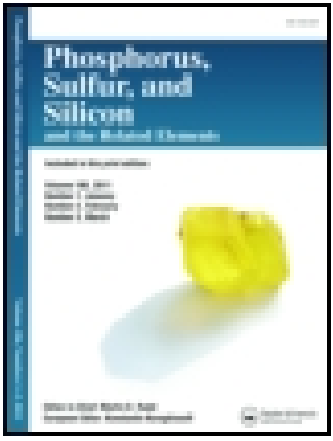

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Microwave Induced One-Pot Synthesis of Some New Thiopyrano[2,3-b]quinolin-2-ones under Solvent-Free Conditions

M. Raghavendra [a] , Halehatty S. Bhojya Naik [a] & Bailure S. Sherigara [a]

[a] Department of P G Studies and Research in Industrial Chemistry, School of Chemical Sciences , Kuvempu University , Shankaraghatta, Karnataka, India

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M. Raghavendra, Halehatty S. Bhojya Naik, and Bailure S. Sherigara
Department of P G Studies and Research in Industrial Chemistry, School of Chemical Sciences, Kuvempu University, Shankaraghatta, Karnataka, India

A series of some new thiopyrano[2,3-b]quinolin-2-one ***2a-i*** *have been synthesized by the one pot reaction between 2-mercaptoquinoline-3-carbaldehyde* ***1a-i*** *and phenoxyacetic acid using TEA catalyst under microwave irradiation in solvent free conditions. The procedure is simple, environmentally benign and occurs in good yields. All the newly synthesized compounds were characterized by elemental analyses, IR,* ^{1}*H NMR and mass spectral data.*

Keywords 2-Mercaptoquinoline-3-carbaldehyde; phenoxyacetic acid; solvent free; thiopyrano[2,3-*b*]quinolin-2-one

INTRODUCTION

Five- and six-membered heterocyclic compounds, containing one or two heteroatoms, fused to quinoline ring in a linear fashion are found in natural products, as well as in synthetic compounds of biological interest.[1,2] They are known to exhibit antiallergenic, antifungal,hypocholesterolemic, hypolemic, antibacterial, and antiviral properties.[3–7] In addition, various fused system of quinolines were studied for their intercalative DNA binding properties.

A literature survey reveals the 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.[8] The antitumor drugs that

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Address correspondence to Halehatty S. Bhojya Naik, Department of P G Studies and Research in Industrial Chemistry, School of Chemical Sciences, Kuvempu University, Shankaraghatta 577-451, Karnataka, India. E-mail: hsb_naik@rediffmail.com

intercalate DNA are of growing interest in the field of anticancer derivatives. Generally, they are characterized 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.[9] DNA binding studies of pyrimidothienoquinolines have been recently reported in the literature.[10]

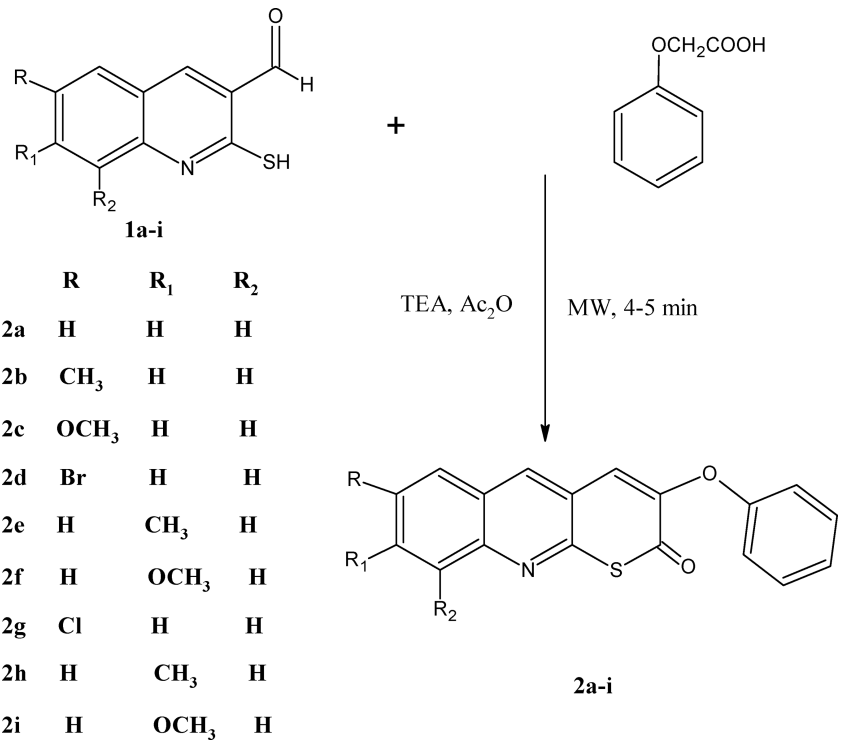
The beneficial effects of microwave irradiation are playing an increasing role in process chemistry, especially in cases where classical methods require forcing conditions or prolonged reaction times. When processes involve sensitive reagents, or there is the possibility of compound decomposition under prolonged reaction conditions. Solvent-free reaction techniques were successfully coupled with microwave because they avoid the use of low boiling point solvents, which may sometimes lead to explosions. Additionally, it can also avoid the use of poisonous and expensive solvents, and as such can be environmentally benign, and make manipulations much easier. The use of microwave for the synthesis of organic compounds under solvent-free conditions proved to be an efficient safe and environmentally benign techniques that with shorter reaction time, high yields, and easier manipulation.[11–14]

