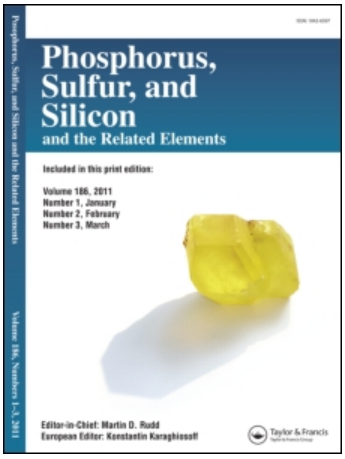

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Microwave Assisted Synthesis of Some Novel Thiopyrano[2,3-*b*]quinolines as a New Class of Antimicrobial Agent

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Microwave Assisted Synthesis of Some Novel Thiopyrano[2,3-*b*]quinolines as a New Class of Antimicrobial Agent

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*A series of novel substituted thiopyrano[2,3-*b*]quinolines **4a–e**, **5a–e**, and **6a–e** were prepared from substituted 3-formyl-2-mercapto quinolines **2a–e**, on reaction with ethyl acetoacetate, diethyl malonate, and ethyl cyanoacetate **3a–c** by microwave irradiation in the presence of piperidine. Synthesized compounds were evaluated for antimicrobial activities. Among the compounds tested, 7-chloro-2-oxo-2H-thiopyrano[2,3-*b*]quinoline-3-carbonitrile **6d** and 7-nitro-2-oxo-2H-thiopyrano[2,3-*b*]quinoline-3-carbonitrile **6e** were highly active against S. aureus and M. roseus.*

Keywords Antimicrobial agent; diethyl malonate; ethyl acetoacetate; ethyl cyanoacetate; microwave irradiation; thiopyrano[2,3-*b*]quinolines

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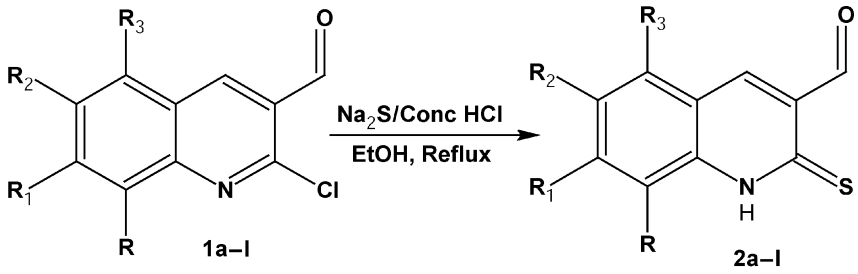
INTRODUCTION

Quinoline and its derivatives have been reported to be associated with interesting pharmacological properties.[1–5] They are found in numerous commercial products, including pharmaceuticals, fragrances, and dyes. Quinoline alkaloids, such as quinine, chloroquine, mefloquine, and amodia quine, are used as efficient drugs for the treatment of maleria.[6–13] A literature survey shows that there is evidence that antitumor activity is due to the intercalation between the base pairs of DNA and interferences with the normal functioning of enzyme topoisomerase II, which is involved in the breaking and releasing of DNA strands.[14] The antitumor drugs that intercalate DNA are of growing interest in the field of anticancer derivatives. Generally, they are chacterized by planar chromophore, which is often constituted by three or four condensed rings, which can intercalate into base pairs. Results of these various binding studies have been useful in designing new and promising anticancer agent for clinical use.[15] DNA binding studies of pyrimidothienoquinolines have been recently reported in the literature.[16–17]

The latest developments in dedicated MW equipment have attracted the attention of chemical companies, and their heightened interest has become obvious as exemplified recently in the application of microwaves in the combinatorial chemistry arena that rapidly generates a library of potentially useful chemical entities.[18] A chemical reaction performed using microwave assisted organic synthesis techniques, which has attracted a substantial amount of attention in the past few years.[19] Moreover, it is an environmentally friendly technique and is believed to be a step toward green chemistry,[20] because the reactions are performed at higher temperatures than their conventional counterparts. MW-based synthesizers can achieve a temperature of up to 250°C and pressure up to 20 bars, allowing reactions to be carried out at higher temperatures than their reflux counterparts. These features recently also have attracted interest from the drug discovery and medicinal chemistry communities, for which reaction speed is of great importance.[21–26]

In continuation of our work on condensed heterocycles.[27–28] and in view of our growing interest in the field of anticancer agents, herein we wish to report an efficient synthesis of novel title compounds **4a–e**, **5a–e**, and **6a–e** by the application of microwave energy and their profile of antimicrobial activity.

