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AYSEL GÜRSOY

BANU ÜNAL

NİLGÜN KARALI

GÜLTEN ÖTÜK

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Synthesis, Characterization and Primary Antimicrobial Activity Evaluation of 3-Phenyl-6-methyl-4(3H)-quinazolinone-2-yl-mercaptoacetic Acid Arylidenehydrazides

Aysel GÜRSOY[1*], Banu ÜNAL[1], Nilgün KARALI[1], Gülten ÖTÜK[2]
[1] *İstanbul University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, 34116 Beyazıt, İstanbul-TURKEY*
e-mail: ayselgursoy@yahoo.com
[2] *İstanbul University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, 34116 Beyazıt, İstanbul-TURKEY*

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3-Phenyl-6-methyl-4(3H)-quinazolinone-2-yl-mercaptoacetic acid hydrazide (**3**) was reacted with substituted aldehydes in absolute ethanol to obtain a new series, 3-phenyl-6-methyl-4(3H)-quinazolinone-2-yl-mercaptoacetic acid arylidenehydrazides (**4a-q**). The structures of **4a-q** were elucidated by elemental analyses and from spectrometric (UV, IR, ^{1}H-NMR, ^{13}C-NMR and EIMS) data. Then **4a-q** were evaluated for antibacterial, antifungal and antitubercular activities. No significant activity was observed against the selected microorganisms.

Key Words: 4(3H)-Quinazolinone, arylidenehydrazide, synthesis, antimicrobial activity.

Introduction

Compounds containing the 4(3H)-quinazolinone ring have been reported to possess different biological activities such as antibacterial[1], antifungal[2,3], antitubercular[4], antiviral[5], anticancer[6,7]and anticonvulsant[8] activity depending on the substituents in the ring system. In addition, literature surveys show that quinazolinone hydrazones exhibit antimicrobial[9,10] and anticonvulsant[11,12] activity. In view of the above considerations we planned the present study to further investigate this ring system.

Experimental

Melting points were estimated with a Büchi 530 melting point apparatus in open capillaries and are uncorrected. Elemental analyses were performed on a Carlo Erba 1106 elemental analyzer. UV spectra

*Corresponding author

were determined on a Shimadzu UV-1601. IR spectra were recorded on KBr disks, using a Perkin-Elmer Model 1600 FT-IR spectrometer. ^{1}H-NMR and ^{13}C-NMR spectra were obtained on a Bruker AC 200 (200 MHz and 50.3 MHz) spectrophotometer. EIMS were determined on a VG Zab Spec (70 eV) mass spectrometer.

Synthesis of 3-phenyl-6-methyl-4(1H,3H)-quinazolinone-2-thione (1)[13]

To a solution of 5-methylantranilic acid (0.05 mol) in 30 mL of absolute ethanol was added phenyl isothiocyanate (0.05 mol). The reaction mixture was refluxed on a water bath for 5.5 h. The products formed were filtered and recrystallized from ethanol.

Synthesis of 3-phenyl-6-methyl-4(3H)-quinazolinone-2-ylmercaptoacetic acid ethyl ester (2)[14]

To a solution of **1** (0.02 mol) in 30 mL of dimethylformamide were added ethyl bromoacetate (0.024 mol) and 10 g of K_2CO_3 . The reaction mixture was refluxed on a water bath for 2 h, poured into ice-water and allowed to stand overnight. The precipitate was filtered and recrystallized from ethanol.

Synthesis of 3-phenyl-6-methyl-4(3H)-quinazolinone-2-ylmercaptoacetic acid hydrazide (3)[14]

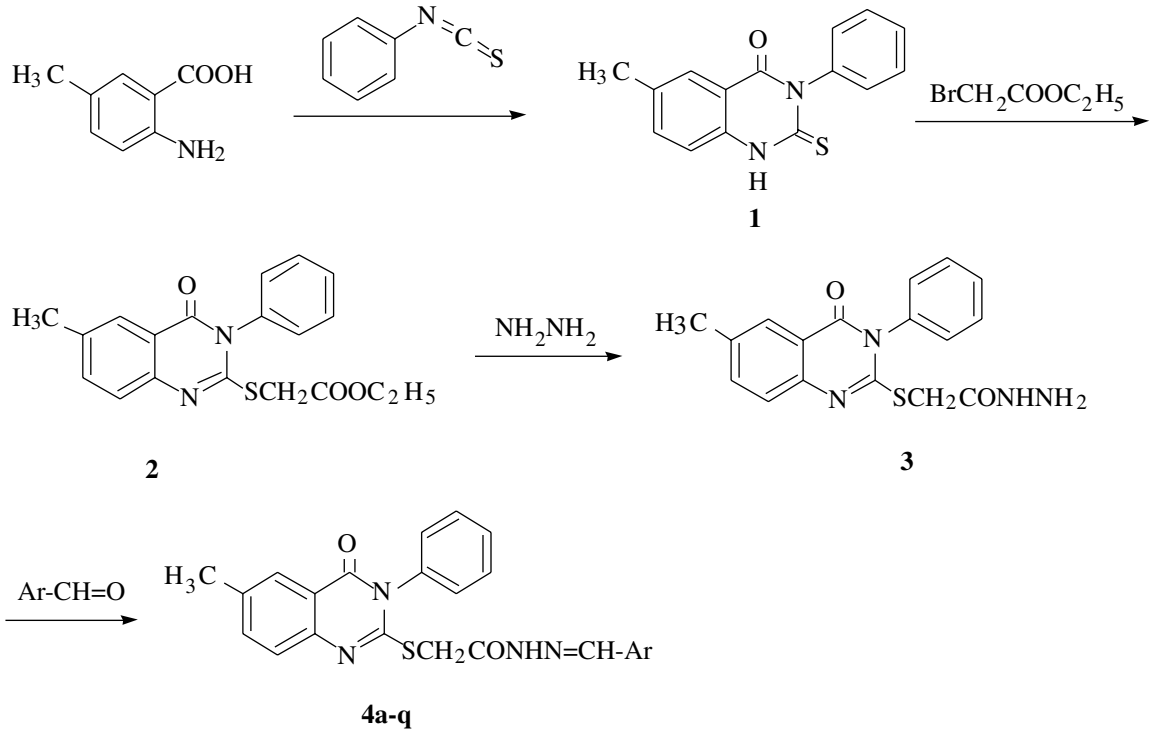
To a solution of **2** (0.01 mol) in 50 mL of absolute ethanol was added hydrazine hydrate (0.02 mol). The reaction mixture was refluxed on a water bath for 4 h and allowed to stand overnight. The crystals formed were filtered, washed and after drying recrystallized from ethanol.

