J. Chem. Sci. Vol. 124, No. 5, September 2012, pp. 1043–1048.

Synthesis and antimicrobial activities of new oxime carbamates of 3-aryl-2-thioquinazolin-4(3H)-one

SURESH S PATIL[a,*], SWATI D JADHAV[a] and M B DESHMUKH[b]

[a]Organic Research Laboratory, Padmabhushan Dr. Vasantraodada Patil College, Tasgaon, Dist. Sangli 416 312, India

[b]Department of Chemistry, Shivaji University, Kolhapur 416 004, India

e-mail: sanyujapatil@yahoo.com

MS received 4 September 2011; revised 24 April 2012; accepted 11 May 2012

Abstract. S-alkylation of 3-aryl-2-thioquinazolin-4(3H)-one (**1**) with chloroacetone gave 2-(propanonyl thio)-3-arylquinazol-4(3H)ones (**2**). Further, the treatment of compound (**2**) with hydroxylamine hydrochloride gave the corresponding oximes (**3**) which on reaction with phenyl isocyanate in THF yielded corresponding oxime carbamates **4**. The synthesized compounds have been confirmed using IR and ^{1}H NMR, mass spectral data together with elemental analysis. All newly synthesized compounds have been tested for their antibacterial and antifungal activities.

Keywords. Thioquinazolinones; oximes; oxime carbamates; phenyl isocyanate; hydroxylamine hydrochloride.

1. Introduction

Natural products containing quinazolinone moiety possess a broad spectrum of biological activities,[1,2] especially antimicrobial,[3] antiulcer,[4] pesticidal,[5] antifungal,[6,7] insecticidal,[8] antibacterial,[9] anticonvulsant,[10,11] antithrombic,[12] antitubercular,[13] antitumour,[14] etc. In this paper, we report a new route for the synthesis of 2-thio-3-aryl derivatives of quinazolinone.

2. Experimental

All ^{1}H NMR spectra were scanned on a Bruker A-300 F-NMR spectrometer. IR spectra were recorded on a Perkin Elmer-783 spectrophotometer. All chemicals used were of AR grade and are used without further purification. Melting points are uncorrected and were measured on a DBK programmable melting point apparatus. Purity of the products was checked by TLC.

The starting compounds **1a–f** were prepared by reported method.[15]

2.1 *3-(4-methylphenyl)-2-[(2-oxopropyl)sulfanyl]quinazolin-4(3H)-one* (**2a**)

The compound **1a** (2.84 g, 0.01 mol) and chloroacetone (0.93 g, 0.01 mol) in dry acetone (10 ml), to which anhydrous potassium carbonate was added and reaction mixture refluxed for 18 h (monitored by TLC). The mixture was cooled and separated solid was extracted with 20 ml ether. After removal of ether under reduced pressure gave solid, which was recrystallized from ethanol to furnish **2a**; Yield: 70%; m.p. 100°C. (Found: C, 66.65; H, 4.95; N, 8.69 $C_{18}H_{16}O_2N_2S$ requires: C, 66.64; H, 4.97; N, 8.64%); IR (KBr) cm^{-1}: 1718 (C=O), 1680 (cyclic amide C=O), 1615(C=N); ^{1}H NMR ($CDCl_3$): δ 2.23 (3H, s, -$COCH_3$), 2.41 (3H, s, Ar-CH_3), 3.91 (2H, s, S-CH_2), 7.21–8.10 (8H, m, ArH) ppm; MS (m/z): 324(M^+), 309, 281, 267, 235(100%), 233, 91, 43; ^{13}C NMR: 23.7 (Ar-**C**H_3), 29.6 (**C**H_3-C=O), 37.4 (S-**C**H_2-C=O), 120.2 (C_9), 121.3 ($C_{2'}$ and $C_{6'}$), 122.5 (C_8), 127.9 (C_6), 128.8(C_5), 129.1 ($C_{1'}$), 129.4 ($C_{3'}$ and $C_{5'}$), 133.7 (C_7), 134.4 ($C_{4'}$), 147.3 (C_{10}), 162.3 (C_4), 164.0 (C_2), 202.1 (CH_3-**C**=O).

Compounds **2b** to **2f** were prepared by using same method.

2.2 *2-[2-(Hydroxyimino)propyl]sulfanyl-3-(4-methylphenyl)quinazolin-4(3H)-one* (**3a**)

To a mixture of compound **2a** (0.5 g, 0.0018 mol) and hydroxylamine hydrochloride (0.1 g, 0.0036 mol) in ethanol (10 ml), sodium hydroxide (1 g) was added slowly in a small portion at a time and constant stirring with cooling the reaction mixture. The same reaction mixture was refluxed further for about 10 min,