In conclusion, we have shown that the application of microwave irradiation improves yields of title compounds and significantly reduces reaction times. The described procedure is simple, less time consuming, and economically viable, and the product is obtained in good yield and pure form.



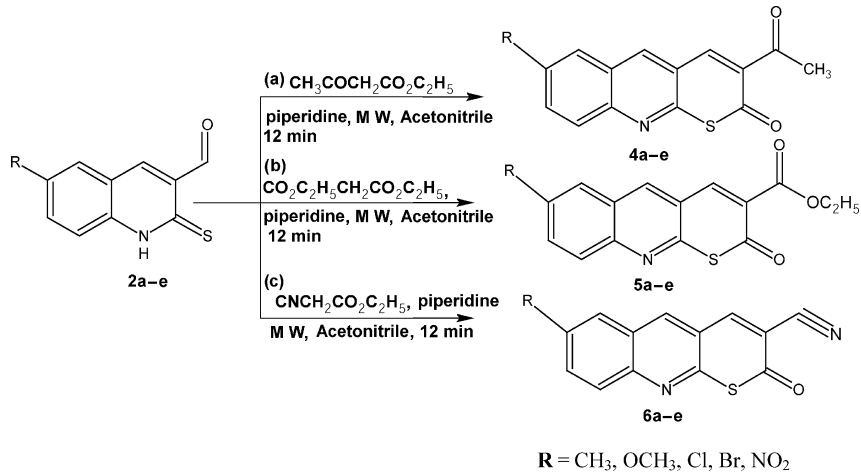
	R	R_1	R_2	R_3
a.	H	H	H	H
b.	H	H	CH_3	H
c.	H	CH_3	H	H
d.	CH_3	H	H	H
e.	H	H	OCH_3	H
f.	H	OCH_3	H	H
g.	OCH_3	H	H	H
h.	H	H	Br	H
i.	H	H	Cl	H
j.	H	Cl	H	H
k.	H	OCH_3	OCH_3	H
l.	H	OCH_3	OCH_3	OCH_3

SCHEME 1 The general synthetic procedure of 3-formyl-2-mercapto quinolines derivatives **2a–l**.

RESULTS AND DISCUSSION

Numerous condensed quinolines have various bioactivities, which render them valuable pharmacological activities as mentioned earlier, and, therefore, they are a useful material in drug research. Hence, In continuation of our study in developing condensed quinolines derivaties due to their significant biological activates, it appeared expedient to synthesize a series of systematically condensed and appropriately funtionalized thiopyrano quinolines in the present study.

In order to synthesize compounds **4a–e**, **5a–e**, and **6a–e**, the compounds 3-formyl-2-mercapto quinolines **2a–e** were allowed to react with ethyl acetoacetate **3a**, diethyl malonate **3b**, and ethyl cyanoacetate **3c** in the presence of a catalytic amount of piperidine in acetonitrile as a solvent, which afforded thiopyrano[2,3-*b*]quinolin-2-one derivaties **4a–e**, **5a–e**, and **6a–e** in good yields (Scheme 2). The structure of all the new thiopyrano quinolines have been elucidated by elemental analysis, and



SCHEME 2 The general synthetic procedure of thiopyrano[2,3-*b*]quinolines derivatives **4a–e**, **5a–e**, and **6a–e**.