Synthesis of 3-phenyl-6-methyl-4(3H)-quinazolinone-2-ylmercaptoacetic acid arylidenehydrazides (4a-q)

To a solution of **3** (0.01 mol) in absolute ethanol was added substituted benzaldehyde (0.01 mol). The reaction mixture was refluxed on a water bath for 4 h. The product formed after cooling was filtered and recrystallized from ethanol.

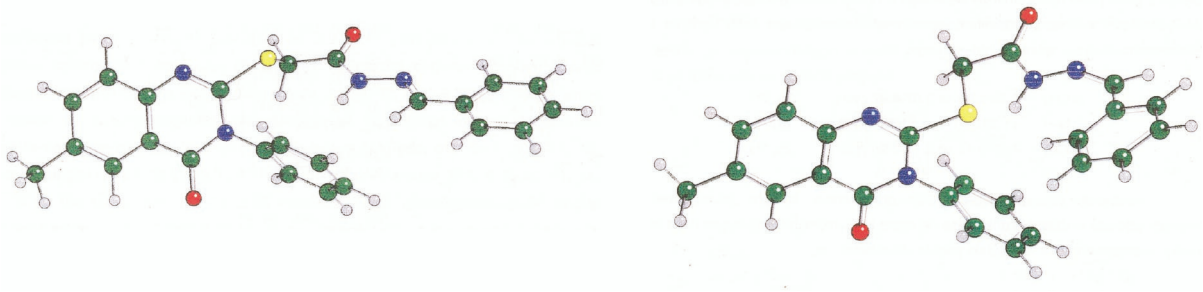
Results and Discussion

In this research, 3-phenyl-6-methyl-4(1H,3H)-quinazolinone-2-thione (**1**)[13] synthesized from the reaction of 5-methylantranilic acid with phenylisothiocyanate was reacted with ethyl bromoacetate in alkaline medium to yield 3-phenyl-6-methyl-4(3H)-quinazolinone-2-yl-mercaptoacetic acid ethyl ester (**2**)[14]. Subsequent treatment of **2** with hydrazine hydrate in absolute ethanol afforded 3-phenyl-6-methyl-4(3H)-quinazolinone-2-yl-mercaptoacetic acid hydrazide (**3**)[14]. Then **3** was reacted with aldehydes in absolute ethanol to obtain 17 new 3-phenyl-6-methyl-4(3H)-quinazolinone-2-yl-mercaptoacetic acid arylidenehydrazides (**4a-q**). The structures of the new compounds were confirmed by elemental analyses and from spectrometric (UV, IR, ^{1}H-NMR, ^{13}C-NMR and EIMS) data (Scheme 1) (Tables 1-5).



Scheme 1

The maxima observed in the UV spectra were associated with the parent molecule and incorporation of the arylidene moiety brought about no significant change. Only slight bathochromic shifts were observed in **4a-q,** where the arylidene moiety had electron donating and electron attracting groups. IR spectra of **4a-q** showed 2 bands resulting from the CO stretching bands of the lactam and arylidenehydrazide functions in the 1697-1667 and 1693-1641 cm^{-1} regions, respectively[15,16]. In the spectra of the compounds the NH and N=CH bands of the arylidenehydrazide function were observed in the 3230-3108 and 1620-1606 cm^{-1} regions, respectively[14,17] The ^{1}H-NMR spectra in DMSO-d_6 revealed the existence of 2 isomers. Restricted rotation about the N=CH linkage led to the formation of E and Z isomers. Thus the resonances associated with the SCH_2CO, N=CH and CONH were observed as 2 singlets, which integrated to give 2H, 1H, and 1H, respectively. The isomeric ratio was calculated using the integral values of the peak pairs. The dominating isomer was assigned to the E structure, where the steric effects of the functional groups were minimum. It was also the more stable structure with lower energy (Figure).



E isomer Z isomer

Figure. The formation of E and Z isomers of **4a**.

Table 1. Formulae, physical constants and elemental analysis of **4a-q**.

