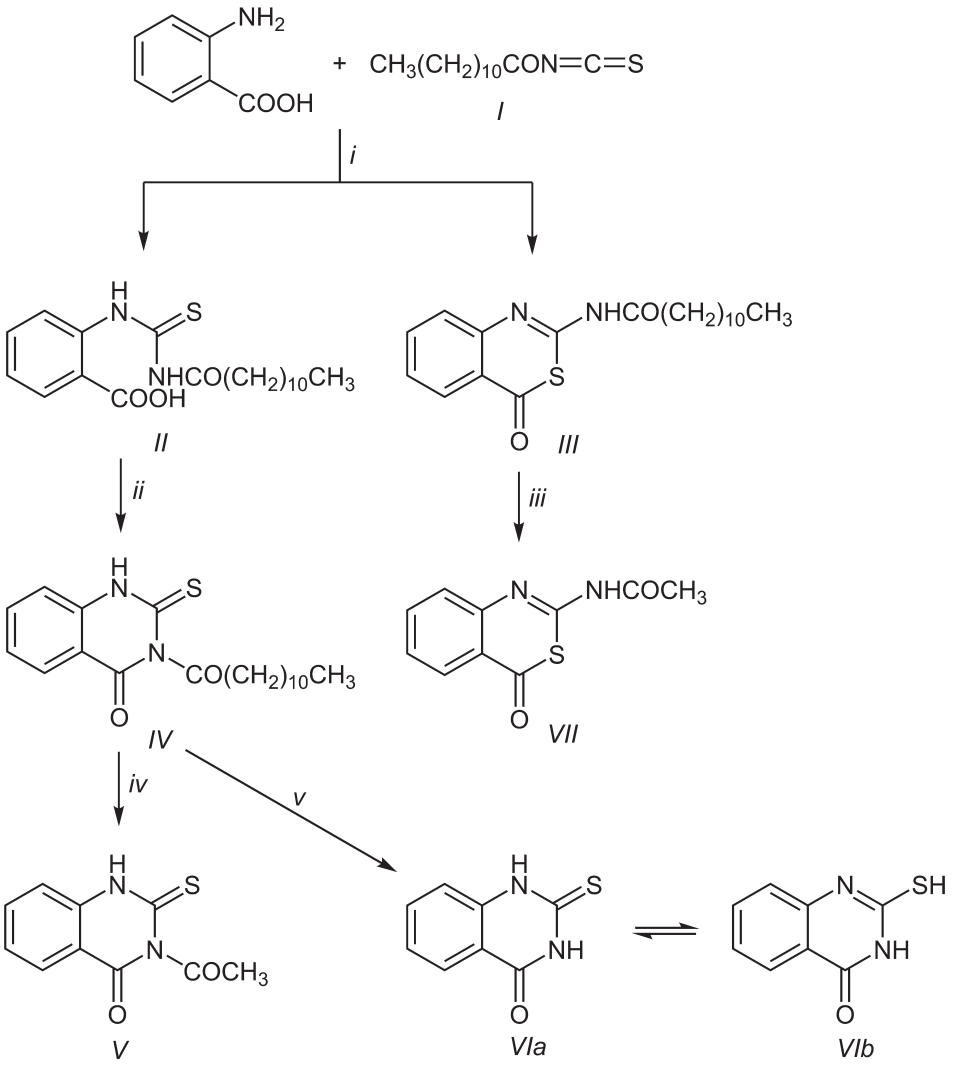

Fig. 1. Synthesis of compounds *II*–*VII*. Reaction conditions: *i*) MeCN, reflux; *ii*) Ac_2O, reflux, 1 h; *iii*) Ac_2O; *iv*) Ac_2O, reflux, 3 h; *v*) butan-1-ol, triethylamine, reflux.

Ac_2O afforded 3-acetyl-2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (*V*) with a good yield. In addition, 2-thioxo-2,3-dihydroquinazolin-4(1*H*)-one (*VI*) was obtained upon the heating of compound *IV* in butan-1-ol in the presence of a catalytic amount of triethylamine. On the other hand, *N*-(4-oxo-4*H*-benzo[*d*][1,3]thiazin-2-yl)acetamide (*VII*) was obtained upon the heating of benzothiazine derivative *III* in Ac_2O (Fig. 1).

The structures of compounds *II*–*VII* were confirmed from their microanalytical and spectral data. The IR spectra showed the absorption frequencies for N—H, C═O, C═N and C═S groups. ^{1}H NMR spectra displayed signals for aliphatic and aromatic protons as well as acidic OH, NH and SH protons in the downfield region that were exchangeable with D_2O. The structure of thiazine derivative *III* was based on the relatively high absorption value of the carbonyl group at 1721 cm^{-1} and the appearance of the fragment ion at m/z 162 in the mass spectrum corresponding to the benzothiazine moiety. Inspection of the ^{1}H NMR spectrum of *III* revealed the presence of two signals for NH protons exchangeable with D_2O (integration ratio of 85 : 15) integrated to one proton; this observation endorses the existence of compound *III* in DMSO-d_6 as an equilibrium mixture of tautomers *IIIa* and *IIIb*, respectively, in a ratio of approximately 6 : 1 as shown in Fig. 2. The ^{1}H NMR spectrum of compound *VI* revealed two broad singlets δ 12.66 and 12.42 exchangeable with D_2O corresponding to two NH groups. Moreover, an extra signal at δ 4.06 exchangeable with D_2O, corresponds to the SH proton. This confirms the existence of compound *VI* in DMSO-d_6 solution as thione–thiol tautomers *VIa* and *VIb* in the ratio of 74 : 26 (see Fig. 1). The mass spectra of the synthesised compounds revealed molecular ion peaks consistent with their proposed structures. The formation of the derivatives of thiazine *III* and quinazoline *IV* obviously proceeded via the cyclisation of thiourea derivative *II* by removing a molecule of water. Hence, the thiol tautomer of adduct *II* con-