*For correspondence

cooled and then poured into dil. HCl (50 ml). The separated solid was filtered, washed with water, and recrystallized from ethanol, Yield: 87%, m. p. 268°C. (Found: C, 63.75; H, 5.09; N, 12.39 $C_{18}H_{17}O_2N_3S$ requires: C, 63.70; H, 5.05; N, 12.38%); IR(KBr)cm^{-1}: 3460–3340 (oxime -OH), 1672 (cyclic amide C=O), 1620 and 1612 (C=N)cm^{-1}; ^{1}H NMR: δ 2.12 (3H, s, -N=C-CH_3), 2.32 (3H, s, Ar-CH_3), 4.16 (2H, s, S-CH_2), 7.03–8.11(8H, m, Ar-H), 10.42 (1H, s, -OH) ppm; MS (m/z): 339(M^+), 324, 308, 248, 235(100%), 104, 91; ^{13}C NMR: 17.3, (**C**H_3-C=N), 24.3 (Ar-**C**H_3), 32.1 (S-**C**H_2-), 120.9 (C_9), 120.8 ($C_{2'}$ and $C_{6'}$), 121.7 (C_8), 127.2 (C_6), 128.8 (C_5), 129.2 ($C_{1'}$), 129.6 ($C_{3'}$ and $C_{5'}$), 134.0 (C_7), 134.1 ($C_{4'}$), 147.1 (C_{10}), 161.1 (C_4), 163.6 (C_2), 169.0 (**C**=N-OH).

Compounds **3b** to **3f** were prepared by operating same method.

2.3 *2-[2′-(O-phenylcarbamoylimino) propylidene thio] 3-(p-methylphenyl) quinazolin-4(3H)one* (**4a**)

The equimolar mixture of **3a** (0.20 g, 0.0006 mol) and phenylisocynate (0.07 g, 0.0006 mol) in THF (10 ml) was heated on a steam bath at 70°C for 2 h, cooled and the separated solid was filtered and recrystallized from ethanol, Yield: 90%, m. p. 235°C. (Found: C, 65.52; H, 4.82; N, 12.25 $C_{25}H_{22}O_3N_4S$ requires: C, 65.49; H, 4.84; N, 12.22%); IR(KBr) cm^{-1}: 1710 (carbamate C=O), 1676 (cyclic amide C=O), 1610 and 1612 (C=N) cm^{-1}; ^{1}H NMR: δ 2.15 (3H, s, -N=C-CH_3), 2.35 (3H, s, Ar-CH_3), 4.12(2H, s, S-CH_2), 7.20–8.11(13H, m, Ar-H), 8.61 (1H, s, -NH) ppm; MS (m/z): 458(M^+), 367, 366, 322(100%), 235, 223, 136, 91, 77; ^{13}C NMR: 23.1, (**C**H_3-C=N), 24.3 (Ar-**C**H_3), 24.9 (S-**C**H_2-), 119.9 (C_9), 121.5 ($C_{2''}$ and $C_{6''}$), 121.8 ($C_{2'}$ and $C_{6'}$), 122.7 (C_8),124.6 ($C_{4''}$), 127.2 (C_6), 128.4 (C_5), 127.2 ($C_{1'}$), 129.0 ($C_{3''}$ and $C_{5''}$), 129.3 ($C_{3'}$ and $C_{5'}$), 133.9 (C_7), 134.0 ($C_{4'}$), 135.8 ($C_{1''}$), 146.9 (C_{10}), 151.8 (O-**C**=O-NH), 161.1 (C_4), 163.2 (C_2), 164.5 (-**C**=N-O).

Compounds **4b** to **4f** were prepared by operating same method.

2.4 *Antimicrobial activity*

The antimicrobial screening of synthesized compounds was carried out by paper disc diffusion method at 100 ppm against Gram +ve bacteria *B. substilis, S. aureus* and Gram −ve bacteria like *E. coli, P. vulgaris*. The antifungal activity of the compounds was assayed using fungal species *Aspergillus niger* and *Phytophora.* Standard antibacterial streptomycin and antifungal griseofulvin were also screened under similar condition for comparison.

The results indicate that the compounds **2e**, **2f**, **3e**, **3f**, **4e** and **4f** exhibited good antimicrobial activity against above bacteria and fungal species, while the compounds **2d**, **3a**, **3d** and **4d** have moderate antimicrobial activity against both Gram +ve and −ve bacteria and fungal species (table 1).

The generalization can be made from these observations that the compounds with substituent groups like -Cl and -Br enhance the antimicrobial activity than the other substituted compounds.

2.5 *Analytical data of synthesized compounds*

2.5a *3-(2-Methylphenyl)-2-[(2-oxopropyl)sulfanyl] quinazolin-4(3H)-one* (**2b**): Yield: 76%; m.p. 100°C; (Found: C, 66.65; H, 4.95; N, 8.69 $C_{18}H_{16}O_2N_2S$ requires: C, 66.64; H, 4.97; N, 8.64%); IR (KBr) cm^{-1}: 1718 (C=O), 1676 (cyclic amide C=O), 1612(C=N); ^{1}H NMR ($CDCl_3$): δ 2.51 (3H, s, -$COCH_3$), 2.42 (3H, s, Ar-CH_3), 4.91 (2H, s, S-CH_2), 7.03–8.11(8H, m, Ar-H) ppm. ^{13}C NMR: 15.2 (Ar-**C**H_3), 29.6 (**C**H_3-C=O), 37.6 (S-**C**H_2-C=O), 120.1 (C_{10}), 122.2 ($C_{6'}$) 122.6 (C_8), 124.4 ($C_{4'}$), 125.8 ($C_{5'}$), 127.6 (C_6), 128.2($C_{3'}$), 128.9(C_5), 135.1($C_{2'}$), 135.6 ($C_{1'}$), 136.9 (C_7), 147.4 (C_9), 161.1 (C_4), 163.8 (C_2), 201.4 (CH_3-**C**=O).