Comp.	Ar	Formula (M.W.)	Yield %	m.p. °C	Analyses (Calc./Found.)			
					C	H	N	S
4a	C_6H_5	$C_{24}H_{20}N_4O_2S$ (428.51)	80	248-51	67.27 67.55	4.70 4.77	13.07 13.14	7.48 7.21
4b	(4-CH_3)C_6H_4	$C_{25}H_{22}N_4O_2S$ (442.53)	65	241-2	67.85 67.95	5.01 4.87	12.66 12.50	7.25 6.98
4c	(2-OH)C_6H_4	$C_{24}H_{20}N_4O_3S$ (444.51)	98	272-3	64.85 65.05	4.54 4.76	12.60 12.10	7.21 6.88
4d	(3-OCH_3)C_6H_4	$C_{25}H_{22}N_4O_3S$ (458.53)	77	262-4	65.48 65.63	4.84 5.42	12.22 11.93	6.99 6.86
4e	(4-OCH_3)C_6H_4	$C_{25}H_{22}N_4O_3S$ (458.53)	85	230-1	65.48 65.48	4.84 4.30	12.22 11.89	6.99 6.62
4f	(2-OCH_3)(5-OCH_3)C_6H_3	$C_{26}H_{24}N_4O_4S$ (488.56)	79	255-7	63.92 64.05	4.95 5.02	11.47 11.30	6.56 6.29
4g	(3-OCH_3)(4-OH)C_6H_3	$C_{25}H_{22}N_4O_4S$ (474.53)	53	238-9	63.28 63.49	4.67 5.09	11.81 11.67	6.76 6.74
4h	(3-OC_2H_5)(4-OH)C_6H_3	$C_{26}H_{24}N_4O_4S$ (488.56)	89	255-6	63.92 64.27	4.95 5.32	11.47 11.15	6.56 6.23
4i	(2-OH)(5-Br) C_6H_3	$C_{24}H_{19}BrN_4O_3S$ (523.40)	93	251-2	55.07 54.93	3.66 3.75	10.70 10.31	6.13 5.60
4j	(4-Br)C_6H_4	$C_{24}H_{19}BrN_4O_2S$ (507.40)	98	250-2	56.81 57.38	3.77 3.27	11.04 11.04	6.32 6.01
4k	(4-Cl)C_6H_4	$C_{24}H_{19}ClN_4O_2S$ (462.95)	76	252-3	62.26 61.94	4.14 4.47	12.10 11.86	6.93 6.70
4l	(3-Cl)(4-Cl)C_6H_3	$C_{24}H_{18}Cl_2N_4O_2S$ (497.40)	85	260-3	57.95 58.07	3.65 3.54	11.26 11.14	6.45 6.27
4m	(4-F)C_6H_4	$C_{24}H_{19}FN_4O_2S$ (446.50)	61	233-6	64.56 64.97	4.29 4.43	12.55 12.18	7.18 6.76
4n	(4-CF_3)C_6H_4	$C_{25}H_{19}F_3N_4O_2S$ (496.51)	72	248-50	60.48 60.85	3.86 4.12	11.28 11.01	6.46 6.28
4o	(2-NO_2)C_6H_4	$C_{24}H_{19}N_5O_4S$ (473.51)	77	242-3	60.88 60.96	4.04 4.21	14.79 14.55	6.77 6.86
4p	(4-NO_2)C_6H_4	$C_{24}H_{19}N_5O_4S$ (473.51)	94	246-7	60.88 61.22	4.04 4.02	14.79 14.57	6.77 6.39
4q	5-nitrofurfural	$C_{22}H_{17}N_5O_5S$ (463.47)	20	209-12	57.01 57.90	3.70 4.14	15.11 14.82	6.92 6.36

Table 2. UV, IR and ^{1}H-NMR data of **4a-q**.

