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Full Length Research Paper

Synthesis of novel 2-quinolone derivatives

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In this work, N-amino quinoline-2-one (2) has been synthesized by the reflux of coumarin (1) with hydrazine hydrate (99%) in ethanol for 12 h. The azomethines (3-6) were prepared from the corresponding aryl aldehydes and ketones. Tetrazine derivative (7) was prepared from the reaction of compound (2) with CS2 and hydrazine hydrate in the presence of potassium hydroxide. However, the reaction of compound (2) with thiol compounds afforded the derivatives (8-14). Finally, condensation of compound (11) with 4-hydroxy benzaldehyde brought about the derivative (15). The structures of the synthesized compounds were deduced by using some spectroscopic methods, FT-IR, UV-Visible and NMR.

Key words: 2-quinolone, Schiff bases, hydrazine hydrate.

INTRODUCTION

2-quinolone derivatives were found to be associated with various biological activities such as antitumor (Joseph et al., 2002), antimalarial (Xiao et al., 2001), antiplatelet (Nishi et al., 2000), antidepressant (Oshiro et al., 2000), antiulcer (Banno et al., 1988), plant virucides (Hung et al., 1996; Dia et al., 2004), antioxidant activity (Al-Omar et al., 2006) and herbicides (Khan et al., 2003). Many substituted quinoline-2-one derivatives have recently craned great interest in chemotherapy as ant tumor drugs (Jin et al., 2005; Wissner et al., 2000). Also a number of quinolones are excellent reservoir of bioactive substances (Al-Bayati et al., 2004). 2-Quinolones are also valuable intermediates in organic synthesis, since they are easily converted into 2-chloro and 2-amino-quinoline derivatives (Godard et al., 1994).

Some Schiff bases bearing heterocyclic residues possess biological activities, such as analgesic, antiviral, antifungal and anticancer (Jarrahpour et al., 2004).

In the present study, N-amino quinoline-2-one was allowed to react with aryl aldehydes and ketones, carbondisulfide and then hydrazine hydrate and thiol compounds (Scheme 1).

EXPERIMENTAL

General

Melting points were determined on GallenKamp (MFB-600) melting point apparatus and were uncorrected. The IR spectra of the compounds were recorded on a shimadzu FT-IR-8300 spectro-meter as KBr disk. The UV spectra were performed on Cintra-5-Gbes scientific equipment. The 1H-NMR and 13C-NMR spectra (solvent DMSO-d6) were recorded on Bruker 400 MHz spectrophotometer using TMS as internal standard.

Synthesis of N-amino quinoline-2-one (2)

Coumarin (1.46 g, 0.01 mol) with excess hydrazine hydrate (99%) (3.2 g, 0.1 mol) in absolute ethanol (25 ml) was refluxed for 12 h, it was then cooled and the formed solid was collected and recrystallized from chloroform (Table 1).

Synthesis of Schiff bases (3-8)

A mixture of compound 2 (0.8 g, 0.005 mol) and the appropriate aryl aldehyde or ketone (0.005 mol) or (0.0025 mol) of Terphthaldehyde was refluxed in absolute ethanol (25 ml) for 6 to 8 h. The reaction mixture was cooled and the product obtained was recrystallized from appropriate solvent (Table 1).

Synthesis of compound (7)

To a solution of compound 2 (0.5 g, 0.003 mol) in absolute ethanol (20 ml) was added potassium hydroxide (0.003 mol) and carbon disulphide (2.2 ml). The mixture was stirred for 1 h at 15 to 20˚C, to the stirred mixture was added hydrazine hydrate (0.03 mol) and stirring continued at 45 to 55℃ for 1 h. On the addition of water, a solid was separated and was recrystallized from ethanol (Table 1).

Synthesis of compounds (8-14)

