September 2007 Volume 3 Issue 3

Trade Science Inc.

Organic CHEMISTRY

An Indian Journal

Full Paper

OCAIJ, 3(3), 2007 [134-137]

Microwave Induced One Pot Synthesis Of Some New 3-(Phenylthio)-2*H*-Thiopyrano[2,3-b]Quinolin-2-One Under Solvent Free Condition

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Received: 12th May, 2007 ; Accepted: 17th May, 2007

ABSTRACT

A series of some new 3-(phenylthio)-2H-thiopyrano[2,3-b]quinolin-2-one have been synthesised by the one pot reaction between 2-mercaptoquinoline-3-carbaldehyde and (phenylthio)acetic 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 synthesised compounds were characterized by elemental analyses, IR, ^{1}H-NMR and mass spectral data.

KEYWORDS

2-mercaptoquinoline-3-carbaldehyde;
Phenylthio acetic acid;
3-(Phenylthio)-2H-thiopyrano[2,3-b] quinolin-2-one

INTRODUCTION

Quinoline moiety is a characteristic component of a large number of antibacterial and/or anticancer agents[1–5], also they possess antimitotic activity[6–8]. Particularly Several tricyclic compounds containing quinoline moiety have been reported to act as antitumoral agents[9-12]. The activity of these compounds seems to be due to their interaction with DNA[13,14].

The antitumor drugs that intercalate DNA are of growing interest in the field of anticancer derivatives as said earlier, they are Generally 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[15].

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 using of low boiling point solvents, which may sometimes lead to explosions. Additionally, it can also avoid the use of poisonous and expensive solvent, 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[16-19].

EXPERIMENTAL

Melting points are 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 3-(phenylthio)-2*H*-thiopyrano[2,3-b]quinolin-2-one (2a-i)

Mixture of substituted quinoline **(1a)**(0.180g, 0.001mol), (phenylthio)acetic acid(0.168g, 0.001mol) and acetic anhydride (0.0015mol) were taken in 50ml beaker mixed well with glass rod then the contents were irradiated under microwave oven for about 4 minutes at an interval of 30sec at 160W. The completion of reaction was monitored by TLC, the product **(2a)** was poured into ice-cold water. The obtained yellow colour solid was filtered washed with water then recrystallised from acetonitrile, results in 80% yield. The same procedure was used for the synthesis of **(2b-i)**.

Conventional method

Mixture of substituted quinoline **(1a)**(0.180g, 0.001mol) and(phenylthio)acetic acid (0.168 g, 0.001mol) acetic anhydride(0.0015mol) and 20ml of anhydrous DMF were taken in 100 ml round bottom flask, kept for reflux for about 10hours after the completion of the reaction confirmed by TLC, reaction mixture was concentrated then poured into ice cold water. The obtained yellow colour solid was filtered washed with water then recrystallised from acetonitrile. The same procedure was used for the synthesis of**(2b-i)**.

Physical and spectral data of the products

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

Solid, mp.184-186^{0}C; Yield 80% (MW), 60% (Conventional); ^{1}H-NMR(400MHz, DMSO-d6) δ(ppm): 9.05(s, 1H, H4), 8.70(s, 1H, H5), 7.20-8.40(m, 9H, Ar-H); IR(KBr) ν(cm^{-1}): 1635 (C=O); MS, m/z 321 [M+], Anal.Calcd for $C_{18}H_{11}NOS_2$: C, 67.28; H, 3.42; N, 4.36. Found: C, 67.30; H, 3.46; N, 4.39.

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

Solid, m.p.215-217^{0}C; Yield 82%(MW), 62% (Conventional); ^{1}H-NMR(400MHz, DMSO-d6) δ(ppm): 3.90(s OCH_3 protons), 9.0(s, 1H, H4), 8.80(s, 1H, H5), 7.15-8.35(m, 11H, Ar-H); IR (KBr) ν(cm^{-1}): 1645(C=O); MS, m/z 351[M$^+$], Anal.Calcd for $C_{19}H_{13}NO_2S_2$: C, 64.95; H, 3.70; N, 3.98. Found: C, 64.91; H, 3.75; N, 3.94.