Comp.	UV[$\lambda_{max.}^{EtOH}$ nm (Σ)]	IR [γ cm^{-1} , KBr]	^{1}H-NMR [200 MHz, dmso-d$_6$]
4a	220 (50950) 280 (40451) 338 (4285)	3187 (NH) 1677 (lactam C=O) 1641 (amide C=O)	2.43 (3H, s, quin. C_6-CH_3), 3.98, 4.45 (2H, 2s, SCH_2CO), 7.43-7.70 (12H, m, quin. C_3-C_6H_5, quin. $C_{7,8}$-H, ar.), 7.88 (1H, s, quin. C_5-H), 8.05, 8.26 (1H, 2s, N=CH), 11.57 (1H, s, CONH)
4b	223 (100454) 283 (80629) 339 (9205)	3188 (NH) 1694 (lactam C=O) 1670 (amide C=O)	2.34 (3H, s, ar.C_4-CH_3), 2.43 (3H, s, quin. C_6-CH_3), 3.24, 3.97 (2H, 2s, SCH_2CO), 7.23 (2H, d, J:7.82 Hz, ar. $C_{3,5}$-H), 7.40 (1H, d, J:8.36 Hz, quin. C_8-H), 7.45 (1H, d, J:7.27 Hz, quin. C_7-H), 7.54-7.64 (7H, m, quin. C_3-C_6H_5, ar. $C_{2,6}$-H), 7.88 (1H, s, quin. C_5-H), 8.01, 8.21 (1H, 2s, N=CH), 11.48 (1H, s, CONH)
4c	231 (55164) 280 (38850) 323 (17691)	3181 (NH) 1678 (lactam and amide C=O)	2.43 (3H, s, quin. C_6-CH_3), 3.99, 4.43 (2H, 2s, SCH_2CO), 6.79-6.92 (2H, m, ar. $C_{3,5}$-H), 7.23, 7.30 (1H, dd, J:6.95, 6.83 Hz, ar. C_4-H), 7.45 (1H, d, J:6.73 Hz, quin. C_8-H), 7.46 (1H, d, J:6.97 Hz, quin. C_7-H), 7.52-7.63 (6H, m, quin. C_3-C_6H_5, ar. C_6-H), 7.88 (1H, s, quin. C_5-H), 8.33, 8.46 (1H, 2s, N=CH), 10.04, 10.98 (1H, 2s, ar. C_2-OH), 11.51, 11.89 (1H, 2s, CONH, D-exch.)
4d	220 (55345) 281 (41038) 321 (14765)	3194, 3126 (NH) 1682 (lactam C=O) 1658 (amide C=O)	2.42 (3H, s, quin. C_6-CH_3), 3.78 (3H, s, ar. C_3-OCH_3), 3.98, 4.46 (2H, 2s, SCH_2CO), 6.98 (1H, d, J:7.56 Hz, ar. C_4-H), 7.24- 7.41 (2H, m, ar. C_2-H, quin. C_8-H), 7.43-7.46 (2H, m, ar. $C_{5,6}$-H), 7.45 (1H, d, J:6.99 Hz, quin. C_7-H), 7.53-7.57 (5H, m, quin. C_3-C_6H_5), 7.87 (1H, s, quin. C_5-H), 8.01, 8.23 (1H, 2s, N=CH), 11.61 (1H, s, CONH)
4e	226 (72218) 283 (54840) 309 (41772)	3205 (NH) 1695 (lactam C=O) 1670 (amide C=O)	2.42 (3H, s, quin. C_6-CH_3), 3.79 (3H, s, ar. C_4-OCH_3), 3.95, 4.43 (2H, 2s, SCH_2CO), 6.98, 6.99 (2H, dd, J:8.71, 8.69 Hz, ar. $C_{3,5}$-H), 7.39-7.67 (7H, m, quin. C_3-C_6H_5, quin. $C_{7,8}$-H), 7.45, 7.47 (2H, dd, J:8.92, 6.11 Hz, ar. $C_{2,6}$-H), 7.87 (1H, s, quin. C_5-H), 7.97, 8.17 (1H, 2s, N=CH), 11.52, 11.61 (1H, 2s, CONH)
4f	209 (63610) 278 (28766) 323 (1094)	3188 (NH) 1678 (lactam and amide C=O)	2.43 (3H, s, quin. C_6-CH_3), 3.72 (3H, s, ar. C_5-OCH_3), 3.81 (3H, s, ar. C_2-OCH_3), 3.95, 4.46 (2H, 2s, SCH_2CO), 7.02 (1H, dd, J:6.03, 2.72 Hz, ar. C_4-H), 7.05 (1H, d, J:8.93 Hz, ar. C_3-H), 7.27, 7.33 (1H, 2d, J:2.37, 2.32 Hz, ar. C_6-H), 7.39 (1H, d, J:6.42 Hz, quin. C_8-H), 7.44 (1H, d, J:7.39 Hz, quin. C_7-H), 7.52-7.67 (5H, m, quin. C_3-C_6H_5), 7.88 (1H, s, quin. C_5-H), 8.33, 8.57 (1H, 2s, N=CH), 11.51, 11.66 (1H, 2s, CONH)

Table 2. Contunied.