Compound 2 (0.65g, 0.004 mol) and appropriate thiol compounds

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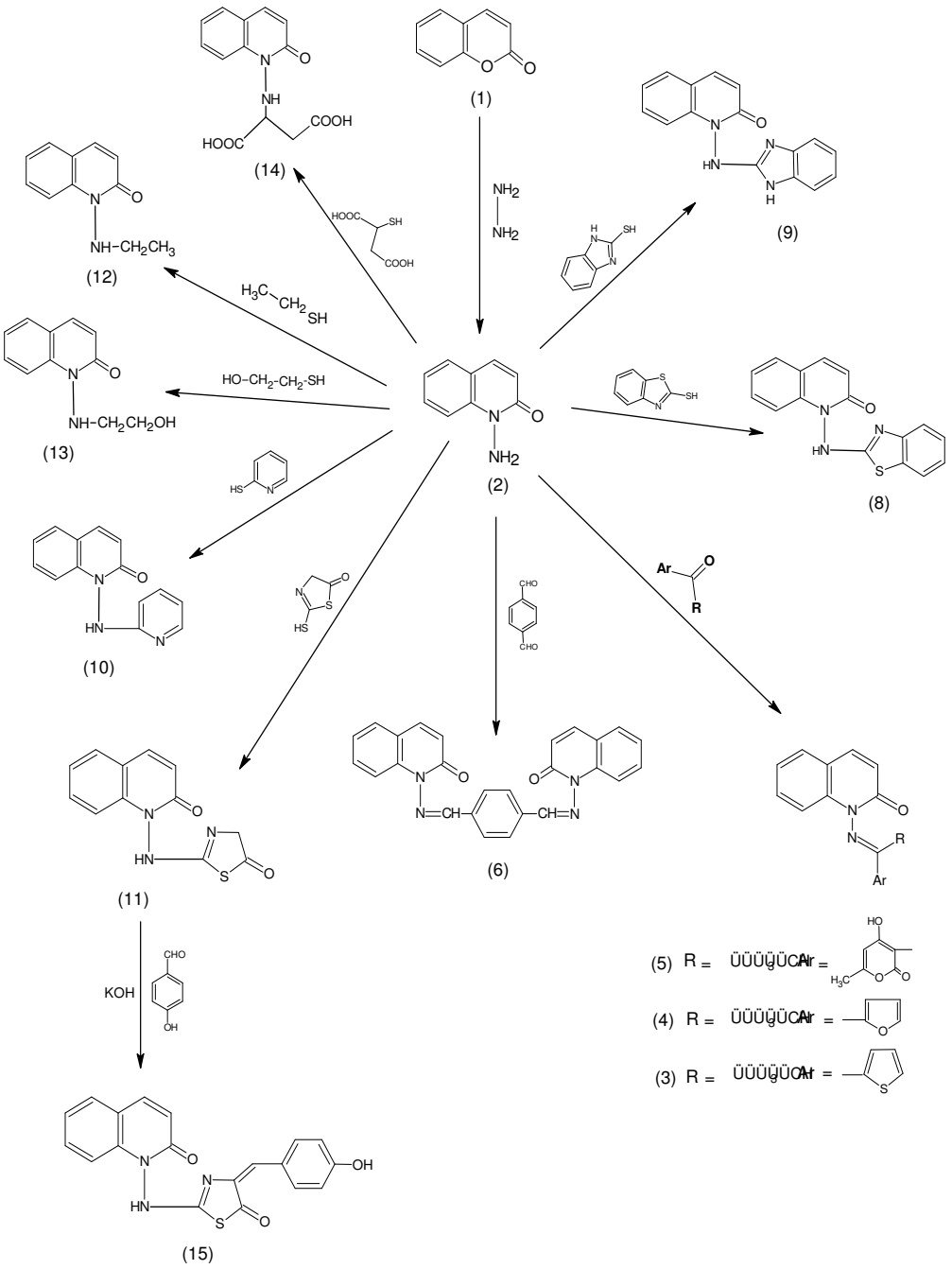

Scheme 1. The reaction of N-amino quinoline-2-one with aryl aldehydes and ketones, carbondisulfide and then hydrazine hydrate and thiol compounds.

(0.004 mol) in absolute ethanol (30 ml) were refluxed, and the time of the reaction was monitored by lead acetate paper. After that the reaction mixture was left to cool and then the solid was separated and recrystallized from the proper solvent (Table 1).

Synthesis of compound (15)

To a solution of compound 11 (0.77 g, 0.003 mol) and potassium hydroxide (0.7 g) in absolute ethanol (30 ml), 4-hydroxy benzaldehyde (0.003 mol) was added and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was neutralized (pH = 6-7) by adding a 10% hydrochloric acid. The precipitate was obtained and filtered off and was then recrystallized from ethanol (Table 1).

RESULTS AND DISCUSSION

N-amino quinoline-2-one (2) was obtained by heating a mixture of coumarin with large excess of hydrazine hydrate in boiling absolute ethanol for 12 h with yield 91%.

Table 1. Physical properties of synthesized compounds.

Comp. no.	M. P (°C)	Yield %	Recryst. Solvent
2	131 - 133	91	Chloroform
3	85 - 87	72	Ethanol
4	60 - 62	80	Ethanol
5	80 - 82	84	Ethanol
6	280 dec	84	Ethanol
7	172 - 174	93	Ethanol
8	72 - 74	92	Ethanol
9	106 - 108	91	Ethanol
10	Oily	87	Ben-MeOH (7:3)*
11	102 - 104	85	Ethanol
12	158 - 160	89	Acetone
13	Oily	80	Ben-MeOH (7:3)*
14	Oily	78	Ben-MeOH (7:3)*
15	90 - 92	72	Ethanol

* Column chromatography.