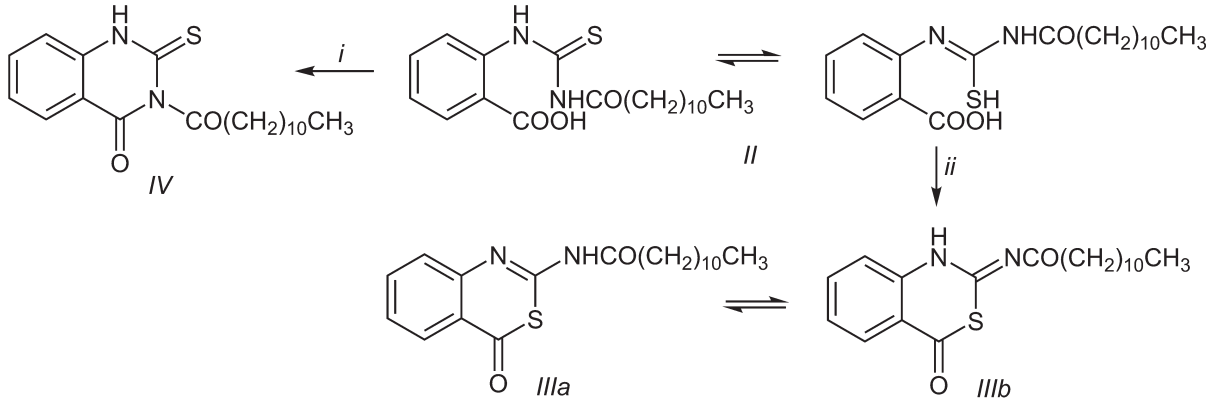

Fig. 2. Proposed mechanism for formation of compounds *II* and *III*. Reaction conditions: *i*) Ac_2O (loss of water molecule); *ii*) MeCN, reflux (loss of water molecule).

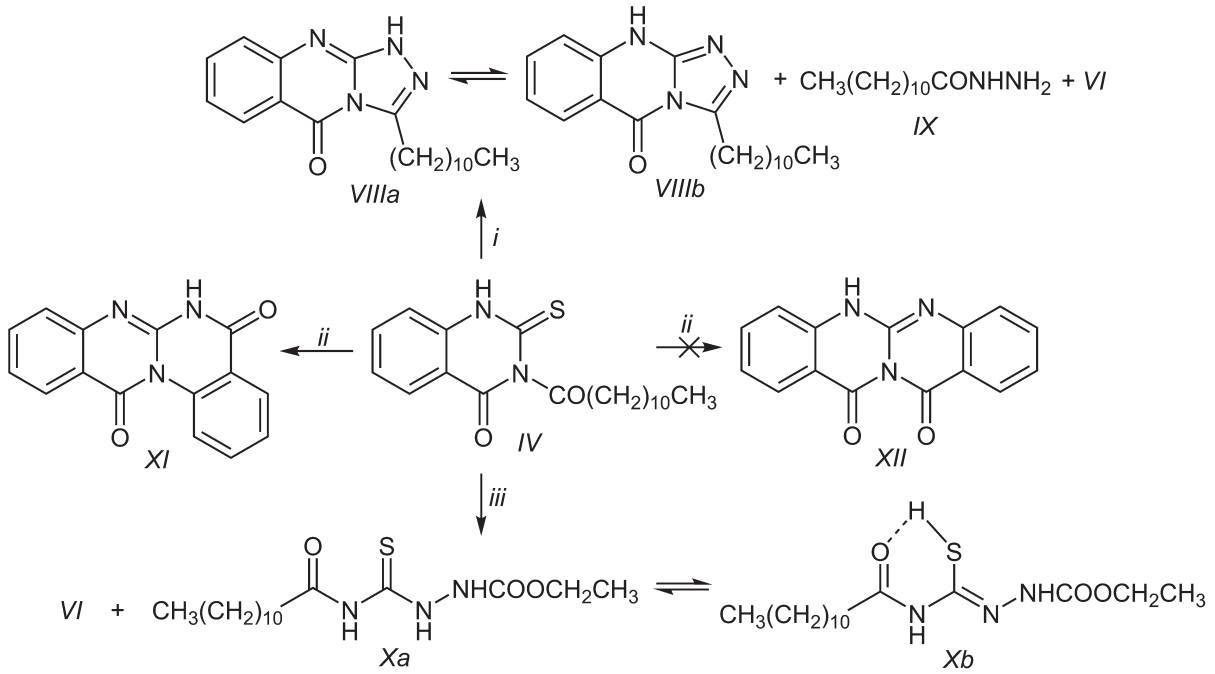

Fig. 3. Synthesis of compounds *VIII–XI*. Reaction conditions: *i*) hydrazine hydrate, butan-1-ol; *ii*) anthranilic acid, butan-1-ol, triethylamine; *iii*) ethyl carbazate, butan-1-ol, triethylamine.

tributes largely to the formation of compound *III*; in addition, compound *IV* was obtained from the thione tautomer of compound *II* as shown in Fig. 2.

The treatment of compound *IV* with hydrazine hydrate in butan-1-ol afforded a mixture of 3-undecyl-[1,2,4]triazolo[3,4-*b*]quinazolin-5(10*H*)-one (*VIII*), dodecanehydrazide (*IX*) and quinazoline *VI*. A similar treatment of *IV* with ethyl carbazate produced *VI* as a major product besides a minor amount of 4-dodecanoyl-1-ethoxycarbonylthiosemicarbazide (*X*) as depicted in Fig. 3. The heating of quinazoline *IV* and anthranilic acid in butan-1-ol under reflux in the presence of a few drops of triethylamine afforded 6*H*-quinazolino[3,2-*a*]quinazoline-5,12-dione (*XI*). The formation of the isomeric 5*H*-quinazolino [2,3-*b*]quinazoline-11,13-dione (*XII*) is excluded on the basis of its melting point (m.p. > 300 °C; Butler & Partridge, 1959; Shestakov et al., 2015). The reaction was accompanied by the release of gaseous H_2S, as detected by the change in colour to black of a paper soaked in lead acetate solution.

The IR spectra of compounds *VIII–XI* showed absorption bands corresponding to the N—H and C=O groups. The ^{1}H NMR spectra exhibited signals characteristic of aromatic and aliphatic protons. In addition, NH protons exchangeable with D_2O were observed in the downfield region. Inspection of the ^{1}H NMR spectrum of *VIII* revealed its existence as a mixture of tautomers *VIIIa* and *VIIIb* in the ratio of 43 : 57. The relatively high ratio of *VIIIb* is in agreement with the