2.5b *3-(3-Methylphenyl)-2-[(2-oxopropyl)sulfanyl] quinazolin-4(3H)-one* (**2c**): Yield: 81%; m.p. 145°C; (Found: C, 66.65; H, 4.95; N, 8.69 $C_{18}H_{16}O_2N_2S$ requires: C, 66.64; H, 4.97; N, 8.64%); IR (KBr) cm^{-1}: 1720 (C=O), 1674 (cyclic amide C=O), 1612(C=N); ^{1}H NMR ($CDCl_3$): δ, 2.3 (3H, s, -$COCH_3$), 2.5 (3H, s, Ar-CH_3), 4.0 (2H, s, S-CH_2), 7.1–8.0(8H, m, Ar-H) ppm. ^{13}C NMR: 23.7 (Ar-**C**H_3), 29.3 (**C**H_3-C=O), 36.9 (S-**C**H_2-C=O), 118.2($C_{6'}$), 121.1 (C_{10}), 122.1 (C_8), 123.4 ($C_{2'}$), 124.6 ($C_{4'}$), 128.2($C_{5'}$), 127.3 (C_6), 128.9 (C_5), 135.2 ($C_{1'}$), 138.8 ($C_{3'}$), 134.9 (C_7), 147.9 (C_9), 162.0 (C_4), 164.1 (C_2), 200.4 (CH_3-**C**=O).

2.5c *3-(4-Methoxyphenyl)-2-[(2-oxopropyl)sulfanyl] quinazolin-4(3H)-one* (**2d**): Yield: 78%; m.p. 168°C; (Found: C, 63.45; H, 4.67; N, 8.29 $C_{18}H_{16}O_3N_2S$ requires: C, 63.51; H, 4.74; N, 8.23%); IR (KBr) cm^{-1}: 1720 (C=O), 1676 (cyclic amide C=O), 1610(C=N); ^{1}H NMR ($CDCl_3$): δ 2.13 (3H, s, -$COCH_3$), 3.24 (3H, s, Ar-OCH_3), 3.80 (2H, s, S-CH_2), 7.21–8.12(8H, m, Ar-H) ppm. ^{13}C NMR: 29.9 (**C**H_3-C=O), 38.1 (S-**C**H_2-C=O), 56.7 (Ar-O**C**H_3), 114.4 ($C_{3'}$ and $C_{5'}$), 120.7 (C_{10}), 121.9 (C_8), 122.6($C_{2'}$ and $C_{6'}$), 125.3 ($C_{1'}$), 127.1

Table 1. Antimicrobial screening data of the compounds **2**, **3** and **4** (diameter of the zones of inhibition in mm).

Compounds	R	Bacteria				Fungi	
		E. coli	*P. valgaris*	*B. subtilis*	*S. aureus*	*Aspergillus niger*	*Phytophora* spp.
2a	p-CH_3	12	14	12	14	13	14
2b	o-CH_3	10	13	12	13	12	15
2c	m-CH_3	12	13	11	11	13	14
2d	p-OCH_3	16	15	18	17	17	18
2e	p-Cl	22	23	21	20	21	18
2f	p-Br	23	21	19	18	21	22
3a	p-CH_3	16	15	17	15	15	11
3b	o-CH_3	11	16	15	15	13	14
3c	m-CH_3	09	12	11	10	12	13
3d	p-OCH_3	17	19	16	17	19	17
3e	p-Cl	22	23	20	21	20	19
3f	p-Br	21	22	21	22	23	24
4a	p-CH_3	14	16	15	13	14	12
4b	o-CH_3	14	13	17	14	15	15
4c	m-CH_3	14	12	13	14	11	12
4d	p-OCH_3	18	19	16	18	17	19
4e	p-Cl	23	21	22	20	23	21
4f	p-Br	24	22	22	21	23	24
				Standards			
1	Streptomycin	24	23	22	23	–	–
2	Griseofulvin	–	–	–	–	25	23

Activity: Good: above 20 mm; moderate: 15–20 mm; low: below 15 mm.

(C_6), 128.2(C_5), 134.1 (C_7), 147.2 (C_9), 156.1 ($C_{4'}$), 162.3 (C_4), 163.2 (C_2), 201.5 (CH_3-**C**=O).