IR, ^{1}H, NMR, and mass spectral data. The IR spectrum of compound **4a** showed an absence of SH, NH, and CHO stretching frequency in the region of 3100–3400 and 1648 cm^{-1}, which appeared in the 3-formyl-2-mercapto quinoline; an appearance of new peaks in the region of 1620–1625 cm^{-1} attributed to a thiopyrano ring carbonyl and another at 1644 cm^{-1} assigned to —$COCH_3$ in the newly formed ring was the indication of the ring closure. The ^{1}H NMR spectrum of **4a** exhibited a singlet at δ 2.46 (s, 3H, Ar-CH_3), which corresponds to three protons due to a methyl group present on an aromatic ring. It also showed a singlet integrated for three protons at δ 2.6–2.61 (s, 3H, —$COCH_3$) attributed to a methyl group of the —$COCH_3$ in the newly formed thiopyrano ring system on the quinoline nucleus. The signals due to aromatic protons appeared at 7.40 (s, C_4-H), 7.72 (d, $J = 9$ Hz, C_{12}-H), 7.82 (s, C_{14}-H), 7.84 (d, $J = 9$ Hz, C_{11}-H), and 8.64 (s, C_{10}-H). The mass spectrum of compound **4a** exhibited a peak at m/z 269. Similarly, the structures of all the compounds **4b–e** were assigned on the basis of their spectral data and were placed in appropriate places.

In light of the foregoing result, the reaction of 3-formyl-2-mercapto quinoline with diethyl malonate **3b** in acetonitrile containing a catalytic amount of piperidine afforded **5a**. Structure **5a** was confirmed on the basis of spectral data. The IR spectrum of **5a** exhibited absorption bands at 1621–1623 cm^{-1} due to —S—CO— of the thiopyrano ring, a band at 1716–1719 cm^{-1} corresponding to —$COOC_2H_5$ of the newly formed thiopyrano ring on a quinoline nucleus. No band at 3410–3490 cm^{-1} corresponds to the —SH and —NH groups. The ^{1}H NMR spectrum of

compound **5a** showed a triplet at 1.34–1.46 (t, $J = 7$ Hz, $-OCH_2CH_3$), which corresponds to $-CH_3$ of $-OCH_2CH_3$ and a quartet at 4.3–4.5 (q, $J = 7.1$ Hz, $-OCH_2$) attributed $-CH_2$ of $-OCH_2CH_3$. A singlet at δ2.45 (s, 3H, Ar-CH_3) methyl group on carboxylic ring. The signals due to aromatic protons seen between 7.45 (s, C_4-H), 7.73 (d, $J = 9$ Hz, C_{12}-H), 7.79 (d, $J = 9$ Hz, C_{11}-H), 7.83 (s, C_{14}-H), and 8.59 (s, C_{10}-H). Mass spectrum of compound **5a** consistent with structure assigned to the molecule m/z 299. A peak was observed at m/z 299, on the basis of which it was assigned the structure ethyl-7-methyl-2-oxo-2*H*-thiopyrano[2,3-*b*]quinoline-3-carboxylate **5a**. Similarly, structures of all the compounds **5b–e** were assigned on the basis of their spectral data and were placed in appropriate places.

By a similar route, the treatment of 3-formyl-2-mercapto quinoline with ethyl cyanoacetate **3c** afforded **6a**. The IR spectrum of **6a** shows absorption bands at 2210–2213 cm^{-1} corresponding to a cyano group stretching frequency. 1618–1625 cm^{-1} corresponding to —S—CO— of the thiopyrano ring. The ^{1}H NMR spectrum of compound **6a** exhibited usual signals at δ2.59 (s, 3H, Ar-CH_3), which correspond to 3 protons of methyl group present on a carbocyclic ring. Signals due to aromatic protons appeared at 7.56 (s, C_4-H), 7.71 (d, $J = 9$ Hz, C_{12}-H), 7.83 (s, C_{14}-H), 7.87 (d, $J = 9$ Hz, C_{11}-H), and 8.65 (s, C_{10}-H). Further, the structure; was confirmed by its mass spectrum; it gave at m/z 252. Similarly, the structures of **6b–e** were assigned and given in an appropriate place.

EXPERIMENTAL

All melting points were determined in an open capillary and are uncorrected. The purity of the compounds was checked by TLC on silica gel and were purified by column chromatography. ^{1}H NMR spectra (300 MHz) were recorded on a Bruker supercon FT NMR instrument using TMS as internal standard, and chemical shifts are expressed in δ units. IR spectra on a Perkin Elmer 157 Infrared spectrophotometer and mass spectra on a Jeol JMS-D 300 mass spectrometer operating at 70 eV (Table I).