Table 1. Characterisation data of newly prepared compounds

Compound	Formula	M_r	w_i(calc.)/% w_i(found)/%			Yield	M.p.
			C	H	N	%	°C
II	$C_{20}H_{30}N_2O_3S$	378.53	63.46	7.99	7.40	55	102–104
			63.38	7.81	7.12		
III	$C_{20}H_{28}N_2O_2S$	360.51	66.63	7.83	7.77	38	208–210
			66.42	7.65	7.46		
IV	$C_{20}H_{28}N_2O_2S$	360.51	66.63	7.83	7.77	88	153–155
			66.29	7.71	7.59		
V	$C_{10}H_8N_2O_2S$	220.25	54.53	3.66	12.72	76	228–230
			54.61	3.48	12.43		
VI	$C_8H_6N_2OS$	178.21	53.92	3.39	15.72	76	289–290[a]
			53.99	3.33	15.65		
VII	$C_{10}H_8N_2O_2S$	220.25	54.53	3.66	12.72	78	268–270
			54.28	3.44	12.61		
VIII	$C_{20}H_{28}N_4O$	340.46	70.56	8.29	16.46	41	195–197
			70.24	8.37	16.12		
IX	$C_{12}H_{26}N_2O$	214.35	67.24	12.23	13.07	26	104–106[b]
			66.96	12.42	12.76		
X	$C_{16}H_{31}N_3O_3S$	345.50	55.62	9.04	12.16	18	54–56
			55.47	8.77	11.87		
XI	$C_{15}H_9N_3O_2$	263.25	68.44	3.45	15.96	72	258–260[c]
			68.53	3.27	15.82		
XIII	$C_{19}H_{30}N_2O_2S$	350.52	65.10	8.63	7.99	76	145–147
			64.84	8.41	7.68		
XIV	$C_{19}H_{28}N_2OS$	332.50	68.63	8.49	8.42	78	108–110
			68.36	8.23	8.11		

a) Leistner et al. (1990) reported m.p. of 304–305 °C; *b*) El-Sayed and Khairou (2015) reported m.p. of 115–117 °C; *c*) Butler and Partridge (1959) reported m.p. of 255–255.5 °C.

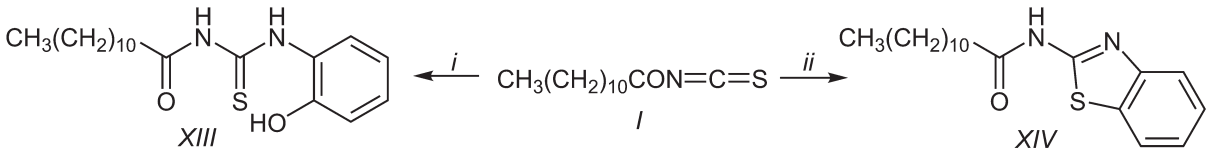

Fig. 4. Synthesis of compounds *XIII–XIV*. Reaction conditions: *i*) 2-aminophenol, MeCN; *ii*) 2-aminothiophenol, MeCN (loss of hydrogen sulfide molecule).

aromatic structure of the triazole ring. The ^{1}H NMR spectrum of *X* revealed an extra signal at δ 3.28 corresponding to the SH proton. This suggests the presence of *X* in the DMSO-d_6 solution as an equilibrium mixture of thione–thiol tautomers *Xa* and *Xb* in the ratio of 46 : 54. The relatively high ratio of thiol from *Xb* may be attributed to its stabilisation by the H-bond as shown in Fig. 3. The extra signal at δ 152.91 in the ^{13}C NMR spectrum corresponding to the C=N group is also supportive of thione–thiol tautomers *Xa* and *Xb*. Moreover, the mass spectral data of compounds *VIII–XI* are in accord with their proposed structures as they show the molecular ion peaks as well as some important fragmentation peaks. The formation of *VIII* and *XI* can be rationalised on the basis of the cyclocondensation of *IV* with hydrazine molecule or anthranilic acid, followed by the expulsion of dodecanoic acid with the latter. The formation of compound *X* is achieved by pyrimidine-ring cleavage under the reaction conditions (reagent and the high-boiling point butan-1-ol with triethylamine) (Okuda et al., 2010).

The reaction of *I* with 2-aminophenol and 2-aminothiophenol was also studied (Uher et al., 1983). 1-Dodecanoyl-3-(2-hydroxyphenyl)thiourea (*XIII*) was obtained upon the treatment of *I* with 2-aminophenol. On the other hand, *N*-(benzo[*d*]thiazol-2-yl)dodecanamide (*XIV*) was obtained when *I* was allowed to react with 2-aminothiophenol (Fig. 4). The formation of compound *XIV* was accompanied by the release of gaseous H_2S. The structures of *XIII* and *XIV* were assigned on the basis of the spectral data.

Conclusions

Dodecanoyl isothiocyanate was used in the synthesis of 3,1-benzothiazine, quinazoline, benzothiazole and thiourea derivatives bearing the dodecanoyl (lauroyl) group. The lipophilic character of this group (a hydrocarbon moiety) favours the permeation of these compounds through lipid barriers in the fungal cell