RESULTS AND DISCUSSION

As mentioned earlier, condensed quinolines have a wide range of biological activities, therefore, they are useful materials in drug research. Hence, in continuation of our studies in the synthesis of condensed quinoline derivatives,[15–18] due to their significant biological activities, it appeared expedient to synthesize a condensed quinoline that is presented here in the present study.

2-Mercaptoquinoline-3-carbaldehyde**1a–i**, were found to be excellent starting materials for the synthesis of novel thiopyrano[2,3-*b*]quinolin-2-one derivatives. The starting compounds were prepared according to the literature method.[19] Then cyclization of **1a–i** with phenoxyacetic acid under microwave irradiation, in the presence of basic conditions in one pot furnished the title compounds **2a–i**, in good to excellent yields (Scheme 1). The structure of the compounds was confirmed based on elemental analysis and spectral data (Experimental section).

The IR spectrum of compound **2a–i** showed an absence of SH, NH, and CHO stretching frequency in the region 3100–3400 and between 1650–1670 cm^{-1}, which appeared in the substituted 3-formyl-2-mercapto quinolines.[19] In addition IR (KBr) spectra of (**2a–i)** exhibiting absorption bands in the region 1630–1645 cm^{-1} due to (C = O) group. The ^{1}H NMR (DMSO-d6) spectrum of the compound **2a**–**i** displayed



	R	R_1	R_2
2a	H	H	H
2b	CH_3	H	H
2c	OCH_3	H	H
2d	Br	H	H
2e	H	CH_3	H
2f	H	OCH_3	H
2g	Cl	H	H
2h	H	CH_3	H
2i	H	OCH_3	H

SCHEME 1

a singlet in the region δ 9.0–9.2 (s, 1H, H4), another singlet in the region 8.75–8.95 (s, 1H, H5) and the aromatic protons were resonated between δ 7.20–8.60, indicates the attachment of the reactive partner to the quinoline moiety. Finally, above stated compound confirmed by mass spectral data (Experimental section)

CONCLUSION

In conclusion, a simple efficient and environmentally benign method has been developed for the synthesis of thiopyrano[2,3-*b*]quinolin-2-one under microwave irradiation in solvent-free conditions. This microwave irradiation method is superior from the view of a yield and reaction time compared to the conventional (thermal) method (experimental section).

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. The FT-IR spectra were recorded on NICOLETAVATAR 360-FTIR

instrument by using KBr pellets. The ^{1}H NMR were recorded on a BRUCKER AMX-400 spectrometer operating at 400 MHz. Mass spectra were recorded on AGILENT LC-MSD-TRAP-XCT mass spectrometer Elemental analyses were done on Vario EL. CHNOS elemental analyzer.