8-Methoxy-3-(phenylthio)-2H-thiopyrano[2,3-b]quinolin-2-one (2c)

Solid, m.p. 197-199^{0}C; Yield 84%(MW), 59% (Conventional); ^{1}H-NMR (400MHz, DMSO-d6) (ppm): 3.95(s OCH_3 protons) 9.05(s, 1H, H4), 8.75(s, 1H, H5), 7.25-8.45(m, 11H, Ar-H); IR (KBr) ν(cm^{-1}): 1640(C=O); MS, m/z 351[M$^+$], Anal.Calcd for $C_{19}H_{13}NO_2S_2$: C, 64.95; H, 3.70; N, 3.98. Found: C, 64.98; H, 3.75; N, 3.92.

9-Methyl-3-(phenylthio)-2H-thiopyrano[2,3-b]quinolin-2-one (2d)

Solid, m.p. 205-207^{0}C; Yield 82%(MW), 65% (Conventional); ^{1}H-NMR(400MHz, DMSO-d6) δ(ppm): 2.30(s CH_3 protons), 9.10(s, 1H, H4), 8.80(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 $C_{19}H_{13}NOS_2$: C, 68.05; H, 3.88; N, 4.18. Found: C, 68.09; H, 3.92; N, 4.20.

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

Solid, m.p. 201-203^{0}C; Yield 85%(MW), 62%(Conventional); ^{1}H-NMR(400MHz, DMSO-d6) (ppm): 2.35(s CH_3 protons), 9.05(s, 1H, H4), 8.70(s, 1H, H5), 7.25-8.45(m, 11H, Ar-H); IR(KBr) ν(cm^{-1}): 1645(C=O); MS, m/z 335[M$^+$], Anal.Calcd for

$C_{19}H_{13}NOS_2$: C, 68.05; H, 3.88; N, 4.18. Found: C, 68.01; H, 3.84; N, 4.22.

7-Bromo-3-(phenylthio)-2H-thiopyrano[2,3-b]quinolin-2-one (2f)

Solid, m.p. 243-245^{0}C; Yield 83%(MW), 58%(Conventional); ^{1}H-NMR(400MHz, DMSO-d6) (ppm): 9.0(s, 1H, H4), 8.70(s, 1H, H5), 7.20-8.40(m, 8H, Ar-H); IR(KBr) ν(cm^{-1}): 1645(C=O); MS, m/z 400[M$^+$], Anal.Calcd for $C_{18}H_{10}BrNOS_2$: C, 54.00; H, 2.50; N, 3.50. Found: C, 54.04; H, 2.56; N, 3.55.

8-Methyl-3-(phenylthio)-2H-thiopyrano[2,3-b]quinolin-2-one (2g)

Solid, m.p.190-192^{0}C; Yield 82%(MW), 62% (Conventional); ^{1}H-NMR(400MHz, DMSO-d6) (ppm): 2.35(s CH_3 protons), 9.10(s, 1H, H4), 8.70(s, 1H, H5), 7.15-8.35 (m, 1H, Ar-H); IR (KBr) ν(cm^{-1}): 1640(C=O); MS, m/z 335[M$^+$], Anal. Calcd for $C_{19}H_{13}NOS_2$: C, 68.05; H, 3.88; N, 4.18. Found: C, 68.08; H, 3.92; N, 4.21.