The General Procedure for the Synthesis of 3-Acetyl-7-methyl-2*H*-thiopyrano[2,3-*b*]quinolin-2-one (4a)

A mixture of 3-formyl-2-mercapto quinoline **2a** (0.01 mole) and ethyl acetoacetate **3a** (0.01 mole) containing piperidene (5 drops) was taken in a mortar and mixed thoroughly with 5 mL of acetonitrile. All these

TABLE I Characterization Data of the Newly Synthesised Compounds

Compound no.	M.P. (°C)	Microwave irradiation		Mol. formula Mol. Wt.	Elemental analysis. Calcd./found (%)			
		Yield (%)	Time (Min)		C	H	N	S
4a	212	80	12	$C_{15}H_{11}NO_2S$	66.89	4.12	5.20	11.91
				269	66.75	4.10	5.37	11.81
4b	213	78	10	$C_{15}H_{11}NO_3S$	63.14	3.89	4.91	11.24
				285	63.23	3.78	4.82	11.35
4c	215	72	11	$C_{14}H_8BrNO_2S$	50.32	2.41	4.19	9.60
				334	50.45	2.39	4.27	9.29
4d	213	75	11	$C_{14}H_8ClNO_2S$	58.04	2.78	4.83	11.07
				289	50.13	2.62	4.75	11.13
4e	218	68	12	$C_{14}H_8N_2O_4S$	56.00	2.69	9.33	10.68
				300	56.08	2,53	9.55	10.57
5a	212	78	12	$C_{16}H_{13}NO_3S$	64.20	4.38	4.68	10.71
				299	64.13	4.29	6.85	10.89
5b	214	76	11	$C_{16}H_{13}NO_4S$	60.94	4.16	4.44	10.17
				315	60.89	4.29	4.25	10.29
5c	215	73	10	$C_{15}H_{10}BrNO_3S$	49.47	2.77	3.85	8.80
				364	48.98	2.86	3.75	8.78
5d	214	74	11	$C_{15}H_{10}ClNO_3S$	56.34	3.15	4.38	10.03
				319	56.29	3.25	4.32	10.25
5e	216	69	12	$C_{15}H_{10}N_2O_5S$	54.54	3.05	8.48	9.71
				330	54.49	3.12	8.39	9.69
6a	213	79	12	$C_{14}H_8N_2OS$	66.65	3.20	11.10	12.71
				252	66.55	3.29	11.15	12.89
6b	213	77	9	$C_{14}H_8N_2O_2S$	62.67	3.01	10.44	11.95
				268	62.57	3.10	10.39	11.89
6c	214	73	10	$C_{13}H_5BrN_2OS$	49.23	1.59	8.83	10.1
				317	49.28	1.51	8.85	10.07
6d	213	74	10	$C_{13}H_5ClN_2OS$	57.25	1.85	10.27	11.76
				272	57.12	1.83	10.18	11.64
6e	216	65	11	$C_{13}H_5N_3O_3S$	55.12	1.78	14.83	11.32
				283	55.18	1.72	14.79	11.28

contents were taken in a 100-mL beaker. The reaction mixture was placed in a microwave oven and irradiated for 8–12 min by using a Whirlpool M 542 domestic microwave oven specially designed for organic synthesis. The completion of the reaction was monitored by means of TLC; the reaction mixture **4a** was poured into ice-cold water, stirred well, filtered, and dried. An obtained brown solid was recrystallized from ethyl acetate/benzene.

3-Acetyl-7-methoxy-2*H*-thiopyrano[2,3-*b*]quinolin-2-one (4b)

As described in the general procedure, **4b** was obtained as a brown solid. The isolated compound **4b** was washed and recrystallized from ethyl acetate/benzene. IR (KBr) (cm^{-1}): 1622–1623 (C=O), 1642–1646 (–$COCH_3$). ^1H NMR (300 MHz) (DMSO-d_6) (δ) ppm; 2.6–2.62 (s, 3H, –$COCH_3$), 4.0 (s, 3H, –OCH_3), 7.41 (s, C_4–H), 7.68 (d, $J =$ 9 Hz, C_{12}-H), 7.89 (s, C_{14}-H), 7.84 (d, $J = 9$ Hz, C_{11}-H), and 8.68 (s, C_{10}–H).