General MW Procedure for the Synthesis of Substituted Thiopyrano[2,3-*b*]quinolin-2-one 2a–i

Mixture of substituted quinoline **1a** (0.180 g, 0.001 mol), phenoxyacetic acid (0.152 g, 0.001 mol), TEA (0.1515 g, 0.0015 mol) and acetic anhydride (0.306 g, 0.003 mol) were taken in 50 ml beaker, mixed well. The contents were irradiated under microwave oven for about 4 min at an interval of 30 s at 160 W. The completion of reaction was monitored by TLC, the product **2a** was poured into ice-cold water. The obtained yellow color solid was filtered washed with water then recrystallized from acetonitrile, gave 80% yield. The same procedure was used for the synthesis of (**2b–i**)

Conventional Method

A mixture of substituted quinoline **1a** (0.180 g, 0.001 mol) and phenoxyacetic acid (0.152 g, 0.001 mol) TEA (0.1515 g, 0.0015 mol), acetic anhydride (0.306 g, 0.003 mol) and 20 ml of anhydrous DMF were taken in 100 ml round-bottom flask, refluxed for 10 h. After completion of the reaction confirmed by TLC, reaction mixture was concentrated, then poured into ice-cold water. The obtained yellow color solid was filtered, washed with water then recrystallized from acetonitrile, gave 59% yield. The same procedure was used for the synthesis of (**2b–i**).

Physical and Spectral Data of the Products

3-Phenoxy-2H-thiopyrano[2,3-b]quinolin-2-one (2a)

Solid, m.p. 194–196°C; Yield 80% (MW), 59% (Conventional); Irradiation time 4 min (MW), reflux 10 h (conventional); ^{1}H NMR (400 MHz, DMSO-d6) δ (ppm): 9.10 (s, 1H, H4), 8.80 (s, 1H, H5), 7.30–8.50 (m, 9H, Ar−H); IR (KBr) ν (cm^{-1}): 1630 (C = O); MS, m/z 305 [M+], Anal. Calcd.. for $C_{18}H_{11}NO_2S$: C, 70.81; H, 3.60; N, 4.59. Found: C, 70.79; H, 3.62; N, 4.57.

7-Methyl-3-phenoxy-2H-thiopyrano[2,3-b]quinolin-2-one (2b)

Solid, m.p. 213–215°C; Yield 84% (MW), 63% (Conventional); Irradiation time 5 min (MW), reflux 10 h (conventional); ^{1}H NMR (400 MHz, DMSO-d6) δ (ppm): 2.35 (s CH_3 protons), 9.2 (s, 1H, H4), 8.90 (s, 1H,

H5), 7.30–8.55 (m, 11H, Ar−H); IR (KBr) ν (cm^{-1}): 1635 (C = O); MS, m/z 319 [M+], Anal. Calcd. for $C_{19}H_{13}NO_2S$: C, 71.47; H, 4.07; N, 4.38. Found: C, 71.49; H, 4.09; N, 4.35.

7-Methoxy-3-phenoxy-2H-thiopyrano[2,3-b]quinolin-2-one (2c)

Solid, m.p. 224–226°C; Yield 81% (MW), 60% (Conventional); Irradiation time 4 min (MW), reflux 10 h (conventional); ^{1}H NMR (400 MHz, DMSO-d6) δ (ppm): 3.90 (s OCH_3 protons), 9.10 (s, 1H, H4), 8.85 (s, 1H, H5), 7.25–8.45 (m, 11H, Ar−H); IR (KBr) ν (cm^{-1}): 1640 (C = O); MS, m/z 335 [M+], Anal. Calcd. for $C_{19}H_{13}NO_3S$: C, 68.05; H, 3.88; N, 4.18. Found: C, 68.02; H, 3.40; N, 4.21.

7-Bromo-3-phenoxy-2H-thiopyrano[2,3-b]quinolin-2-one (2d)

Solid, m.p. 245–247°C; Yield 82% (MW), 55% (Conventional); Irradiation time 4 min (MW), reflux 10 h (conventional); ^{1}H NMR (400 MHz, DMSO-d6) δ (ppm): 9.0 (s, 1H, H4), 8.80 (s, 1H, H5), 7.35–8.60 (m, 8H, Ar−H); IR (KBr) ν (cm^{-1}): 1635 (C = O); MS, m/z 384 [M+], Anal. Calcd. for $C_{18}H_{10}BrNO_2S$: C, 56.25; H, 2.60; N, 3.64. Found: C, 56.23; H, 2.58; N, 3.62.