2.5d *3-(4-Chlorophenyl)-2-[(2-oxopropyl)sulfanyl] quinazolin-4(3H)-one* (**2e**): Yield: 75%; m.p. 180°C; (Found: C, 59.20; H, 3.84; N, 8.10 $C_{17}H_{13}O_2N_2SCl$ requires: C, 59.21; H, 3.80; N, 8.12%); IR (KBr) cm^{-1}: 1722 (C=O), 1681 (cyclic amide C=O), 1615(C=N); ^{1}H NMR ($CDCl_3$): δ 2.31 (3H, s, -$COCH_3$), 3.90 (2H, s, S-CH_2), 7.10–8.10(8H, m, ArH) ppm. ^{13}C NMR: 29.7 (**C**H_3-C=O), 37.8 (S-**C**H_2-C=O), 120.1 (C_{10}), 122.9 (C_8), 123.1($C_{2'}$ and $C_{6'}$), 127.8 (C_6), 129.1(C_5), 129.7 ($C_{4'}$), 129.2 ($C_{3'}$ and $C_{5'}$), 131.1 ($C_{1'}$), 134.1 (C_7), 148.6 (C_9), 162.3 (C_4), 163.2 (C_2), 201.5 (CH_3-**C**=O).

2.5e *3-(4-Bromophenyl)-2-[(2-oxopropyl)sulfanyl] quinazolin-4(3H)-one* (**2f**): Yield: 74%; m.p. 183°C, (Found: C, 52.44; H, 3.39; N, 7.24 $C_{17}H_{13}O_2N_2SBr$ requires: C, 52.45; H, 3.37; N, 7.20%); IR (KBr) cm^{-1}: 1716 (C=O), 1680 (cyclic amide C=O), 1612(C=N); ^{1}H NMR ($CDCl_3$): δ 2.11(3H, s, -$COCH_3$), 4.02 (2H, s, S-CH_2), 7.22–8.16(8H, m, ArH) ppm. ^{13}C NMR: 29.1 (**C**H_3-C=O), 37.1 (S-**C**H_2-C=O), 120.1 ($C_{4'}$), 121.3 (C_{10}), 122.1 (C_8), 122.8($C_{2'}$ and $C_{6'}$), 127.1 (C_6), 129.6(C_5), 130.9 ($C_{1'}$), 132.2 ($C_{3'}$ and $C_{5'}$), 134.3 (C_7), 147.2 (C_9), 161.3 (C_4), 162.9 (C_2), 200.5 (CH_3-**C**=O).

2.5f *2-[2-(Hydroxyimino)propyl]sulfanyl-3-(2-methylphenyl)quinazolin-4(3H)-one* (**3b**): Yield: 93%, m.p. 242°C; (Found: C, 63.72; H, 5.04; N, 12.37 $C_{18}H_{17}O_2N_3S$ requires: C, 63.70; H, 5.05; N, 12.38%); IR(KBr) cm^{-1}: 3500–3310 (oxime -OH), 1667 (cyclic amide C=O), 1618 and 1610 (C=N) cm^{-1}; ^{1}H NMR: δ 2.15 (3H, s, -N=C-CH_3), 2.30 (3H, s, Ar-CH_3), 4.10 (2H, s, S-CH_2), 7.12–8.13(8H, m, Ar-H), 10.20 (1H, s, -OH) ppm. ^{13}C NMR: 16.2 (Ar-**C**H_3), 22.6 (**C**H_3-C=N), 25.6 (S-**C**H_2-C=N), 121.1 (C_{10}), 121.2 ($C_{6'}$), 121.8(C_8), 124.1 ($C_{4'}$), 126.7 ($C_{5'}$), 127.3 (C_6), 128.6(C_5), 129.1($C_{3'}$), 134.6 (C_7), 134.7($C_{2'}$), 135.1 ($C_{1'}$), 147.2 (C_9), 161.0 (C_4), 164.2 (C_2), 165.2 (**C**=N-OH).

2.5g *2-[2-(Hydroxyimino)propyl]sulfanyl-3-(3-methylphenyl)quinazolin-4(3H)-one* (**3c**): Yield: 90%, m. p. 246°C; (Found: C, 63.74; H, 5.05; N, 12.35 $C_{18}H_{17}O_2N_3S$ requires: C, 63.70; H, 5.05; N, 12.38%); IR(KBr) cm^{-1}: 3495–3362 (oxime -OH), 1670 (cyclic amide C=O), 1622 and 1611 (C=N) cm^{-1}; ^{1}H NMR: δ 2.20 (3H, s, -N=C-CH_3), 2.25 (3H, s, Ar-CH_3), 4.12 (2H, s, S-CH_2), 6.90–8.05(8H, m, Ar-H), 10.30 (1H, s, -OH) ppm. ^{13}C NMR: 22.7 (**C**H_3-C=N), 24.3 (Ar-**C**H_3), 25.3 (S-**C**H_2-C=N), 119.2($C_{2'}$), 120.8 (C_{10}), 121.3 ($C_{2'}$), 122.16 (C_8), 123.9 ($C_{4'}$), 127.5 (C_6), 127.8

(C_5), 128.7($C_{3'}$), 133.2 ($C_{1'}$), 134.3 (C_7), 138.2 ($C_{5'}$), 147.2 (C_9), 162.0 (C_4), 164.2 (C_2), 165.4 (**C**=N-OH).