Table 2. Spectral data of newly prepared compounds

Compound	Spectral data
II	IR, $\tilde{\nu}$/cm^{-1}: 3413–2854 (br, O—H), 3242, 3138 (N—H), 3088, 3025 (H—C_{aryl}), 2921, 2852 (H—C_{alkyl}), 1713, 1683 (C═O), 1169 (C═S), 745 (δ_{4H}, benzene ring) ^{1}H NMR (DMSO-d_6), δ: 0.85 (t, 3H, CH_3, J = 6.0 Hz, J = 6.9 Hz), 1.16–1.25 (m, 16H, $CH_3(C\underline{H}_2)_8CH_2$), 1.54–1.56 (m, 2H, $(CH_2)_8C\underline{H}_2CH_2$), 2.44 (t, 2H, CH_2CO, J = 7.5 Hz, J = 7.2 Hz), 7.34 (t, 1H, J = 7.5 Hz, J = 7.8 Hz), 7.58 (t, 1H, J = 8.1 Hz, J = 7.8 Hz), 7.89 (dd, 1H, J = 2.1 Hz, J = 1.8 Hz), 8.09 (d, 1H, J = 7.8 Hz), 11.33, 12.94 (2brs, each 2H, 2 × NH, exchangeable), 13.30 (brs, 1H, OH, exchangeable) ^{13}C NMR (DMSO-d_6), δ: 14.39, 22.53, 24.75, 28.86, 29.13, 29.15, 29.31, 29.42, 29.46, 31.73, 36.15, 125.07, 126.54, 127.82, 130.78, 132.27, 138.41, 167.46 (C═O), 174.92 (C═O), 179.88 (C═S) MS, m/z (I_r/%): 378 (0) (M^+), 371 (0.4), 336 (0.3), 254 (0.7), 241(0.4), 198 (0.6), 183 (0.3), 155 (0.2), 138 (0.7), 128 (2), 114 (2.9), 72 (26), 59 (100)
III	IR, $\tilde{\nu}$/cm^{-1}: 3162 (N—H), 3068 (H—C_{aryl}), 2977, 2925, (H—C_{alkyl}), 1721 (C═O), 1630 (C═N), 757 (δ_{4H}, benzene ring) ^{1}H NMR (DMSO-d_6), δ: 0.85 (t, 3H, CH_3, J = 6.5 Hz), 1.18–1.24 (m, 16H, $CH_3(C\underline{H}_2)_8CH_2$), 1.56–1.57 (m, 2H, $(CH_2)_8C\underline{H}_2CH_2$), 2.44 (t, 2H, CH_2CO, J = 7.4 Hz), 7.43 (t, 1H, J = 7.8 Hz, J = 7.2 Hz), 7.68 (t, 1H, J = 7.2 Hz, J = 7.8 Hz), 7.86 (d, 1H, J = 7.8 Hz), 7.91 (d, 1H, J = 8.4 Hz); for *IIIa*: 9.54 (brs, 1H, NH, exchangeable); for *IIIb*: 8.88 (brs, 1H, NH, exchangeable) MS, m/z (I_r/%): 360 (0) (M^+), 267 (93) ([M· − C_6H_{13}]$^+$), 261 (22) ([M· − C_7H_{15}]$^+$), 247 (4) ([M· − C_8H_{17}]$^+$), 233 (21) ([M· − C_9H_{19}]$^+$), 219 (27) ([M· − $C_{10}H_{21}$]$^+$), 177 (36) ([M− $C_{11}H_{23}CO$]$^+$), 162 (100) ([M· − $C_{11}H_{23}CONH$]$^+$), 146 (28), 134 (26), 120 (56), 90 (49), 77 (31)
IV	IR, $\tilde{\nu}$/cm^{-1}: 3228, 3197 (N—H), 3059, 3010 (H—C_{aryl}), 2918, 2848 (H—C_{alkyl}), 1701, (C═O), 752 (δ_{4H}, benzene ring) ^{1}H NMR (DMSO-d_6), δ: 0.84 (t, 3H, CH_3, J = 5.4 Hz, J = 6.9 Hz), 1.14–1.23 (m, 16H, $CH_3(C\underline{H}_2)_8CH_2$), 1.54 (t, 2H, $(CH_2)_8C\underline{H}_2CH_2$, J = 6.3 Hz), 2.42 (t, 2H, CH_2CO, J = 7.5 Hz, J = 7.2 Hz), 7.51 (t, 1H, J = 7.2 Hz, J = 7.5 Hz), 7.59 (d, 1H, J = 7.8 Hz), 7.68 (t, 1H, J = 7.8 Hz, J = 7.5 Hz), 8.04 (d, 1H, J = 7.8 Hz), 11.81 (brs, 1H, NH, exchangeable) ^{13}C NMR (DMSO-d_6), δ: 14.38, 22.52, 24.74, 28.83, 29.07, 29.15, 29.25, 29.41, 31.72, 35.82, 119.85, 124.78, 127.44, 129.31, 136.79, 148.08, 153.39 (C═O), 174.23 (C═O), 185.03 (C═S) MS, m/z (I_r/%): 360 (44) (M^+), 345 (4) ([M· − CH_3]$^+$), 331 (28) ([M$^{+\cdot}$ − C_2H_5]$^+$), 317 (7) ([M· − C_3H_7]$^+$), 303 (6) ([M· − C_4H_9]$^+$), 289 (11) ([M· − C_5H_{11}]$^+$), 275 (8) ([M· − C_6H1_3]$^+$), 261 (4) ([M· − C_7H_{15}]$^+$), 247 (12) ([M· − C_8H_{17}]$^+$), 233 (46) ([M· − C_9H_{19}]$^+$), 220 (68) ([M· − $C_{10}H_{20}$]$^+$), 205 (14) ([M· − $C_{11}H_{23}$]$^+$), 192 (33), 177 (100), 145 (35), 120 (90), 90 (46), 57 (98)
V	IR, $\tilde{\nu}$/cm^{-1}: 3211, 3197 (N—H), 3062 H—C_{aryl}), 2918 (H—C_{alkyl}), 1700, 1657 (C═O), 756 (δ_{4H}, benzene ring) ^{1}H NMR (DMSO-d_6), δ:2.14 (s, 3H, CH_3CO), 7.52 (t, 1H, J = 7.2 Hz, J = 7.8 Hz), 7.59 (d, 1H, J = 8.4 Hz), 7.87 (t, 1H, J = 7.5 Hz, J = 8.4 Hz), 8.04 (d, 1H, J = 6.3 Hz), 11.88 (brs, 1H, NH, exchangeable) MS, m/z (I_r/%): 220 (40) (M^+), 221 (7) ([M· + 1]$^+$), 205 (9) ([M· − CH_3]$^+$), 192 (23) ([M· − CO]$^+$), 177 (100) ([M· − CHCO]$^+$), 162 (93), 159 (55), 145 (31), 120 (64), 90 (42), 55 (88)
VI	IR, $\tilde{\nu}$/cm^{-1}: 3218, 3122 (N—H), 3078, 3035 (H—C_{aryl}), 2944 (H—C_{alkyl}), 1690, (C═O), 1165 (C═S), 761 (δ_{4H}, benzene ring) ^{1}H NMR (DMSO-d_6), δ: 4.06 (brs, 1H, SH, exchangeable); 7.51 (t, 1H, J = 7.2 Hz, J = 7.5 Hz), 7.36 (d, 1H, J = 8.1 Hz), 7.72 (t, 1H, J = 8.4 Hz, J = 7.5 Hz), 7.92 (d, 1H, J = 7.8 Hz), 12.42, 12.66 (2brs, each 2H, 2 × NH, exchangeable) MS, m/z (I_r/%): 178 (12) (M^+), 177 (100) ([M − H]$^+$), 145 (43) ([M − SH]$^+$), 118 (23), 117 (29), 104 (86), 88 (33)
VII	IR, $\tilde{\nu}$/cm^{-1}: 3163 (N—H), 3063, 3005 (H—C_{aryl}), 2776 (H—C_{alkyl}), 1657 (C═O), 1582 (C═N), 765 (δ_{4H}, benzene ring) ^{1}H NMR (DMSO-d_6), δ: 2.14 (s, 3H, CH_3), 7.51 (t, 1H, J = 7.2 Hz, J = 7.8 Hz), 7.59 (d, 1H, J = 7.8 Hz), 7.87 (t, 1H, J = 7.2 Hz, J = 7.8 Hz), 8.04 (d, 1H, J = 8.4 Hz), 11.83 (brs, 1H, NH, exchangeable) MS, m/z (I_r/%): 220 (97) (M^+), 221 (10) ([M· + 1]$^+$), 222 (4) ([M· + 2]$^+$), 205 (8), 192 (6), 178 (100) ([M· − CH_2CO]$^+$), 177 (11) ([M· − CH_3CO]$^+$), 162 (97) ([M· − CH_3CONH]$^+$), 150 (84), 145 (59), 120 (94), 90 (78), 63 (36)
VIII	IR, $\tilde{\nu}$/cm^{-1}: 3384, 3281 (N—H), 3046 (H—C_{aryl}), 2951, 2920, 2851 (H—C_{alkyl}) 1714 (C═O), 1670, 1652 (C═N), 756 (δ_{4H}, benzene ring) ^{1}H NMR (DMSO-d_6), δ: 0.84 (t, 3H, CH_3, J = 7.2 Hz), 1.22–1.27 (m, 16H, $CH_3(C\underline{H}_2)_8CH_2$), 1.57–1.60 (m, 2H, $(CH_2)_8C\underline{H}_2CH_2$), 2.34 (t, 2H, CH_2CO, J = 7.5 Hz), 7.10 (t, 1H, J = 7.8 Hz, J = 6.9 Hz), 7.19 (d, 1H, J = 8.7 Hz), 7.58 (t, 1H, J = 8.4 Hz, J = 7.2 Hz), 7.86 (d, 1H, J = 8.1 Hz), for tautomer *VIIIa*: 12.32 (brs, 1H, NH, exchangeable); for tautomer *VIIIb*: 10.46 (brs, 1H, NH, exchangeable). ^{13}C NMR (DMSO-d_6), δ: 14.40, 22.54, 24.80, 29.08, 29.18, 29.29, 29.38, 29.47, 29.48, 31.75, 33.80, 117.13, 121.80, 124.42, 129.94, 134.95, 150.85, 152.85 (C═N), 159.87 (C═N), 172.82 (C═S) MS, m/z (I_r/%): 340 (47) (M^+), 341 (11) ([M· + 1]$^+$), 325 (4) ([M· − CH_3]$^+$), 311 (17) ([M· − C_2H_5]$^+$), 297 (17) ([M· − C_3H_7]$^+$), 283 (11) ([M· − C_4H_9]$^+$), 269 (37) ([M· − C_5H_{11}]$^+$), 255 (77) ([M· − C_6H_{13}]$^+$), 241 (16) ([M· − C_7H_{15}]$^+$), 227 (21) ([M· − C_8H_{17}]$^+$), 213 (100) ([M· − C_9H_{19}]$^+$), 187 (7), 145 (39), 130 (13), 76 (17)
IX	IR, $\tilde{\nu}$/cm^{-1}: 3316, 3292, 3179 (N—H), 2957, 2920, 2850 (H—C_{alkyl}) 1698 (C═O) ^{1}H NMR (DMSO-d_6), δ: 0.86 (t, 3H, CH_3, J = 6.3 Hz, J = 6.9 Hz), 1.24–1.27 (m, 16H, $CH_3(C\underline{H}_2)_8CH_2$), 1.47–1.49 (m, 2H, $(CH_2)_8C\underline{H}_2CH_2$), 1.97 (t, 2H, CH_2CO, J = 7.2 Hz, J = 7.8 Hz), 4.28 (brs, 2H, NH_2, exchangeable), 8.84 (brs, 1H, NH, exchangeable) MS, m/z (I_r/%): 214 (48) (M^+), 200 (18), 183 (100), 176 (73), 165 (23), 145 (56), 123 (87)