3-Acetyl-7-bromo-2*H*-thiopyrano[2,3-*b*]quinolin-2-one (4c)

As described in the general procedure, **4c** was obtained as a brownish red solid. The isolated compound **4c** was washed and recrystallized from ethyl acetate. IR (KBr) (cm^{-1}): 1619–1624 (C=O), 1640–1643 (–$COCH_3$). ^1H NMR (300 MHz) (DMSO-d_6) (δ) ppm: 2.5–2.60 (s, 3H, –$COCH_3$), 7.40 (s, C_4-H), 7.67 (d, $J = 9$ Hz, C_{12}-H), 7.82 (s, C_{14}-H), 7.86 (d, $J = 9$ Hz, C_{11}-H), and 8.69 (s, C_{10}-H).

3-Acetyl-7-chloro-2*H*-thiopyrano[2,3-*b*]quinolin-2-one (4d)

As described in the general procedure, **4d** was obtained as an brown solid. The isolated compound **4d** was subjected to silica gel chromatography using methanol. IR (KBr) (cm^{-1}): 1620–1624 (C=O), 1638–1640 (–$COCH_3$). ^1H NMR (300 MHz) (DMSO-d_6) (δ) ppm; 2.4–2.72 (s, 3H, –$COCH_3$), 7.42 (s, C_4-H), 7.67 (d, $J = 9$ Hz, C_{12}-H), 7.84 (s, C_{14}-H), 7.88 (d, $J = 9$ Hz, C_{11}-H), and 8.64 (s, C_{10}-H).

3-Acetyl-7-nitro-2*H*-thiopyrano[2,3-*b*]quinolin-2-one (4e)

As described in the general procedure, **4e** was obtained as an orange solid. The isolated compound **4e** was washed and recrystallized in ethyl acetate/carbontetrachloride. IR (KBr) (cm^{-1}): 1621–1625 (C=O), 1643–1645 (–$COCH_3$). ^1H NMR (300 MHz) (DMSO-d_6) (δ) ppm: 2.5–2.78 (s, 3H, –$COCH_3$) 7.41 (s, C_4–H), 7.70 (d, $J = 9$ Hz, C_{12}-H), 7.86 (s, C_{14}-H), 7.89 (d, $J = 9$ Hz, C_{11}-H), and 8.70 (s, C_{10}-H).

The General Procedure for the Synthesis of Ethyl-7-methyl-2-oxo-2*H*-thiopyrano[2,3-*b*]quinoline-3-carboxylate (5a)

A mixture of 3-formyl-2-mercapto quinoline **2a** (0.01 mole) and diethyl malonate **4a** (0.01 mole) containing a catalytic amount of piperidene was taken in a mortar and mixed thoroughly with 5 mL of acetonitrile.

All these contents were taken in a 100-mL beaker. The reaction mixture was placed in a microwave oven and irradiated for 10–12 min by using a Whirlpool M 542 domestic microwave oven specially designed for organic synthesis. The progress of the reaction was monitored by means of TLC (eluent:ethyl acetate/benzene,1:4). The mixture was cooled at r.t. and poured on crushed ice. The precipitate **5b** thus obtained was collected by filtration, washed with water, and dried; the crude product was subjected to column chromatography using methanol. Similarly, compounds **5b–e** were synthesized.

Ethyl-7-methoxy-2-oxo-2*H*-thiopyrano[2,3-*b*]quinoline-3-carboxylate (5b)

The compound **5b** was synthesized by using the same procedure as described for **5a**. The solid compound was isolated by the extractive isolation technique, washed and recrystallized from ethanol. IR (KBr) (cm^{-1}): 1622–1625 (C=O), 1718–1720 ($-CO_2C_2H_5$). ^1H NMR (300 MHz) (DMSO-d_6) (δ) ppm: 1.31–1.47 (t, $J = 7$ Hz, OCH_2CH_3), 4.1 (3H, s, $-OCH_3$). 4.3-4.6 (q, $J = 7.1$ Hz, $-OCH_2$), 7.46 (s, C_4-H). 7.72 (d, $J = 9$ Hz, C_{12}-H), 7.83 (d, $J = 9$ Hz, C_{11}-H), 7.85 (s, C_{14}-H), and 8.65 (s, C_{10}-H).