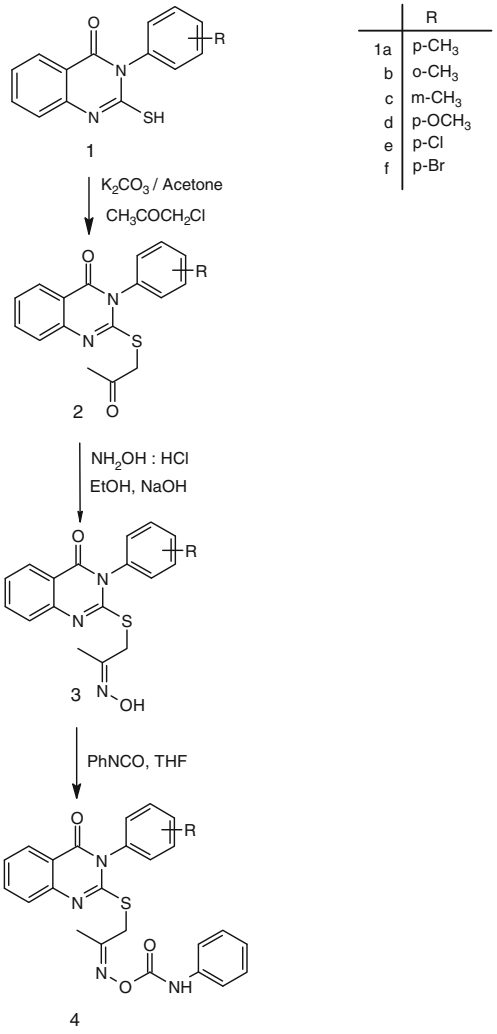
2.5h *2-[2-(Hydroxyimino)propyl]sulfanyl-3-(4-methoxyphenyl)quinazolin-4(3H)-one* (**3d**): Yield: 90%, m. p. 250°C; (Found: C, 60.85; H, 4.87; N, 11.87 $C_{18}H_{17}O_3N_3S$ requires: C, 60.83; H, 4.82; N, 11.82%); IR(KBr) cm^{-1}: 3445–3310 (oxime -OH), 1668(cyclic amide C=O), 1620 and 1614 (C=N) cm^{-1}; ^{1}H NMR: δ 2.22 (3H, s, -N=C-CH_3), 3.45 (3H, s, Ar-OCH_3), 4.00 (2H, s, S-CH_2), 7.10–8.20(8H, m, Ar-H), 10.62 (1H, s, -OH) ppm. ^{13}C NMR: 22.9 (**C**H_3-C=N), 26.1 (S-**C**H_2-C=N), 55.8 (Ar-O**C**H_3), 115.1 ($C_{3'}$ and $C_{5'}$), 121.2 (C_{10}), 121.6 ($C_{2'}$ and $C_{6'}$), 122.2 (C_8), 125.1 ($C_{1'}$), 127.4 (C_6), 127.8(C_5), 133.5 (C_7), 146.1 (C_9), 155.2 ($C_{4'}$), 160.8 (C_4), 164.1 (C_2), 164.9 (**C**=N-OH).

2.5i *2-[2-(Hydroxyimino)propyl]sulfanyl-3-(4-chlorophenyl)quinazolin-4(3H)-one* (**3e**): Yield: 84%, m. p. 248°C; (Found: C, 56.77; H, 3.90; N, 11.64 $C_{17}H_{14}O_2N_3SCl$ requires: C, 56.74; H, 3.92; N, 11.68%); IR(KBr) cm^{-1}: 3483–3312 (oxime -OH), 1665 (cyclic amide C=O), 1618 and 1614 (C=N) cm^{-1}; ^{1}H NMR: δ 2.25 (3H, s, -N=C-CH_3), 4.20 (2H, s, S-CH_2), 7.11–8.21(8H, m, Ar-H), 10.50 (1H, s, -OH) ppm. ^{13}C NMR: 23.1 (**C**H_3-C=N), 25.5 (S-**C**H_2-C=N), 122.3 (C_{10}), 122.8($C_{2'}$ and $C_{6'}$), 122.8 (C_8), 127.4 (C_6), 129.0(C_5), 129.8 ($C_{3'}$ and $C_{5'}$), 130.1 ($C_{4'}$), 130.7 ($C_{1'}$), 133.7 (C_7), 148.1 (C_9), 162.6 (C_4), 164.1 (C_2), 165.4 (**C**=N-OH).

2.5j *2-[2-(Hydroxyimino)propyl]sulfanyl-3-(4-bromophenyl)quinazolin-4(3H)-one* (**3f**): Yield: 87%, m. p. 252°C; (Found: C, 50.54; H, 3.47; N, 10.36 $C_{17}H_{14}O_2N_3SBr$ requires: C, 50.50; H, 3.49; N, 10.39%); IR(KBr) cm^{-1}: 3500–3292 (oxime -OH), 1667 (cyclic amide C=O), 1615 and 1610 (C=N) cm^{-1}; ^{1}H NMR: *δ* 2.22 (3H, s, -N=C-CH_3), 2.31 4.20 (2H, s, S-CH_2), 7.02–8.25(8H, m, Ar-H), 10.64 (1H, s, -OH) ppm. ^{13}C NMR: 22.9 (**C**H_3-C=N), 25.1 (S-**C**H_2-C=N), 121.9 (C_8), 122.1 (C_{10}), 122.9($C_{2'}$ and $C_{6'}$), 127.2 (C_6), 128.3 (C_5), 129.3 ($C_{3'}$ and $C_{5'}$), 130.2 ($C_{1'}$), 133.1 (C_7), 138.9 ($C_{4'}$), 147.8 (C_9), 161.2 (C_4), 164.0 (C_2), 164.3 (**C**=N-OH).