4g	232 (56706) 284 (33644) 320 (32268)	3165 (NH) 1667 (lactam and amide C=O)	2.43 (3H, s, quin. C_6-CH_3), 3.79 (3H, s, ar. C_3-OCH_3), 3.95, 4.44 (2H, 2s, SCH_2CO), 6.81 (1H, d, J:8.08 Hz, ar. C_5-H), 7.10 (1H, d, J:8.14 Hz, ar. C_6-H), 7.25 (1H, s, ar. C_2-H), 7.41 (1H, d, J:8.19 Hz, quin. C_8-H), 7.44 (1H, d, J:7.03 Hz, quin. C_7-H), 7.53-7.64 (5H, m, quin. C_3-C_6H_5), 7.88 (1H, s, quin. C_5-H), 7.92, 8.12 (1H, 2s, N=CH), 9.39 (1H, s, ar C_4-OH), 11.36, 11.44 (1H, 2s, CONH)
4h	232 (51152) 285 (30535) 320 (28825)	3176 (NH) 1673 (lactam and amide C=O)	1.34 (3H, t, J:6.93 Hz, ar. C_3-$OCH_2C\underline{H}_3$), 2.43 (3H, s, quin. C_6-CH_3), 4.04 (2H, q, J:6.85 Hz, ar. C_3-$OC\underline{H}_2CH_3$), 3.95, 4.44 (2H, 2s, SCH_2CO), 6.82 (1H, d, J:8.10 Hz, ar. C_5-H), 7.06 (1H, d, J:8.14 Hz, ar. C_6-H), 7.24 (1H, s, ar. C_2-H), 7.41 (1H, d, J:8.10 Hz, quin. C_8-H), 7.47 (1H, d, J:6.08 Hz, quin. C_7-H), 7.53-7.67 (5H, m, quin. C_3-C_6H_5), 7.88 (1H, s, quin. C_5-H), 7.90, 8.11 (1H, 2s, N=CH), 9.32 (1H, s, ar. C_4-OH), 11.35, 11.43 (1H, 2s, CONH)
4i	232 (50665) 281 (31666) 334 (13137)	3177 (NH) 1697 (lactam C=O) 1666 (amide C=O)	2.43 (3H, s, quin. C_6-CH_3), 3.99, 4.46 (2H, 2s, SCH_2CO), 6.88 (1H, d, J:8.71 Hz, ar. C_3-H), 7.38 (1H, s, ar. C_6-H), 7.41 (1H, d, J:7.45 Hz, quin. C_8-H), 7.49 (1H, d, J:8.37 Hz, quin. C_7-H), 7.58 (5H, s, quin. C_3-C_6H_5), 7.74-7.81 (1H, m, ar. C_4-H), 7.88 (1H, s, quin. C_5-H), 8.28, 8.43 (1H, 2s, N=CH), 8.84 (1H, s, ar. C_2-OH), 11.57 (1H, s, CONH, D-exch.)
4j	223 (48609) 288 (41911) 338 (3805)	3170 (NH) 1693 (lactam C=O) 1671 (amide C=O)	2.43 (3H, s, quin. C_6-CH_3), 3.98, 4.44 (2H, 2s, SCH_2CO), 7.40 (1H, d, J:8.56 Hz, quin. C_8-H), 7.44 (1H, d, J:9.11 Hz, quin. C_7-H), 7.46-7.60 (4H, m, ar. $C_{3,5}$-H, ar. $C_{2,6}$-H), 7.63 (5H, s, quin. C_3-C_6H_5), 7.88 (1H, s, quin. C_5-H), 8.02, 8.24 (1H, 2s, N=CH), 11.63 (1H, s, CONH)
4k	222 (46202) 281 (37730) 336 (3472)	3188 (NH) 1694 (lactam C=O) 1674 (amide C=O)	2.43 (3H, s, quin. C_6-CH_3), 3.98, 4.45 (2H, 2s, SCH_2CO), 7.40 (1H, d, J:8.39 Hz, quin. C_8-H), 7.44 (2H, d, J:8.58 Hz, ar. $C_{3,5}$-H), 7.48 (1H, d, J:7.24 Hz, quin. C_7-H), 7.58 (5H, s, quin. C_3-C_6H_5), 7.70 (2H, d, J:8.58 Hz, ar. $C_{2,6}$-H), 7.88 (1H, s, quin. C_5-H), 8.04, 8.26 (1H, 2s, N=CH), 11.61 (1H, s, CONH)
4l	228 (67149) 282 (49093) 336 (4974)	3134 (NH) 1682 (lactam C=O) 1674 (amide C=O)	2.43 (3H, s, quin. C_6-CH_3), 3.98, 4.46 (2H, 2s, SCH_2CO), 7.43 (1H, d, J:7.61 Hz, quin. C_8-H), 7.45 (1H, d, J:7.54 Hz, quin. C_7-H), 7.51-7.60 (5H, m, quin. C_3-C_6H_5), 7.66 (2H, d, J:5.81 Hz, ar. $C_{5,6}$-H), 7.88 (1H, s, quin. C_5-H), 7.93 (1H, s, ar. C_2-H), 8.02, 8.24 (1H, 2s, N=CH), 11.71, 11.83 (1H, 2s, CONH)

Table 2. Contunied.