Table 2. U.V and FT-IR spectral data for compound (2).

Comp. no.	U.V ethanol		Characteristic bands of FT-IR (cm^{-1} , KBr disk)				
	λ_{max} (nm)	ε_{max}	Cυ= O	υC=C_{ar}	υC—H_{ar}	υC— N	Others
2	280 227	0.93 1.8	1645	1595 1452	3045	1242	uNH_2 3200,3300

The structure of compound (2) was confirmed from its spectral data. The IR spectrum showed two strong absorption bands at 3290 to 3300 cm^{-1} and strong band at 1645 cm^{-1}, corresponding to υNH2 and υC=O, respectively (Table 2). 1H-NMR: 4.1(s, 2H, -NH2), 6.7(t, Ar-H), 7.4(d, Ar-H) and 7.1(d,Ar-H). 13C-NMR: 126, 127, 127.8, 128, 123.3, 128.5, 129, 155 and 157.

Reaction of compound (2) with aromatic aldehydes and ketones in boiling absolute ethanol afforded 3-arylidene derivatives (3-6). IR spectra of these derivatives showed the disappearance of the absorption bands for NH2, while it showed bands due to C=O and C=N groups at 1662 to 1683 and 1583 to 1621 cm^{-1}, respectively (Table 3) . 1H-NMR of compound (3) showed: 2.3(s, 3H, -CH3), 7.6(d, Ar-H), 7.5(d,Ar-H), 7.1(t, Ar-H), 7.9(d, -C=C-H) and 7.97(d, -C=C-H). 13C-NMR: 15, 23, 126, 128, 128.2, 129, 129.8, 130, 131, 131, 133, 135, 143, 144 and 157. reaction of compound (2) with carbon disulfide and hydrazine hydrate in the presence of potassium hydroxide afforded the tetrazine derivative (7). The FT-IR spectrum of this compound showed disappearance of the absorption bands for NH2 and carbonyl group and appearance of bands at 3254 and 3147 cm-1 due to NH groups and band at 1232 cm^{-1} for thion group.

Reaction of compound (2) with thiol compounds in absolute ethanol brought about the compounds (8-14). The releasing of H2S gas indicates the nucleophilic shift of thiol group by amino group of compound (2). FT-IR spectrum of these compounds showed the disappearance of absorption bands for NH2 group and showed bands at 3113 to 3217 cm^{-1} due to NH group, and other bands in Table 4. 13C -NMR of compound (9) showed: 109, 115, 115.9, 119, 122, 122.3, 122.7, 125.1, 125.9, 128, 129, 157 and 168. 1H-NMR of compound (12) showed: 1.4(t , 3H, CH3), 1.9(m, 2H, CH2), 2.4(s, 1H, NH) and 6.7 to 7.3 (m, Ar-H) and the 13C-NMR of this compound showed: 21, 62, 119, 120, 121, 125, 125.8, 128, 129, 130 and 155.

Reaction of compound (11) with 4-hydroxy benzaldehyde in presence of potassium hydroxide brought about derivative (15). This reaction proceeds by formation of carbanion (which attacked the carbonyl group of aldehyde) and then dehydration to give compound (15). The FT-IR spectrum of this compound showed appearance of new band at 3437 cm^{-1} due to phinolic hydroxyl group, as well as bands at 2323 and 1600 cm^{-1} due to NH and C=C groups, respectively, and other bands in Table 5.

Table 3. U.V and FT-IR spectral data for compounds (3-6).

Comp. no.	U.V ethanol		Characteristic bands of FT-IR (cm^{-1} , KBr disk)				
	λ_{max} (nm)	ε_{max}	υC=O	υC=C_{ar}	υCH_{ar}	υC=N	Others
3	339 268 221	1.18 0.72 0.27	1681	1425 1520	3076	1583	υC-H_{alph} 2920 2945
	318 239	1.1 1.9	1662	1564 1458	3051	1606	υC-H_{alph} 2946 2856
5	311 254	1.2 0.8	1685	1556 1458	3043	1604	υC-H_{alph} 2874 2931 υC=O la 1705 υOH 3260
6	333 227	2.2 1.9	1670	1456 1595	3070	1620	---------

Table 4. U.V and FT-IR spectral data for compounds (8-14).