Ethyl-7-bromo-2-oxo-2*H*-thiopyrano[2,3-*b*]quinoline-3-carboxylate (5C)

The compound **5c** was synthesized as a white solid by using the same procedure as described for **5a**. Washed and recrystalized from ethylacetate/chloroform. IR (KBr) (cm^{-1}): 1624–1626 (C=O), 1722–1725 ($-CO_2C_2H_5$). ^1H NMR (300 MHz) (DMSO-d_6) (δ) ppm: 1.30–1.42 (t, $J = 7.1$ Hz, $-OCH_2CH_3$), 4.2–4.4 (q, $J = 7.0$ Hz, OCH_2), 7.47 (s, C_4-H), 7.69 (d, $J = 9$ Hz, C_{12}-H), 7.83 (s, C_{14}-H), 7.85 (d, $J = 9$ Hz, C_{11}-H), and 8.66 (s, C_{10}-H).

Ethyl-7-Chloro-2-oxo-2*H*-thiopyrano[2,3-*b*]quinoline-3-carboxylate (5d)

The compound **5d** was synthesized as a green solid by using the same procedure as described for **5a**. The crude product was subjected to column chromatography for purification using methanol. IR (KBr) (cm^{-1}): 1626–1629 (C=O), 1721–1724 ($-CO_2C_2H_5$). ^1H NMR (300 MHz) (DMSO-d_6) (δ) ppm: 1.33–1.48 (t, $J = 7$ Hz, $-OCH_2CH_3$). 4.3–4.8 (q, $J = 7.1$ Hz, $-OCH_2$), 7.47 (s, C_4-H), 7.70 (d, $J = 9$ Hz, C_{12}-H), 7.81 (s, C_{14}-H), 7.85 (d, $J = 9$ Hz, C_{11}-H), and 8.70 (s, C_{10}-H).

Ethyl-7-nitro-2-oxo-2*H*-thiopyrano[2,3-*b*]quinoline-3-carboxylate (5e)

The compound **5e** was synthesized as a red amorphous solid by using the same procedure as described for **5a**. Washed and recrystalized from ethylacetate. IR (KBr) (cm^{-1}): 1624–1627 (C=O), 1718–1720 ($-CO_2C_2H_5$). ^1H NMR (300 MHz) (DMSO-d_6) (δ) ppm: 1.32–1.40 (t, $J = 7$ Hz, $-OCH_2CH_3$), 4.5–4.9 (q, $J = 7.2$ Hz, $-OCH_2$), 7.45 (s, C_4-H). 7.69 (d, $J = 9$ Hz, C_{12}-H), 7.80 (s, C_{14}-H), 8.69 (s, C_{10}-H).

The General Procedure for the Synthesis of 7-Methyl-2-oxo-2*H*-thiopyrano[2,3-*b*]quinoline-3-carbonitrile (6a)

A mixture of 3-formyl-2-mercapto quinoline **2a** (0.01 mole) and ethyl cyanoacetate, **6a** (0.01 mole) containing piperidene (5 drops) was taken in a mortar and mixed thoroughly with 5 mL of acetonitrile. All of these contents were taken in a 100-mL beaker. The reaction mixture was placed in a microwave oven and irradiated for 9–12 min at an interval of 1 min to avoid excess evaporation of the solvent. The completion of the reaction was monitored by means of TLC; the reaction mixture was poured into crushed ice, stirred well, and filtered; the crude product **4a** was either recrystallized from ethyl acetate/chloroform or subjected to silica gel chromatography using ethyl acetate/carbontetrachloride 5:2 as the eluent.

7-Methoxy-2-oxo-2*H*-thiopyrano[2,3-*b*]quinoline-3-carbonitrile (6b)

As described in the general procedure, **6a** was obtained as a dark solid. The crude product was subjected to silica gel chromatography using methanol. IR (KBr) (cm^{-1}): 1619–1622 (C=O), 2209–2212 (CN). ^1H NMR (300 MHz) (DMSO-d_6) (δ) ppm: 4.2–4.3 (s, 3H, $-OCH_3$), 7.56 (s, C_4-H), 7.59 (s, C_4-H), 7.70 (d, $J = 9$ Hz, C_{12}-H), 7.82 (s, C_{14}-H), 7.87 (d, $J = 9$ Hz, C_{11}-H), and 8.67 (s, C_{10}-H).