4m	219 (45543) 280 (36434) 336 (3349)	3188 (NH) 1693 (lactam C=O) 1672 (amide C=O)	2.43 (3H, s, quin. C_6-CH_3), 3.97, 4.44 (2H, 2s, SCH_2CO), 7.25 (2H, AA' part of AA'BB' system, quasi t, J:8.68 Hz, ar. $C_{3,5}$-H), 7.40 (1H, d, J:8.77 Hz, quin. C_8-H), 7.44 (1H, d, J:8.07 Hz, quin. C_7-H), 7.46-7.58 (5H, m, quin. C_3-C_6H_5), 7.72, 7.75 (2H, BB' part of AA'BB' system, quasi dd, J:8.11, 8.32 Hz, ar. $C_{2,6}$-H), 7.88 (1H, s, quin. C_5-H), 8.04, 8.26 (1H, 2s, N=CH), 11.56, 11.65 (1H, 2s, CONH)
4n	212 (42551) 281 (33316) 336 (3724)	3188 (NH) 1693 (lactam and amide C=O)	2.43 (3H, s, quin. C_6-CH_3), 4.00, 4.47 (2H, 2s, SCH_2CO), 7.40 (1H, d, J:8.68 Hz, quin. C_8-H), 7.43-7.63 (5H, m, quin. C_3-C_6H_5), 7.45 (1H, d, J:7.97 Hz, quin. C_7-H), 7.90 (2H, d, J:8.27 Hz, ar. $C_{3,5}$-H), 7.76 (2H, d, J:8.15 Hz, ar. $C_{2,6}$-H), 7.88 (1H, s, quin. C_5-H), 8.12, 8.34 (1H, 2s, N=CH), 11.76 (1H, s, CONH)
4o	209 (57484) 231 (54169) 278 (32104) 321 (11269)	3171 (NH) 1678 (lactam and amide C=O)	2.42 (3H, s, quin. C_6-CH_3), 3.98, 4.42 (2H, 2s, SCH_2CO), 7.40 (1H, d, J:8.82 Hz, quin. C_8-H), 7.44-7.82 (5H, m, ar. $C_{3,4,5,6}$-H quin. C_7-H), 7.53-7.58 (5H, s, quin. C_3-C_6H_5), 7.87 (1H, s, quin. C_5-H), 8.42, 8.68 (1H, 2s, N=CH), 11.92 (1H, s, CONH)
4p	210 (35040) 232 (36839) 281 (17188) 323 (16052)	3230 (NH) 1694 (lactam C=O) 1656 (amide C=O)	2.42 (3H, s, quin. C_6-CH_3), 4.00, 4.47 (2H, 2s, SCH_2CO), 7.38 (1H, d, J:8.24 Hz, quin. C_8-H), 7.44-7.66 (6H, m, quin. C_7-H, quin. C_3-C_6H_5), 7.87 (1H, s, quin. C_5-H), 7.95 (2H, AA' part of AA'BB' system, quasi d, J: 8.75 Hz, ar. $C_{2,6}$-H), 8.27, 8.28 (2H, BB' part of AA'BB' system, quasi dd, J:8.70, 8.68 Hz, ar. $C_{3,5}$-H), 8.15, 8.36 (1H, 2s, N=CH), 11.97 (1H, s, CONH)
4q	210 (42732) 231 (42176) 279 (18724) 322 (7740)	3108 (NH) 1686 (lactam C=O) 1648 (amide C=O)	2.43 (3H, s, quin. C_6-CH_3), 3.99, 4.43 (2H, 2s, SCH_2CO), 7.24 (1H, d, J:3.84 Hz, furan C_3-H), 7.43 (1H, d, J:8.27 Hz, quin. C_8-H), 7.47 (1H, d, J:7.37 Hz, quin. C_7-H), 7.48 (1H, d, J:3.97 Hz, furan C_4-H), 7.58-7.61 (5H, m, quin. C_3-C_6H_5), 7.88 (1H, s, quin. C_5-H), 8.02, 8.25 (1H, 2s, N=CH), 12.01, 12.12 (1H, 2s, CONH)

Table 3. ^{13}C-NMR proton decoupled [50.3 MHz, dmso-d_6] data of **4b**, **4e** and **4k**.

Carbon	**4b** Ar=(4-CH_3)C_6H_4	**4e** Ar=(4-OCH_3)C_6H_4	**4k** Ar=(4-Cl)C_6H_4
Quin. C_2	155.81	155.78	156.40
Quin. C_4	160.58	160.58	161.15
Quin. C_5	129.36	128.28	129.08
Quin. C_6	135.57	135.52	134.92
Quin. C_7	136.06	136.00	136.74
Quin. C_8	125.83	125.80	126.51
Quin. C_9	145.15	145.13	145.81
Quin. C_{10}	119.17	119.15	119.95
Phenyl C_1	135.69	135.62	136.53
Phenyl $C_2$and C_6	126.99	128.58	129.34
Phenyl C_3andC_5	129.83	129.78	129.05
Phenyl C_4	129.36	129.34	129.54
Aryl C_1	131.34	126.60	133.72
Aryl C_2	129.36	129.34	130.52
Aryl C_3	126.72	114.22	130.06
Aryl C_4	139.62	160.77	136.27
Aryl C_5	126.72	114.22	130.06
Aryl C_6	129.36	129.34	130.52
SCH_2	34.05, 35.28	34.07, 35.28	34.94, 36.21
C(O)NH	163.38,168.63	163.17, 168.43	164.23, 169.43
N=CH-Ar	143.40, 146.77	143.19, 146.64	145.81, 146.07

Table 4. ^{13}C-NMR APT [50.3 MHz, dmso-d_6] data of **4b**, **4e**, **4f** and **4k**.