2.5k *2-[2′-(O-phenylcarbamoylimino) propylidene thio] 3-(2-methylphenyl) quinazolin-4(3H)one* (**4b**): Yield: 82%, m. p. 245°C; (Found: C, 65.50; H, 4.85; N, 12.21 $C_{25}H_{22}O_3N_4S$ requires: C, 65.49; H, 4.84; N, 12.22%); IR(KBr) cm^{-1}: 1713 (carbamate C=O), 1672(cyclic amide C=O), 1611 and 1614 (C=N) cm^{-1}; ^{1}H NMR: δ 2.10 (3H, s, -N=C-CH_3), 2.30(3H, s, Ar-CH_3), 4.10(2H, s, S-CH_2), 7.21–8.03(13H, m, Ar-H), 8.82(1H, s,-NH) ppm. ^{13}C NMR: 16.3 (Ar-**C**H_3), 22.1, (**C**H_3-C=N), 24.6 (S-**C**H_2-), 120.9 (C_{10}), 121.2 ($C_{6'}$), 121.3 ($C_{2''}$ and $C_{6''}$), 121.9 (C_{10}), 122.9 (C_8), 124.1 ($C_{4''}$), 124.3 ($C_{4'}$), 126.3 ($C_{5'}$), 127.3 (C_6), 128.6 (C_5), 129.2 ($C_{3'}$), 129.4 ($C_{3''}$ and $C_{5''}$), 133.8 (C_7), 134.8 ($C_{2'}$), 135.2 ($C_{1'}$), 135.9 ($C_{1''}$), 147.4 (C_9), 151.6 (O-**C**=O-NH), 161.0 (C_4), 163.1 (C_2), 164.7 (-**C**=N-O).

2.5l *2-[2′-(O-phenylcarbamoylimino) propylidene thio] 3-(3-methylphenyl) quinazolin-4(3H)one* (**4c**): Yield: 83%, m. p. 238°C; (Found: C, 65.55; H, 4.80; N, 12.27 $C_{25}H_{22}O_3N_4S$ requires: C, 65.49; H, 4.84; N, 12.22%); IR(KBr) cm^{-1}: 1715 (carbamate C=O), 1675 (cyclic amide C=O), 1610 and 1615 (C=N) cm^{-1}; ^{1}H NMR: δ 2.20 (3H, s, -N=C-CH_3), 2.30 (3H,

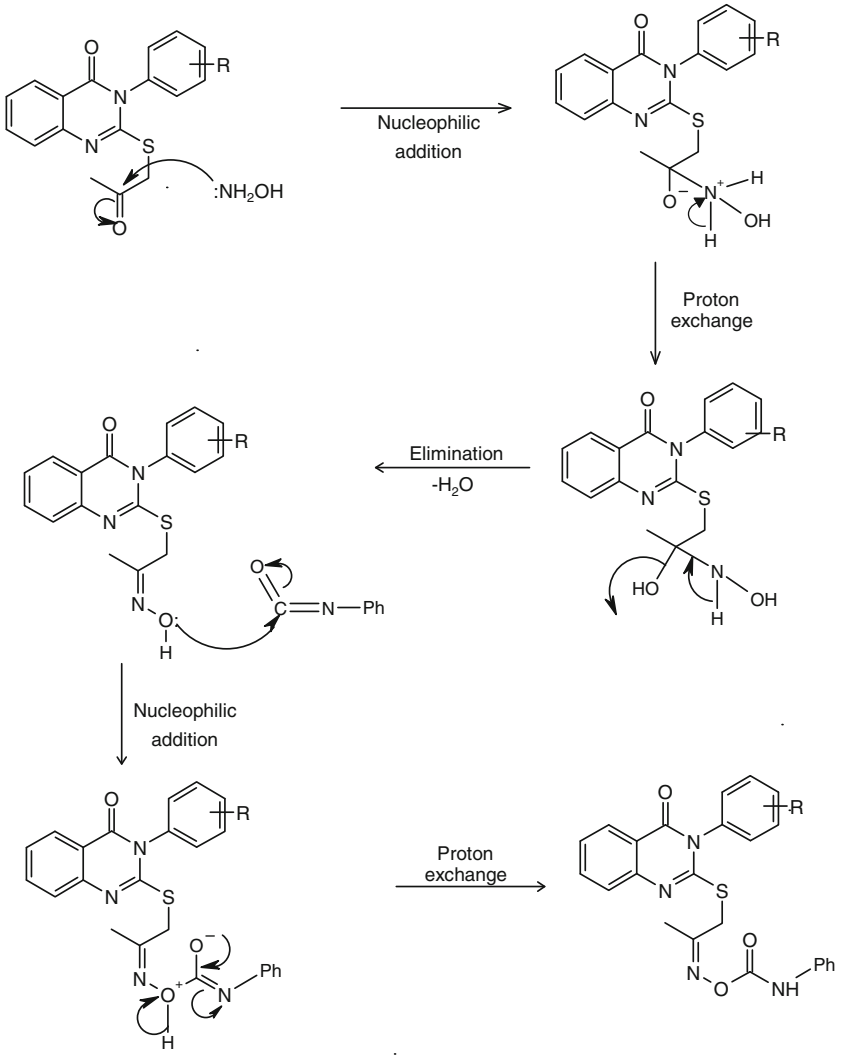


Scheme 1. Synthesis of oximes and oxime carbamates 3-aryl-2-thioquinazolin-4(3H)-one.