Table 2. (continued)

Compound	Spectral data
X	IR, $\tilde{\nu}$/cm^{-1}: 3328, 3288, 3243 (N—H), 2954, 2921, 2851 (H—C_{alkyl}), 1760 (C═O_{ester}), 1692 (C═O_{amide}), 1244 (C═S) ^{1}H NMR (DMSO-d_6), δ: 0.86 (t, 3H, CH_3, J = 5.7 Hz, J = 6.9 Hz), 1.13 (t, 3H, C$\underline{H}_3$CH_2O, J = 5.4 Hz, J = 6.9 Hz), 1.19–1.24 (m, 16H, CH_3(C$\underline{H}_2$)$_8$CH_2), 1.47–1.49 (m, 2H, (CH_2)$_8$C$\underline{H}_2$CH_2), 2.06 (t, 2H, CH_2CO, J = 7.8 Hz, J = 7.5 Hz), 3.28 (brs, 1H, SH, exchangeable), 4.03 (q, 2H, CH_3C$\underline{H}_2$O, J = 7.8 Hz, J = 6.9 Hz, J = 7.5 Hz), 8.86, 9.49, 13.10 (brs, 3H, 3 × NH, exchangeable) ^{13}C NMR (DMSO-d_6), δ: 14.38, 14.95, 22.54, 25.37, 25.43, 26.68, 28.67, 28.93, 28.96, 29.43, 31.73, 33.52, 60.79, 152.91 (C═N), 156.68 (C═O), 166.35 (C═O), 172.28 (C═S) MS, m/z (I_r/%): 345 (2) (M^+), 302 (7) ([$M^{\cdot}$ − C_3H_7]$^+$), 241 (22) ($C_{11}H_{23}CONCS^+$), 183 (100) ($C_{11}H_{23}CO^+$), 146 (37), 104 (86), 57 (94)
XI	IR, $\tilde{\nu}$/cm^{-1}: 3147 (N—H), 3081, 3043 (H—C_{aryl}), 1713, 1706 (C═O), 1628, 1599 (C═N), 756 (δ_{4H}, benzene ring) ^{1}H NMR (DMSO-d_6), δ: 7.41 (t, 1H, J = 7.2 Hz, J = 7.5 Hz), 7.48 (d, 1H, J = 8.1 Hz), 7.58 (t, 1H, J = 7.2 Hz, J = 7.5 Hz), 7.78–7.87 (m, 2H, H_{aryl}), 8.19 (d, 2H, J = 8.1 Hz), 9.20 (d, 1H, J = 9.0 Hz), 12.30 (brs, 1H, NH, exchangeable) MS, m/z (I_r/%): 263 (3) (M^+), 235 (23), ([$M^{+\cdot}$ − CO]$^+$), 173 (16), 118 (58), 104 (86), 88 (33), 67 (79), 51 (100)
XIII	IR, $\tilde{\nu}$/cm^{-1}: 3432 (O—H), 3377, 3213, 3181 (N—H), 3045 (H—C_{aryl}), 2953, 2920, 2850 (H—C_{alkyl}), 1665 (C═O), 1185 (C═S) ^{1}H NMR (DMSO-d_6), δ: 0.85 (t, 3H, CH_3, J = 6.0 Hz), 1.20–1.25 (m, 16H, CH_3(C$\underline{H}_2$)$_8$CH_2), 1.53–1.56 (m, 2H, (CH_2)$_8$C$\underline{H}_2$CH_2), 2.44 (t, 2H, CH_2CO, J = 7.8 Hz), 6.80 (t, 1H, J = 7.2 Hz, J = 8.7 Hz), 6.91 (d, 1H, J = 7.8 Hz), 7.04 (t, 1H, J = 8.1 Hz, J = 7.5 Hz), 8.50 (d, 1H, J = 7.8 Hz), 10.12 and 11.27 (2brs, each 2H, 2 × NH, exchangeable), 12.74 (brs, 1H, OH, exchangeable) MS, m/z (I_r/%): 350 (1.5) (M^+), 333 (0.7), 317 (24), 151 (15), 134 (100), 109 (23), 67 (33)
XIV	IR, $\tilde{\nu}$/cm^{-1}: 3254, 3211 (N—H), 3052 (H—C_{aryl}), 2918, 2851 (H—C_{alkyl}), 1695 (C═O), 754 (δ_{4H}, benzene ring) ^{1}H NMR (DMSO-d_6), δ: 0.84 (t, 3H, CH_3, J = 6.9 Hz, J = 6.3 Hz), 1.23–1.27 (m, 16H, CH_3(C$\underline{H}_2$)$_8$CH_2), 1.59–1.64 (m, 2H, (CH_2)$_8$C$\underline{H}_2$CH_2), 2.45 (t, 2H, CH_2CO, J = 7.2 Hz), 7.29 (t, 1H, J = 7.2 Hz), 7.42 (t, 1H, J = 6.9 Hz), 7.72 (d, 1H, J = 7.8 Hz), 7.95 (d, 1H, J = 7.5 Hz), 12.27 (brs, 1H, NH, exchangeable) ^{13}C NMR (DMSO-d_6), δ: 14.38, 22.53, 24.95, 28.93, 29.11, 29.15, 29.29, 29.41, 29.43, 31.71, 35.55, 120.86, 122.07, 123.84, 126.47, 131.85, 148.97, 158.33(C═N), 172.75 (C═S) MS, m/z (I_r/%): 332 (0) (M^+), 311 (34), 258 (43), 234 (60), 167 (43), 148 (37), 63 (46), 51 (100)