7-Bromo-2-oxo-2*H*-thiopyrano[2,3-*b*]quinoline-3-carbonitrile (6c)

As described in the general procedure, **6c** was obtained as a reddish orange solid. The isolated compound **4d** was washed and recrystallized from ethyl acetate in hexane. IR (KBr) (cm^{-1}): 1622–1625 (C=O), 2212–2215 (CN). ^1H NMR (300 MHz) (DMSO-d_6) (δ) ppm: 7.58 (s, C_4-H), 7.69 (d, $J = 9$ Hz, C_{12}-H), 7.81 (s, C_{14}-H) 8.70 (s, C_{10}-H), and 7.89 (d, $J = 9$ Hz, C_{11}-H).

7-Chloro-2-oxo-2*H*-thiopyrano[2,3-*b*]quinoline-3-carbonitrile (6d)

As described in the general procedure, **6a** was obtained as a orange solid. The crude product was isolated by using the extractive isolation technique, washed, and recrystallized from methanol/ethyl acetate. IR (KBr) (cm^{-1}): 1619–1622 (C=O), 2215–2218 (CN). ^{1}H NMR (300 MHz) (DMSO-d_6) (δ) ppm: 7.57 (s, C_4-H), 7.68 (d, $J = 9$ Hz, C_{12}-H), 7.83 (s, C_{14}-H) 7.88 (d, $J = 9$ Hz, C_{11}-H), and 8.71 (s, C_{10}-H).

7-Nitro-2-oxo-2*H*-thiopyrano[2,3-*b*]quinoline-3-carbonitrile (6e)

As described in the general procedure, **6a** was obtained as a yellowish brown solid. The crude product was subjected to silica gel chromatography using ethanol/ethylacetate. IR (KBr) (cm^{-1}): 1622–1625 (C=O), 2216–2219 (CN). ^{1}H NMR (300 MHz) (DMSO-d_6) (δ) ppm: 7.57 (s, C_4-H), 7.69 (d, $J = 9$ Hz, C_{12}-H), 7.80 (s, C_{14}-H), 7.89 (d, $J = 9$ Hz, C_{11}-H), and 8.62 (s, C_{10}-H).

TABLE II Results of Antimicrobial Activity Tests of Thiopyrano[2,3-*b*]quinolines

Compound no.	Microorganism		
	S. aureus	*M. roseus*	*E. coli*
Ampicillin	20	22	22
4a	5	4	5
4b	4	5	4
4c	4	3	3
4d	3	5	5
4e	5	8	7
5a	3	3	4
5b	4	5	5
5c	5	4	4
5d	3	5	3
5e	3	4	5
6a	2	9	4
6b	4	7	3
6c	8	8	5
6d	15	16	11
6e	17	17	10

Zone of inhibition was expressed in mm.

ANTMICROBIAL ACTIVITY

The in vitro antimicrobial activity was carried out against 24-h-old cultures of three bacteria by the disk diffusion method[29] using ampicillin as the reference. Compounds **4a–e**, **5a–e**, and **6a–e** were tested against Gram positive bacteria (*Staphylococcus aureus*, *Micrococcus roseus*) and a Gram negative bacteria (*Escherichia coli*). The compounds were tested at a concentration of 0.001 mol/mL in DMF against all organisms. The zone of inhibition was compared with the standard drug after 24 h of incubation at 25°C and was measured in mm. The results are reported in Table II, it was found that compounds **6d** and **6e** were highly active against *S. aureus* and *M. roseus* (gram positive) and moderately active against *E. coli* (gram negative). Compound **4e** was slightly active against *M. roseus*, and *E. coli*. Compound **6e** was slightly active against *S. aureus* and *M. roseus*, and compounds **6a** and **6b** were slightly active against *M. roseus.* Other compounds were all inactive against these three pathogenic microorganisms. Hence, further studies in these compounds are planned to obtain clinically useful agents.

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