8-Methyl-3-phenoxy-2H-thiopyrano[2,3-b]quinolin-2-one (2e)

Solid, m.p. 197–199°C; Yield 79% (MW), 62% (Conventional); Irradiation time 5 min (MW), reflux 10 h (conventional); ^{1}H NMR (400 MHz, DMSO-d6) δ (ppm): 2.35 (s CH_3 protons), 9.20 (s, 1H, H4), 8.90 (s, 1H, H5), 7.25–8.50 (m, 11H, Ar−H); IR (KBr) ν (cm^{-1}): 1645 (C = O); MS, m/z 319 [M+], Anal. Calcd. for $C_{19}H_{13}NO_2S$: C, 71.47; H, 4.07; N, 4.38. Found: C, 71.49; H, 4.04; N, 4.41.

8-Methoxy-3-phenoxy-2H-thiopyrano[2,3-b]quinolin-2-one (2f)

Solid, m.p. 203–205°C; Yield 85% (MW), 57% (Conventional); Irradiation time 5 min (MW), reflux 10 h (conventional); ^{1}H NMR (400 MHz, DMSO-d6) δ (ppm): 3.95 (s OCH_3 protons) 9.15 (s, 1H, H4), 8.80 (s, 1H, H5), 7.30–8.55 (m, 11H, Ar−H); IR (KBr) ν (cm^{-1}): 1630 (C = O); MS, m/z 335 [M+], Anal. Calcd. for $C_{19}H_{13}NO_3S$: C, 68.05; H, 3.88; N, 4.18. Found: C, 68.09; H, 3.85; N, 9.15.

7-Chloro-3-phenoxy-2H-thiopyrano[2,3-b]quinolin-2-one (2g)

Solid, m.p. 237–239°C; Yield 84% (MW), 55% (Conventional); Irradiation time 5 min (MW), reflux 10 h (conventional); ^{1}H NMR (400 MHz, DMSO-d6) δ (ppm): 9.10(s, 1H, H4,), 8.75 (s, 1H, H5), 7.20–8.45 (m, 8H, Ar−H); IR (KBr) ν (cm^{-1}): 1635 (C = O); MS, m/z 339 [M+], Anal. Calcd.

for $C_{18}H_{10}ClNO_2S$: C, 63.71; H, 2.94; N, 4.13. Found: C, 63.73; H, 2.97; N, 4.16.

9-Methyl-3-phenoxy-2H-thiopyrano[2,3-b]quinolin-2-one (2h)

Solid, m.p. 217–219°C; Yield 83% (MW), 64% (Conventional); Irradiation time 4 min (MW), reflux 10 h (conventional); ^{1}H NMR (400 MHz, DMSO-d6) δ (ppm): 2.30 (s CH_3 protons), 9.20 (s, 1H, H4), 8.90 (s, 1H, H5), 7.35–8.60 (m, 11H, Ar−H); IR (KBr) ν (cm^{-1}): 1630 (C = O); MS, m/z 319 [M+], Anal. Calcd. for $C_{19}H_{13}NO_2S$: C, 71.47; H, 4.07; N, 4.38. Found: C, 71.49; H, 4.05; N, 4.35.

9-Methoxy-3-phenoxy-2H-thiopyrano[2,3-b]quinolin-2-one (2i)

Solid, m.p. 209–211°C; Yield 80% (MW), 61% (Conventional); Irradiation time 5 min (MW), reflux 10 h (conventional); ^{1}H NMR (400 MHz, DMSO-d6) δ (ppm): 3.90 (s OCH_3 protons), 9.15 (s, 1H, H4), 8.95 (s, 1H, H5), 7.30–8.55 (m, 11H, Ar−H); IR (KBr) ν (cm^{-1}): 1635 (C = O); MS, m/z 335 [M+], Anal. Calcd. for $C_{19}H_{13}NO_3S$: C, 68.05; H, 3.88; N, 4.18. Found: C, 68.09; H, 3.92; N, 4.20.

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