9-Methoxy-3-(phenylthio)-2H-thiopyrano[2,3-b]quinolin-2-one (2h)

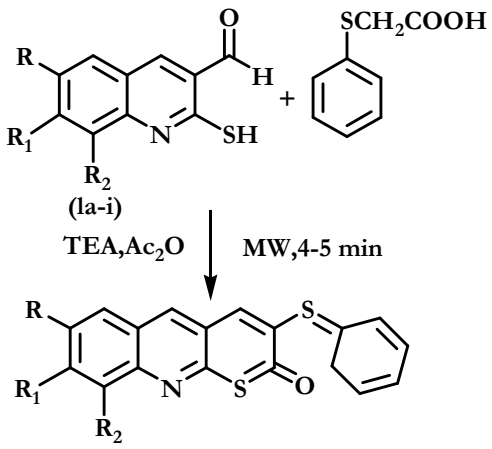
Solid, m.p.193-195^{0}C; Yield 80%(MW), 61%(Conventional); ^{1}H-NMR(400MHz, DMSO-d6) δ(ppm): 3.90(s OCH_3 protons), 9.05(s, 1H, H4), 8.80(s, 1H, H5), 7.20-8.45(m, 11H, Ar-H); IR (KBr) ν(cm^{-1}): 1640 (C=O); MS, m/z 351[M$^+$], Anal.Calcd for $C_{19}H_{13}NO_2S_2$: C, 64.95; H, 3.70; N, 3.98. Found: C, 64.97; H, 3.75; N, 3.93.

7-Chloro-3-(phenylthio)-2H-thiopyrano[2,3-b]quinolin-2-one (2i)

Solid, m.p.225-227^{0}C; Yield 86%(MW), 58%(Conventional); ^{1}H-NMR(400MHz, DMSO-d6) δ(ppm): 9.05(s, 1H, H4,), 8.70(s, 1H, H5), 7.10-8.35(m, 8H, Ar-); IR(KBr) ν(cm^{-1}): 1645 (C=O); MS, m/z 355[M$^+$], Anal.Calcd for $C_{18}H_{10}ClNOS_2$: C, 60.84; H, 2.81; N, 3.94. Found: C, 60.86; H, 2.83; N, 3.97.

RESULTS AND DISCUSSION

As mentioned earlier condensed quinolines have wide range of biological activities, therefore, they are a useful material in drug research. Hence, in continuation of our study in synthesis of condensed



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

SCHEME 1

quinolines derivatives[20-24], due to their significant biological activities, it appeared expedient to synthesize a condensed quinoline in the present study.

2-mercaptoquinoline-3-carbaldehyde **(1a-i)**, were found to be the excellent starting material for the synthesis of novel 3-(phenylthio)-2H-thiopyrano[2,3-b]quinolin-2-one derivatives. The starting compounds were prepared according to literature method[19]. Then cyclisation of **(1a-i)** with (phenylthio)acetic acid, under microwave irradiation, in basic condition in one pot furnished the title compounds **(2a-i)**, in good yields(SCHEME 1). The structure of the compounds were confirmed on the basis of elemental analysis and spectral data (Experimental section).

As an example, the IR spectrum of compound **(2a)** showed an absence of SH, NH, and CHO stretching frequency in the region of 3100-3400 and 1648cm^{-1}, which appeared in the 3-formyl-2-mercaptoquinoline[24].

The IR(KBr) spectra of(2a) exhibiting absorption band in the region 1635cm^{-1} due to (C=O) group. The ^{1}H-NMR(DMSO-d6) spectrum of the compound (**2a**) displayed a singlet at δ9.05(s, 1H, H4), another singlet at 8.70(s, 1H, H5); remaining aromatic protons resonated between δ7.20-8.40(m, 9H, Ar-H),

indicates the attachment of the reactive partner to the quinoline moiety. Finally above stated compound confirmed by the appearance of the molecular peak at m/z 321 (M^+).

CONCLUSION

A simple efficient and environmentally benign method has been developed for the synthesis of 3-(phenylthio)-2H-thiopyrano[2,3-b]quinolin-2-one under microwave irradiation in solvent free condition also compared with the conventional method. The reaction is proceed through initial condensation of aldehyde group of quinoline with the -CH_2 group of acid followed by the dehydration of the water between -OH group of acid with the -SH group of quinolines.

This microwave irradiation method is superior from the view of an yield, reaction time compared to the conventional (thermal) method. (experimental section)

ACKNOWLEDGEMENT

Authors thankful to The Director, Sophosticated instrumentation facility center, IISc, Bangalore, for the spectral data.

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