membrane, thereby appreciably altering the antimicrobial properties of the attached heterocycles (Hemdan et al., 2010). Moreover, as the chain-length of the acyl group is increased, the biological activity could be improved (Gažák et al., 2010; Hadj Salem et al., 2010).

References

Alagarsamy, V., & Pathak, U. S. (2007). Synthesis and antihypertensive activity of novel 3-benzyl-2-substituted-3*H*-[1,2,4]triazolo[5,1-*b*]quinazolin-9-ones. *Bioorganic & Medicinal Chemistry*, *15*, 3457–3462. DOI: 10.1016/j.bmc.2007.03.007.

Alagarsamy, V., Murugesan, S., Dhanabal, K., Murugan, M., & de Clercq, E. (2007). AntiHIV, antibacterial and antifungal activities of some novel 2-methyl-3-(substituted methylamino)-(3*H*)-quinazolin-4-ones. *Indian Journal of Pharmaceutical Sciences*, *69*, 304–307. DOI: 10.4103/0250-474x.33167.

Balzarini, J., Van Daele, I., Negri, A., Solaroli, N., Karlsson, A., Liekens, S., Gago, F., & Van Calenbergh, S. (2009). Human mitochondrial thymidine kinase is selectively inhibited by 3′-thiourea derivatives of β-thymidine: Identification of residues crucial for both inhibition and catalytic activity. *Molecular Pharmacology*, *75*, 1127–1136. DOI: 10.1124/mol.108.053785.

Barluenga, J., Tomás, M., Ballesteros, A., & López, L. A. (1994). A simple approach to pyrimidine and quinazoline derivatives by [4+2] cycloaddition of 1,3-diazadienes and enamines. *Heterocycles*, *37*, 1109–1120. DOI: 10.3987/com-93-s123.

Bukvić Krajačić, M., Perić, M., Smith, K. S., Ivezić Schönfeld, Z., Žiher, D., Fajdetić, A., Kujundžić, N., Schönfeld, W., Landek, G., Padovan, J., Jelić, D., Ager, A., Milhous, W. K., Ellis, W., Spaventi, R., & Ohrt, C. (2011). Synthesis, structure–activity relationship, and antimalarial activity of ureas and thioureas of 15-membered azalides. *Journal of Medicinal Chemistry*, *54*, 3595–3605. DOI: 10.1021/jm2001585.

Butin, A. V., Tsiunchik, F. A., Abaev, V. T., Gutnov, A. V., & Cheshkov, D. A. (2009). Aryl ring migration reaction in the synthesis of 2,4-diaryl-4*H*-3,1-benzothiazines. *Synthesis*, *2009*, 2616–2626. DOI: 10.1055/s-0029-1217399.

Butler, K., & Partridge, M. W. (1959). Cyclic amidines. Part VIII. Derivatives of 12*H*-6:7:12a-triazabenz[*a*]anthracene and 5a*H*-5:6:11a-triazanaphthacene. *Journal of Chemical Society*, *1959*, 1512–1521.

Canon, K. K. (1984). Japan Patent No. JP59197051. Tokyo, Japan: Japan Patent Office.

Chandrika, P. M., Yakaiah, T., Rao, A. R. R., Narsaiah, B., Reddy, N. C., Sridhar, V., & Rao, J. V. (2008). Synthesis of novel 4,6-disubstituted quinazoline derivatives, their anti-inflammatory and anti-cancer activity (cytotoxic) against U937 leukemia cell lines. *European Journal of Medicinal Chemistry*, *43*, 846–852. DOI: 10.1016/j.ejmech.2007.06.010.

Cohen, E., Klarberg, B., & Vaughan, J. R., Jr. (1960). Quinazolinone sulfonamides. A new class of diuretic agents. *Journal of the American Chemical Society*, *82*, 2731–2735. DOI: 10.1021/ja01496a020.

Ding, Q., Liu, X., Yu, J., Zhang, Q., Wang, D., Cao, B., & Peng, Y. (2012). Access to functionalized 4-benzylidene-4*H*-benzo[*d*][1,3]thiazines via tandem addition-cyclization/cross-coupling reactions. *Tetrahedron*, *68*, 3937–3941. DOI: 10.1016/j.tet.2012.03.098.