Comp. no.	U.V ethanol		Characteristic bands of FT-IR (cm^{-1} , KBr disk)				
	λ_{max}	ε_{max}	υ(NH)	υC—H_{ar}	υC=O	υC=C_{ar}	Others
8	338 211	0.9 1.9	3113	3043	1674	1500 1458	υC=N 1597
9	331 232	1.1 2.9	3170	3080	1680	1512 1465	υC=N 1622
10	320 269	1.4 1.9	3182	3072	1668	1573 1456	υC=N 1598
11	338 228	0.7 2.9	3182	3070	1708	1570	υC=N 1604
12	281 209	0.7 1.88	3210	3076	1678	1562 1440	υCH_{alp} 2953 2890
13	305 224	2.1 2.9	3196	3070	1668	1610 1456	υOH 3284 υCHalp 2872 2928
14	282 209	1.4 1.9	3217	3020	1651	1462 1568	υOH 2563-3280 υC=O 1714

Table 5. U.V and FT-IR spectral data for compound (15).

Comp. no.	U.V ethanol		Characteristic bands of FT-IR (cm^{-1} , KBr disk)				
	λ_{max} (nm)	ε_{max}	υC= O	υC=C_{ar}	υC=C	υC—H_{ar}	Others
15	209 282	1.5 1.9	1672	1512 1454	1600	3040	υOH 3437 υ(NH) υ(NH) 3223

REFERENCES

Joseph B, Darro F, Behard A, Lesur B, Collignon F, Decaestecker C, Frydman A, Guillaumet G, Kiss R (2002). 3-aryl-2-quinolone derivatives: Synthesis and characterization of *in vitro* and *in vivo* antitumor effects with emphasis on a new therapeutical target connected with cell migration J. Med. Chem., 45: 2534-2555.

Xiao Z, Waters NC, Woodard CL, Li PK (2001). Design and synthesis of Pfmrk inhibitors as potential antimalarial agents Bioorg. Med. Chem. Lett., 11: 2875-2878.

Nishi T, Kimura Y, Nakagawa K, Yaku-gaku Z (2000). Research and development of cilostazol: An antiplatelet agent, 120: 1247-1260.

Oshiro Y, Sakurai Y, Sato S, Kurahashi N, Tanaka T, Kikuchi T, Tottori K, Uwahodo Y, Miwa T, Nishi T (2000). 3,4-Dihydro-2(1*H*) quinolinone as a novel antidepressant drug: Synthesis and pharmacology of 1-[3-[4-(3 chlorophenyl)-1-piperazinyl]propyl]-3,4 dihydro-5-methoxy-2(1*H*)-quinolinone and Its Derivatives. J. Med. Chem., 43: 177-189.

Banno K, Fujioka T, Kikuchi T, Oshiro Y, Hiyama T, Nakagawa K (1988). Studies on 2(1H)- uinolinonederivatives as neuroleptic agents I. Synthesis and biological activities of (4-phenyl-1-iperazinyl)-propoxy-2(1H)-quinolinone derivatives Chem. Pharm. Bull., 36: 4377-4388.

Hung Q, Ali, Hima JE, Qui DOW (1996). Synthesis of O-(4-Quinazolinyl)oxime Ethers and Their Antiviral Activity. Chem. J. Chin. Univ., pp. 17: 57.

Dia D, Singh A, Sarawagi R (2004). Green chemical multi-component one-pot synthesis of fluorinated 2,3-disubstituted quinazolin-4(3H)-ones under solvent-free conditions and their anti-fungal activity J. fluorine Chem., 125: 1835-1840.

AL-Omar MA, EL-Azab AS, EL-Obeid HA, Abdel H (2006). Synthesis of Some New 4(3H)-Quinazolinone Analogues J. Sandi Chem. Soc., 10: 113.

Khan IA, Hassan G, Ihsanullah KMA (2003). Efficacy of Post-emergence Herbicides for controlling Weeds in Canola. Asian J. Plant Sci., 2: 294.

Jin Y, Li HY, Lin LP, Tan JZ, Ding J, Luo XM, Long YQ (2005). Synthesis and antitumor evaluation of novel 5-substituted-4-hydroxy-8-nitroquinazolines as EGFR signaling-targeted inhibitors Bioorg. Med. Chem., 13: 5613.

Wissner A, Berger DM, Boschelli DH (2000). 4-Anilino-6,7-dialkoxyquinoline-3-carbonitrile Inhibitors of Epidermal Growth Factor Receptor Kinase and Their Bioisosteric Relationship to the 4-Anilino-6,7-dialkoxy- quinazoline Inhibitors J. Med. Chem., 43: 3244.

AL-Bayati RFH, Hassan YK, Hameed SM, AL-Qadisia (2004). Synthesis of Novel quinazolines J. Pure Sci., 10: 90.

Godard A, Fourquez JM, Tamion R, Marsais F, Queguiner GS (1994). New Synthesis of the Streptonigrin Quinoline-5,8-quinone Moiety and Aromatic Cross-Coupling Synlett., p. 235.

Jarrahpour AA, Motamedifar M, Pakshir K, Zarei M (2004). Synthesis of Novel Azo Schiff Bases and Their Antibacterial and Antifungal Activities Molecules, 9: 815-820.