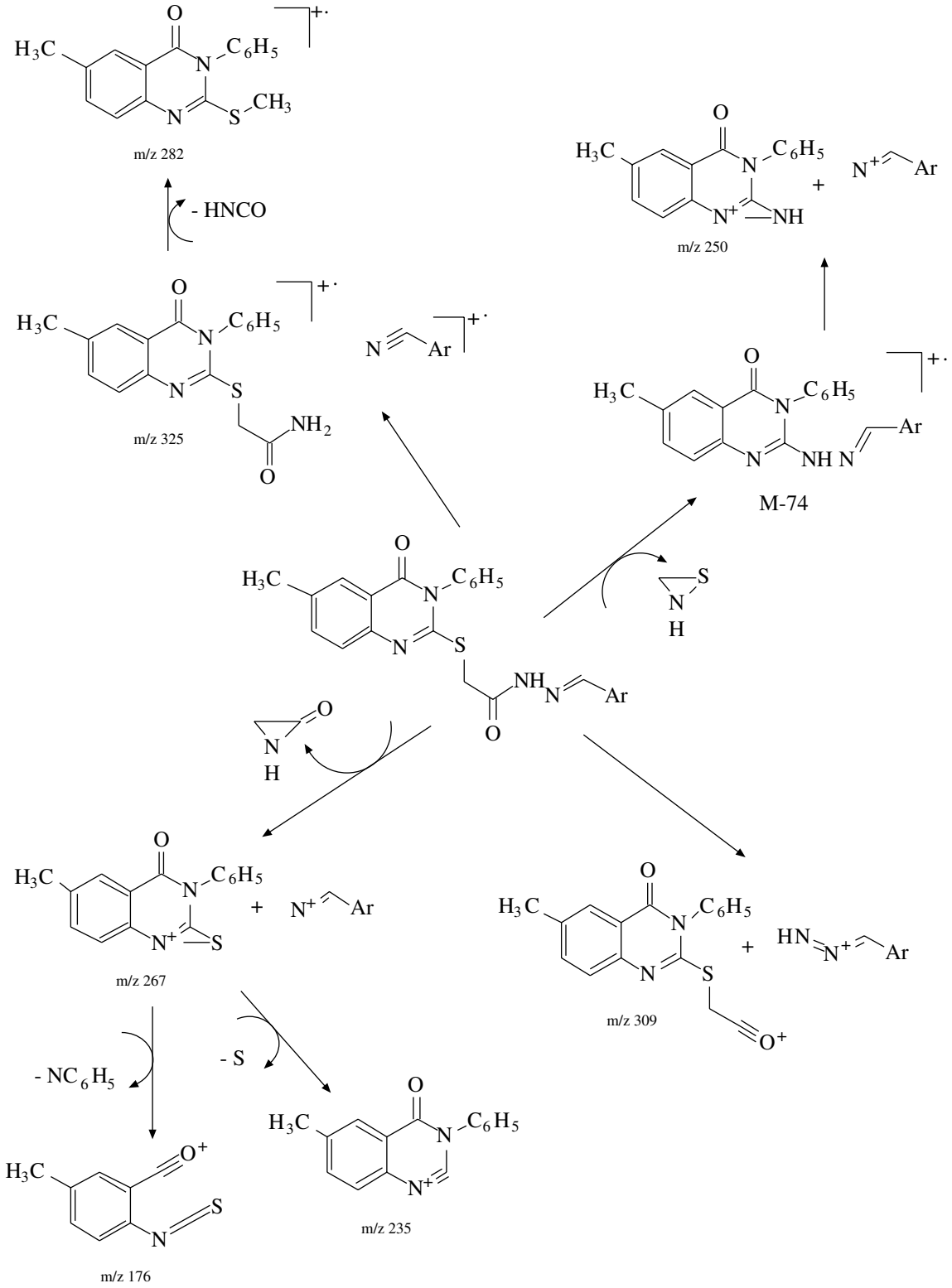
Carbon	**4b** Ar=(4-CH_3)C_6H_4	**4e** Ar=(4-OCH_3)C_6H_4	**4f** Ar=(2-OCH_3) (5-OCH_3)C_6H_3	**4k** Ar=(4-Cl)C_6H_4
Quin. C_2	155.86	155.81	155.73	156.20
Quin. C_4	160.61	160.61	160.50	160.50
Quin. C_5	129.40	128.32	129.74	128.64
Quin. C_6	135.59	135.55	135.93	134.25
Quin. C_7	136.11	136.05	135.49	136.06
Quin. C_8	125.86	125.83	125.77	125.83
Quin. C_9	145.17	145.15	145.08	145.13
Quin. C_{10}	119.18	119.18	119.12	119.18
Phenyl C_1	135.70	135.65	135.50	135.59
Phenyl $C_2$and C_6	127.03	128.61	129.30	128.83
Phenyl C_3andC_5	129.89	129.83	129.30	129.84
Phenyl C_4	129.40	129.38	129.30	128.64
Aryl C_1	131.35	126.62	122.74	133.02
Aryl C_2	129.40	129.38	153.18	129.37
Aryl C_3	126.76	114.25	116.96	128.83
Aryl C_4	139.65	161.00	119.32	136.38
Aryl C_5	126.76	114.25	152.07	128.83
Aryl C_6	129.40	129.38	109.54	129.37
SCH_2	34.08, 35.31	34.11, 35.31	34.21, 35.18	34.00, 35.27
C(O)NH	163.42,168.87	163.20, 168.47	163.30,168.59	163.63, 168.84
N=CH-Ar	143.38, 146.70	143.20, 146.64	138.76, 142.15	142.00, 145.36

Table 5. EIMS data of **4a-q**.

Comp.	M^+ (%)	M-74 (%)	m/z 325	m/z 310	m/z 309	m/z 282	m/z 268	m/z 267	m/z 250	m/z 249	m/z 235	m/z 176	m/z 159	m/z 146	m/z 133	m/z 118	m/z 104
4a	428 (2.3)	354 (6.1)	3.6	29.8	100	6.2	36.3	51.3	7.9	12.8	11.9	5.0	2.5	27.5	12.8	2.9	14.5
4b	442 (1.3)	368 (1.1)	1.9	32.6	100	4.8	29.4	42.2	6.3	9.1	10.2	4.7	1.9	24.1	12.9	5.1	12.6
4c	444 (11.4)	370 (0.6)	-	24.8	100	5.6	51.4	75.9	8.6	10.7	16.8	8.5	5.4	21.3	22.5	-	16.5
4d	458 (2.6)	384 (4.1)	2.4	31.7	100	5.5	35.5	51.2	16.7	15.0	12.1	3.6	1.5	18.7	12.4	-	4.8
4e	458 (0.6)	384 (1.2)	0.8	34.7	100	3.5	17.3	31.6	6.8	7.7	9.3	4.1	2.0	21.8	13.5	1.2	8.0
4f	488 (0.5)	414 (0.9)	0.9	22.8	100	3.3	19.9	30.9	8.8	8.2	9.9	3.4	1.5	14.8	9.5	0.5	6.5
4g	474 (1.1)	400 (1.6)	1.1	45.3	100	5.2	20.5	34.1	7.9	9.8	12.0	6.2	2.5	32.3	13.3	0.8	10
4h	488 (0.6)	414 (2.4)	1.0	38.8	100	3.9	17.3	31.5	6.6	8.5	11.1	4.1	1.8	19.3	9.8	0.4	7.0
4i	522 (4.1) 524 (4.4)	448 (0.1) 450 (0.1)	-	13.6	64.9	5.0	73.5	100	9.0	9.8	18.2	8.5	6.8	14	26.5	-	21.5