s, Ar-CH_3), 4.20(2H, s, S-CH_2), 7.03–8.12(13H, m, Ar-H), 8.65 (1H, s, -NH) ppm. ^{13}C NMR: 22.5, (**C**H_3-C=N), 24.9 (S-**C**H_2-), 26.3 (Ar-**C**H_3), 118.5 ($C_{6'}$), 120.8 (C_{10}), 120.9 (C_{10}), 121.5 ($C_{2'}$), 121.6 ($C_{2''}$ and $C_{6''}$), 122.6 (C_8), 124.1 ($C_{4'}$), 124.4 ($C_{4''}$), 127.7 (C_6), 128.2 (C_5), 128.7 ($C_{5'}$), 129.1 ($C_{3''}$ and $C_{5''}$), 133.2 ($C_{1'}$), 133.6 (C_7), 135.8 ($C_{1''}$), 138.3 ($C_{3'}$), 147.2 (C_9), 151.9 (O-**C**=O-NH), 160.8 (C_4), 163.0 (C_2), 164.6 (-**C**=N-O).

2.5m *2-[2′-(O-phenylcarbamoylimino) propylidene thio] 3-(4-methoxyphenyl) quinazolin-4(3H)one* (**4d**): Yield: 85%, m. p. 220°C; (Found: C, 63.25; H, 4.69; N, 11.85 $C_{25}H_{22}O_4N_4S$ requires: C, 63.28; H, 4.67; N, 11.81%); IR(KBr) cm^{-1}: 1712(carbamate C=O), 1673 (cyclic amide C=O), 1616 and 1610 (C=N) cm^{-1}; ^{1}H NMR: δ 2.22 (3H, s, -N=C-CH_3), 3.35 (3H, s, Ar-OCH_3), 4.20(2H, s, S-CH_2), 7.21–8.14(13H, m, Ar–H), 8.65 (1H, s, -NH) ppm. ^{13}C NMR: 22.8, (**C**H_3-C=N), 25.3 (S-**C**H_2-), 54.8 (Ar-O**C**H_3), 115.3 ($C_{3'}$ and $C_{5'}$), 121.9 (C_{10}), 122.3 ($C_{2''}$ and $C_{6''}$), 123.2 ($C_{2'}$ and $C_{6'}$), 123.7 (C_8), 125.2 ($C_{4''}$), 125.2 ($C_{1'}$), 126.2 (C_6), 127.4 (C_5), 129.7 ($C_{3''}$ and $C_{5''}$), 133.4 (C_7), 135.3 ($C_{1''}$), 147.9 (C_9), 152.3 (O-**C**=O-NH), 156.9 ($C_{4'}$), 160.1 (C_4), 163.1 (C_2), 165.5 (-**C**=N-O).

2.5n *2-[2′-(O-phenylcarbamoylimino) propylidene thio] 3-(4-chlorophenyl) quinazolin -(3H)one* (**4e**): Yield: 81%, m. p. 245°C; (Found: C, 60.21; H, 4.04; N, 11.75 $C_{24}H_{19}O_3N_4SCl$ requires: C, 60.19; H, 4.00; N, 11.70%); IR(KBr) cm^{-1}: 1718 (carbamate C=O), 1680 (cyclic amide C=O), 1620 and 1615 (C=N) cm^{-1}; ^{1}H NMR: δ 2.17 (3H, s, -N=C-CH_3), 4.00 (2H, s, S-CH_2), 7.02–8.14(13H, m, Ar-H), 8.72(1H, s, -NH) ppm. ^{13}C NMR: 23.7 (**C**H_3-C=N), 25.1 (S-**C**H_2-), 121.4 ($C_{2''}$ and $C_{6''}$), 122.2 (C_{10}), 123.8 ($C_{2'}$ and $C_{6'}$), 123.9 (C_8), 124.9 ($C_{4''}$), 127.2 (C_5), 127.8 (C_6), 129.2 ($C_{3''}$ and



Scheme 2. Proposed mechanism for the synthesis of oximes and oxime carbamates 3-aryl-2-thioquinazolin-4(3H)-one.

$C_{5''}$), 129.3 ($C_{3'}$ and $C_{5'}$), 130.2 ($C_{1'}$), 130.9 ($C_{4'}$), 133.9 (C_7), 135.1 ($C_{1''}$), 147.4 (C_9),151.2 (O-**C**=O-NH), 160.6 (C_4), 164.0 (C_2), 164.7 (-**C**=N-O).