Ding, Q., Lin, Y., Ding, G., Liao, F., Sang, X., & Peng, Y. Y. (2013). New simple synthesis of ring-fused 4-alkyl-4*H*-3,1-benzothiazine-2-thiones: Direct formation from carbon disulfide and (*E*)-3-(2-aminoaryl)acrylates or (*E*)-3-(2-aminoaryl)acrylonitriles. *Beilstein Journal of Organic Chemistry*, *9*, 460–466. DOI: 10.3762/bjoc.9.49.

El-Bordany, E. A. (2012). Addition-cyclization of lauroyl isothiocyanate with hydrazine derivatives as a source of 1,2,4-triazoles. *Middle-East Journal of Scientific Research*, *11*, 266–271.

El-Hiti, G. A., Hussain, A., Hegazy, A. S., & Alotaibi, M. H. (2011). Thioxoquinazolines: synthesis, reactions and biological activities. *Journal of Sulfur Chemistry*, *32*, 361–395. DOI: 10.1080/17415993.2011.601417.

El-Sayed, R., & Khairou, K. S. (2015). Propoxylated fatty thiazole, pyrazole, triazole, and pyrrole derivatives with antimicrobial and surface activity. *Journal of Surfactants and Detergents*, *18*, 661–673. DOI: 10.1007/s11743-015-1684-8.

Fahmy, A. F., Ali, N., Abdelhamid, H., Shiba, S., & Hemdan, M. M. (2010). The utility of *p*-*N*-succinimidobenzoyl isothiocyanate in synthesis of benzoxazole, quinazoline, pyrimidine, 1,2,4-triazoline, 1,3-thiazolidine, and thiourea derivatives. *Phosphorus, Sulfur, and Silicon and the Related Elements*, *185*, 1536–1542. DOI: 10.1080/10426500903127557.

Gažák, R., Purchartová, K., Marhol, P., Živná, L., Sedmera, P., Valentová, K., Kato, N., Matsumura, H., Kaihatsu, K., & Křen, V. (2010). Antioxidant and antiviral activities of silybin fatty acid conjugates. *European Journal of Medicinal Chemistry*, *45*, 1059–1067. DOI: 10.1016/j.ejmech.2009.11.056.

Ghorab, M. M., Ismail, Z. H., Abdalla, M., & Radwan, A. A. (2013). Synthesis, antimicrobial evaluation and molecular modelling of novel sulfonamides carrying a biologically active quinazoline nucleus. *Archives of Pharmacal Research*, *36*, 660–670. DOI: 10.1007/s12272-013-0094-6.

Gimbert, C., & Vallribera, A. (2009). A straightforward synthesis of benzothiazines. *Organic Letters*, *11*, 269–271. DOI: 10.1021/ol802346r.

Grover, G., & Kini, S. G. (2006). Synthesis and evaluation of new quinazolone derivatives of nalidixic acid as potential antibacterial and antifungal agents. *European Journal of Medicinal Chemistry*, *41*, 256–262. DOI: 10.1016/j.ejmech.2005.09.002.

Gütschow, M., Schlenk, M., Gäb, J., Paskaleva, M., Alnouri, M. W., Scolari, S., Iqbal, J., & Müller, C. E. (2012). Benzothiazinones: A novel class of adenosine receptor antagonists structurally unrelated to xanthine and adenine derivatives. *Journal of Medicinal Chemistry*, *55*, 3331−3341. DOI: 10.1021/jm300029s.

Hadj Salem, J., Humeau, C., Chevalot, I., Harscoat-Schiavo, C., Vanderesse, R., Blanchard, F., & Fick, M. (2010). Effect of acyl donor chain length on isoquercitrin acylation and biological activities of corresponding esters. *Process Biochemistry*, *45*, 382–389. DOI: 10.1016/j.procbio.2009.10.012.

Hayao, S., Havera, H. J., Strycker, W. G., Leipzig, T. J., Kulp, R. A., & Hartzler, H. E. (1965). New sedative and hypotensive 3-substituted 2,4(1*H*,3*H*)-quinazolinediones. *Journal of Medicinal Chemistry*, *8*, 807–811. DOI: 10.1021/jm00330a017.

Hemdan, M. M., Fahmy, A. F., Ali, N. F., Hegazi, E., & Abd-Elhaleem, A. (2008). Synthesis of some new heterocycles derived from phenylacetyl isothiocyanate. *Chinese Journal of Chemistry*, *25*, 388–391. DOI: 10.1002/cjoc.200890074.

Hemdan, M. M. (2010). Synthesis and antimicrobial activities of some heterocyclic systems from 2-furoyl isothiocyanate. *Phosphorus, Sulfur, and Silicon and the Related Elements*, *185*, 620–627. DOI: 10.1080/10426500902893209.

Hemdan, M. M., Fahmy, A. F., & El-Sayed, A. A. (2010). Synthesis and antimicrobial study of 1,2,4-triazole, quinazoline and benzothiazole derivatives from 1-naphthoylisothiocyanate. *Journal of Chemical Res*earch, *34*, 219–221. DOI: 10.3184/030823410x12707543946812.

Hemdan, M. M., Fahmy, A. F. M., Aly, N. F., Hegazi, I. A., & El-Sayed, A. A. (2012). Utility of phthalimidoacyl isothiocyanate in synthesis of quinazolines, benzoxazoles, benzimidazoles, 1,2,4-triazoles, and oxatriazepines. *Phosphorus, Sulfur, and Silicon and the Related Elements*, *187*, 181–189. DOI: 10.1080/10426507.2011.597804.

Hemdan, M. M., & El-Sayed, A. A. (2015). Synthesis of some new heterocycles derived from novel 2-(1,3-dioxisoindolin-2-yl)benzoyl isothiocyanate. *Journal of Heterocyclic Chemistry*. DOI: 10.1002/jhet.2287. (in press)

Hemdan, M. M., & Abd El-Mawgoude, H. K. (2015a). Uses of 1-(3-cyano-4,5,6,7-tetrahydrobenzo[*b*]-thiophen-2-yl)-3-dodecanoylthiourea as a building block in the synthesis of fused pyrimidine and thiazine systems. *Chemical and Pharmaceutical Bulletin*, *63*, 450–456. DOI: 10.1248/cpb.c15-00047.