Table 5. Contunied.

Comp.	M^+ (%)	M-74 (%)	m/z 325	m/z 310	m/z 309	m/z 282	m/z 268	m/z 267	m/z 250	m/z 249	m/z 235	m/z 176	m/z 159	m/z 146	m/z 133	m/z 118	m/z 104
4j	506 (0.6) 508 (0.6)	432 (1.1) 434 (1.1)	2.2	20.5	100	5.6	51.9	67.9	20.5	14.7	14.9	5.1	3.2	19.6	15.3	2.8	12.2
4k	461 - 463 (0.6)	387 (0.6) 389 (0.6)	2.5	25.0	100	5.8	46.2	61.2	11.7	12.9	12.4	4.9	2.7	23.1	14.2	1.7	10.6
4l	496 (1.3) 498 (2.1)	422 (2.2) 424 (1.4)	4.7	34.4	100	10.6	67.6	66.5	25.8	21.3	19.4	7.2	4.3	30.7	19.6	2.1	15.1
4m	446 (1.7)	372 (1.3)	2.2	22.9	100	4.9	39.2	56.0	8.1	11.0	11.2	4.6	2.2	22.0	11.9	0.9	8.9
4n	496 (11.4)	422 (1.2)	6.6	20.7	100	7.5	90.8	88.3	7.7	13.5	13.2	5.1	3.1	25.2	14.5	2.6	10.2
4o	473 (14.2)	399 (1.1)	22.3	40.7	100	39.6	93.1	91.3	23.7	39.5	40.5	15.5	7.2	51.9	33.6	10.6	30.4
4p	473 (4.6)	399 (2.7)	3.6	19.3	92.1	7.7	100	87.4	27.0	18.0	18.6	7.1	5.0	31.7	21.4	6.7	19.5
4q	463 (2.9)	389 (8.2)	4.6	18.2	87.8	12.6	87.2	100	14.1	20.5	26.7	9.2	6.7	25.2	30.8	2.8	26.1



Scheme 2

In the spectra of **4a-q** the SCH_2CO, N=CH and CONH protons were observed as 2 singlets (3.24-4.00 and 3.97-4.47 ppm; 7.90-8.42 and 8.11-8.68 ppm; 11.35-12.01 and 11.43-12.12 ppm). Quinazolinone C_5-H resonated at 7.87-7.88 ppm as a singlet. Quinazolinone C_7-H and C_8-H displayed 2 different doublets due to ortho interactions at 7.44-7.49 and 7.38-7.45 ppm, respectively[18−20]. Like in the ^{1}H-NMR spectra, in the ^{13}C-NMR spectra of **4b, 4e**, **4f** and **4k,** chosen as prototypes, the resonances of the SCH_2, N=CH and CONH groups were observed as 2 peaks (34.00-34.94 and 35.18-36.21 ppm; 138.76-145.81 and 142.15-146.77 ppm; 163.17-164.23 and 168.43-169.43 ppm) because of the existence of both E and Z isomers[18,20,21]. The molecular ion peaks in the EI-MS of **4a-q** confirmed their molecular weights. In accordance with the literature, the compounds fragmented via 4 common routes, the first and second of which involved the cleavage of the CO-NH or N-N bond. The third and fourth involved the cleavages of SCH_2 or the thioether and amide linkage at the 2 position of quinazolinone, followed by the binding of the rest of the side chain to the ring. The cleavage of the amide bond gave the fragment at m/z 309 as the base peak in **4a-h** and **4j-o,** whereas the cleavage of the SCH_2 bond gave the fragment at m/z 267 as the base peak in **4i** and **4q**[17,21,22] (Scheme 2).

In line with the reports stating that hydrazides and hydrazide-hydrazones possessed antitubercular, antibacterial and antifungal activities, **4a-q** were tested against *Staphylococcus aureus* ATCC 6538, *Staphylococcus epidermidis* ATCC 12228, *Escherichia coli* ATCC 8739, *Klebsiella pneumoniae* ATCC 4352, *Pseudomonas aeruginosa* ATCC 1539, *Proteus mirabilis* ATCC 14153, *Salmonella typhi*, *Shigella flexneri* and *Candida albicans* ATCC 10231[23]. No significant activity was observed against the selected microorganisms. **4a-q** were also tested against *Mycobacterium tuberculosis* $H_{37}R_v$ employing the BACTEC radiometric sensitivity test but were found inactive at 6.5 μg/mL[24,25].

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