2.5o *2-[2′-(O-phenylcarbamoylimino) propylidene thio] 3-(4-bromophenyl) quinazolin-4(3H)one* (**4f**): Yield: 78%, m. p. 271°C; (Found: C, 55.09; H, 3.65; N, 10.75 $C_{24}H_{19}O_3N_4SBr$ requires: C, 55.07; H, 3.66; N, 10.70%); IR(KBr) cm^{-1}: 1720 (carbamate C=O), 1679 (cyclic amide C=O), 1615 and 1619 (C=N) cm^{-1}; ^{1}H NMR: δ 2.20 (3H, s, -N=C-CH_3), 3.90(2H, s, S-CH_2), 7.12–8.04(13H, m, Ar-H), 8.52 (1H, s, -NH) ppm. ^{13}C NMR: 23.2, (**C**H_3-C=N), 24.8 (S-**C**H_2-), 120.3 (C_{10}), 121.1 ($C_{2?}$ and $C_{6''}$), 123.2 ($C_{2'}$ and $C_{6'}$), 123.5 (C_8), 124.7 ($C_{4''}$), 127.6 (C_6), 126.9 (C_5), 128.9 ($C_{3''}$ and $C_{5''}$), 129.1 ($C_{3'}$ and $C_{5'}$), 130.0 ($C_{1'}$), 120.4 ($C_{4'}$), 133.6 (C_7), 134.9 ($C_{1''}$), 147.6 (C_9), 150.8 (O-**C**=O-NH), 160.2 (C_4), 163.8 (C_2), 164.2 (-**C**=N-O).

3. Results and discussion

3-Aryl-2-thioquinazolin-4(3H)-one **1a–f** were used as a key starting material for the synthesis of oximes **3a–f** and oxime carbamates **4a–f** (scheme 1). First, 3-aryl-2-thioquinazolin-4(3H)-one **1a–f** were S-alkylated with chloroacetone in the presence of catalytic amount of potassium carbonate to give 2-(propanonyl thio)-3-arylquinazol-4(3H)ones **2a–f**. The formation compounds **2** have been explained by the appearance of bands at 1716–1722 cm^{-1} due to acyclic >C=O in IR spectrum and two singlet encountered at δ, 2 to 3 and 3 to 4 due to the -$COCH_3$ and –S-CH_2 in the ^{1}H NMR spectrum, respectively. All compounds are obtained in high purity with good yield.

Compounds **2** on nucleophilic addition of hydroxylamine hydrochloride followed by elimination of water furnished oximes **(3)** (scheme 2). The formation of oximes **3** have been established by the appearance of bands at 3500–3292 cm^{-1} and disappearance of bands at 1716–1722 cm^{-1} in its IR spectrum due to –OH of and acyclic carbonyl, respectively. The formation of **3** were also supported by observing additional down field singlets at δ, 10.4–10.7 ppm due to -OH protons in ^{1}H NMR spectrum.

The compounds **3** were transformed into their corresponding oxime carbamates **4** by reacting them with phenyl isocyanate in THF. The disappearance of IR bands at 3500–3292 cm^{-1} and ^{1}H NMR signals due to -OH protons confirmed their formation.

4. Conclusion

In this work, we have reported new oxime carbamate derivatives of 3-Aryl-2-thioquinazolin-4(3H)-one which are characterized by IR, PMR and ^{13}C NMR spectral analysis. Synthesized compounds are screened for their antifungal and antibacterial activity. These compounds show good activity against Gram +ve and −ve bacteria and fungal species.

References

1. Deshmukh M B, Patil S, Patil S S and Jadhav S D 2010 *Indian J. Pharm. Sci.* **72** 500
2. Ammar Y A, El-Sharief A M Sh, Zahran M A, Ali A H and El-Gaby M S A 2001 *Molecules* **6** 267
3. El-Sharief A M Sh, Ammar Y A, Zahram M A and Ali A H 2002 *J. Chem. Res.* **5** 205
4. Patil A, Ganguly S and Suran S 2010 *J. Chem. Sci.* **22** 443
5. Sen Gupta A K and Pandey A K 1989 *Pesticide Sci.* **26** 41
6. Bennur S C, Talawar M B, Laddi U V, Somannavar Y S, Badigear V V and Virupakshaiah H M 1997 *Indian J. Heterocycl. Chem.* **7** 39
7. Ghorab M M 2000 *Farmaco* **55** 249
8. Singh T, Sharma S, Kishore V and Shrivastava K A 2006 *Indian J. Chem.* **45B** 2558
9. Singh S, Dave U and Parikh A R 1994 *J. Indian Chem. Soc.* 159
10. Parmar S S, Chaturvedi A K, Chaudhari A and Brumlene S J 1974 *J. Pharm. Sci.* **63** 356
11. Ghany A E A and Mohammed H A W 2003 *Acta. Pharm.* **53** 127
12. Demer J P, Sulsky R and Klaubert D H 1989 *J. Heterocycl. Chem.* **26** 1535
13. Kunes J, Bazant J, Pour M, Waisser K, Slosarek M and Janota J 2000 *Farmaco* **55** 725
14. Deetz M J, Malerich J P, Beatty A M and Smith B D 2001 *Tet. Lett.* **42** 1851
15. Deshmukh M B, Deshmukh D S and Shirke S D 1997 *J. Indian Chem. Soc.* **74** 422