Hemdan, M. M., & Abd El-Mawgoude, H. K. (2015b). Synthesis and antimicrobial evaluation of thieno[2,3-*d*]-pyrimidine, thieno[2′,3′:4,5]pyrimido[1,2-*a*][1,3,5]triazine, thieno[2,3-*d*]-1,3-thiazine and 1,2,4-triazole systems. *Chemical and Pharmaceutical Bulletin*, *63*, 812–818. DOI: 10.1248/cpb.c15-00463.

Khalil, A. A., Abdel Hamide, S. G., Al-Obaid, A. M., & El-Subbagh, H. I. (2003). Substituted quinazolines, part 2. Synthesis and in-vitro anticancer evaluation of new 2-substituted mercapto-3*H*-quinazoline analogs. *Archiv der Pharmazie*, *336*, 95–103. DOI: 10.1002/ardp.200390011.

Kidwai, M., Kukreja, S., Rastogi, S., & Singhal, K. (2007). Microwave accelerated multicomponent synthesis for a novel scaffold of monastrol analogues. *Letters in Organic Chemistry*, *4*, 357–361. DOI: 10.2174/157017807781212085.

Laddha, S. S., & Bhatnagar, S. P. (2008). Rapid microwave-assisted solution phase synthesis of 6,8-disubstituted 2-phenyl-3-(substituted benzothiazol-2-yl)-4-[3*H*] quinazolinones as novel anticonvulsants. *Phosphorus, Sulfur, and Silicon and the Related Elements*, *183*, 2262–2273. DOI: 10.1080/10426500801957766.

Leistner, S., Michael Gütschow, M., & Stach, J. (1990). Mehrcyclische Azine mit Heteroatomen in 1- und 3-Stellung, 25. Mitt.: 2-Amino-4-oxo-4*H*-3,1-benzothiazine: Darstellung, Dimroth-Umlagerung zu 4-Oxo-2-thioxo-1,2,3,4-tetrahydrochinazolinen und MS/MS-Fragmentierung. *Archiv der Pharmazie*, *323*, 857–862. DOI: 10.1002/ardp.19903231009. (in German)

Maggio, B., Daidone, G., Raffa, D., Plescia, S., Mantione, L., Cutuli, V. M. C., Mangano, N. G., & Caruso, A. (2001). Synthesis and pharmacological study of ethyl 1-methyl-5-(substituted 3,4-dihydro-4-oxoquinazolin-3-yl)-1*H*-pyrazole-4-acetates. *European Journal of Medicinal Chemistry*, *36*, 737–742. DOI: 10.1016/s0223-5234(01)01259-4.

Mosaad, S. M., Mohammed, K. I., Ahmed, M. A., & Abdel-Hamide, S. G. (2004). Synthesis of certain new 6-iodoquin azolines as potential antitubercular agents. *Journal of Applied Sciences*, *4*, 302–307 DOI: 10.3923/jas.2004.302.307.

Obayashi, T., & Okawa, A. (2001). Japan Patent No. JP200125 3172. Tokyo, Japan: Japan Patent Office.

Okuda, K., Zhang, Y. X., Ohtomo, H., Hirota, T., & Sasaki, K. (2010). Polycyclic *N*-heterocyclic compounds. Part 62: Reaction of *N*-(quinazolin-4-yl)amidine derivatives with hydroxylamine hydrochloride and anti-platelet aggregation activity of the products. *Chemical and Pharmaceutical Bulletin*, *58*, 369–374. DOI: 10.1248/cpb.58.369.

Raffa, D., Edler, M. C., Daidone, G., Maggio, B., Merickech, M., Plescia, S., Schillaci, D., Bai, R., & Hamel, E.

(2004). Synthesis, cytotoxicity, and inhibitory effects on tubulin polymerization of a new 3-heterocyclo substituted 2-styrylquinazolinones. *European Journal of Medicinal Chemistry*, *39*, 299–304. DOI: 10.1016/j.ejmech.2003.12.009.

Roopan, S. M., Maiyalagan, T., & Khan, F. N. (2008). Solvent-free syntheses of some quinazolin-4(3*H*)-ones derivatives. *Canadian Journal of Chemistry*, *86*, 1019–1025. DOI: 10.1139/v08-149.

Schleiss, M., Eickhoff, J., Auerochs, S., Leis, M., Abele, S., Rechter, S., Choi, Y., Anderson, Y., Scott, G., Rawlinson, W., Michel, D., Ensminger, S., Klebl, B., Stamminger, T., & Marschall, M. (2008). Protein kinase inhibitors of the quinazoline class exert anti-cytomegaloviral activity in vitro and in vivo. *Antiviral Research*, *79*, 49–61. DOI: 10.1016/j.antiviral.2008.01.154.

Sharma, S. K., Wu, Y., Steinbergs, N., Crowley, M. L., Hanson, A. S., Casero, R. A., Jr., & Woster, P. M. (2010). (Bis)urea and (bis)thiourea inhibitors of lysine-specific demethylase 1 as epigenetic modulators. *Journal of Medicinal Chemistry*, *53*, 5197–5212. DOI: 10.1021/jm100217a.

Shestakov, A. S., Prezent, M. A., Zlatoustovskaya, E. O., Shikhaliev, K. S., Falaleev, A. V., & Sidorenko, O. E. (2015). Alkylation of 1,3-benzothiazin-4-one 2-oxo-, 2-arylimino-, and 2-thioxo derivatives. *Chemistry of Heterocyclic Compounds*, *51*, 370–376. DOI: 10.1007/s10593-015-1709-2.

Simerpreet, & Cannoo, D. S. (2013). Synthesis and biological evaluation of 1,3-thiazines – a review. *Pharmacophore*, *4*, 70–88.

Uher, M., Berkeš, D., Leško, J., & Floch, I. (1983). Reactions of carbonyl isothiocyanates with nucleophilic bifunctional reagents. *Collection of Czechoslovak Chemical Communications*, *48*, 1651–1658. DOI: 10.1135/cccc19831651.

Yadav, L. D. S., Rai, V. K., & Yadav, B. S. (2009). The first ionic liquid-promoted one-pot diastereoselective synthesis of 2,5-diamino-/2-amino-5-mercapto-1,3-thiazin-4-ones using masked amino/mercapto acids. *Tetrahedron*, *65*, 1306–1315. DOI: 10.1016/j.tet.2008.12.050.

Yavari, I., Nematpour, M., & Hossaini, Z. (2010). Ph_3P-mediated one-pot synthesis of functionalized 3,4-dihydro-2*H*-1,3-thiazines from *N*,*N*′-dialkylthioureas and activated acetylenes in water. *Monatshefte für Chemie – Chemical Monthly*, *141*, 229–232. DOI: 10.1007/s00706-009-0247-y.