Indian Journal of Chemistry
Vol. 37B, July 1998, pp. 715 - 716

Note

Synthesis and antibacterial activity of nitrofurylvinylquinazolinones

B Shivarama Holla*[a], M T Padmaja[a], M K Shivananda[a] & P M Akbarali[b]

[a]Department of Chemistry, Mangalore University, Mangalagangotri 574 199, India

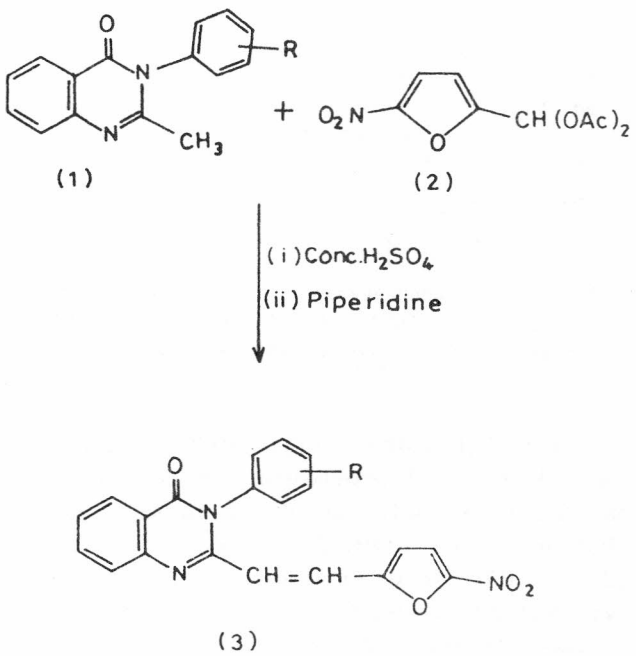
[b]Plama Laboratories Ltd, 120A/B, Industrial Area, Baikampady, New Mangalore 575 011, India

Received 14 October 1996; accepted (revised) 14 July 1997

The reaction of 3-aryl-2-methyl-quinazolin-4-ones **1** with acidified nitrofurfuraldehyde diacetate **2** in the presence of piperidine affords 3-aryl-2-[(5-nitro-2-furyl)vinyl]quinazolin-4-ones **3** in 50-80% yield. These compounds have been characterized by nitrogen analysis, and IR, ^{1}H NMR and mass spectral data. The newly synthesized compounds have been screened for their antibacterial activities.

Quinazolinone derivatives exhibit a wide range of antiparkinson[1], antibacterial[1], anthelmintic[2], CNS depressant[3], antitubercular[4], analgesic[5], antiinflammatory[6], hypoglycemic[7], non-steroidal[8] and fungicidal activities. The 4(3*H*)-quinazolinone[9] moiety constitutes an important structural feature in several useful sedatives, hypnotic and anticonvulsant drugs such as Methaqualone and Mecloqualone. Further, nitrofuran derivatives are being used as potential chemotherapeutic agents[10-11]. In view of these observations and in continuation of our studies on chemotherapeutically important nitrofurans[12-14], it was thought of interest to synthesize novel 3-aryl-2-[(5-nitro-2-furyl)vinyl]-quinazolin-4-ones **3**.

For the present work, various anilines were condensed with 2-methyl-3,1-benzoxazin-4-one in the presence of phosphorus oxychloride employing toluene as solvent. Such condensations afforded 3-aryl-2-methyl-quinazolin-4-ones **1** in 60-70% yield. The required 2-methyl-3,1-benzoxazin-4-one was prepared by the cyclization of anthranilic acid with acetic anhydride. Quinazolinones **1** were characterized by their melting points and reference to literature[15]. 3-Aryl-2-methylquinazolin-4-ones **1** were then condensed with acidified nitrofurfuraldehyde diacetate **2** in the presence of a base such as piperidine to yield **3** (Scheme I). Nitrofurfuraldehyde diacetate **2**, required for this reaction, was obtained by the literature method[16]. Characterization and spectral data of compounds **3** are given in Table I.



Scheme I

Antibacterial Activity. All the newly synthesized compounds were screened for their antibacterial activity against *Bacillus subtilis, Staphylococcus aureus, Escherichia coli* and *Pseudomonas aeruginosa.* All of them showed antibacterial activity at 5 μg/mL to a lesser degree than that of Furacin, a standard drug used for comparison.

Experimental Section

General. Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a Shimadzu FT-IR 157 infrared spectrophotometer, ^{1}H NMR spectra in DMSO-d_6 on a 90 MHz Perkin-Elmer R-32 instrument using TMS as internal reference (chemical shifts in δ, ppm) and mass spectra on a Jeol JMS-D 300 mass spectrometer.

Table I—Characterization data of 3-aryl-2-[(5-nitro-2-furyl)vinyl]quinozolin-4-ones **3***

Compd	R	Yield (%)	m.p. °C	Nature of the compound	Mol. Formula
3a	H	80	254	Orange yellow crystals	$C_{20}H_{13}N_3O_3$
3b	*p*-Bromo†	81	229	Yellow crystals	$C_{20}H_{12}BrN_3O_3$
3c	*p-Methyl*	78	213	Orange crystals	$C_{21}H_{15}N_3O_3$
3d	*m*-Chloro	57	231	Yellowish shining needles	$C_{20}H_{12}ClN_3O_3$
3e	3-Chloro-4-fluoro‡	81	196	Yellow crystals	$C_{20}H_{11}ClFN_3O_3$
3f	*o*-Methoxy	51	191	Light yellow crystals	$C_{21}H_{15}N_3O_4$
3g	*m*-Methyl	68	197	Yellow crystals	$C_{21}H_{15}N_3O_3$
3h	*p*-Nitro	50	242	Brownish orange crystals	$C_{20}H_{12}N_4O_5$
3I	*2,5*-Dichloro	53	226	Light yellow crystals	$C_{20}H_{11}Cl_2N_3O_3$

*Satisfactory elemental analyses (±0.3%) were obtained.
†IR: 1675 (C=O), 1600 (C=C), 1550 and 1340 cm^{-1} (NO_2 *asym* and *sym*)
‡IR: 1681 (C=O), 1600 (C=C), 1545 and 1340 cm^{-1} (NO_2 *asym* and *sym*)

3-Aryl-2-[(5-nitro-2-furyl)vinyl] quinazolin-4-ones 3: General procedure. An equimolecular mixture of suitably substituted quinazolinone **1** (0.01 mole) and 5-nitro-2-furfuraldehyde diacetate (2.43 g, 0.01 mole) in absolute ethanol (20 mL) was treated first with conc. sulphuric acid (0.5 mL) followed by the *addition of piperidine* (10 mL). The mixture was heated under reflux for 1-2 hr. On cooling the reaction mixture, the resultant product was filtered, washed and recrystallized from dimethylformamide. The characterization data of compounds **3** are given in Table I.

As a representative case the spectral data of **3c** are given below: IR: 1680 (C=O), 1600 (C=C), 1540 and 1340 cm^{-1} (NO_2 *asym* and *sym*). ^1H NMR (DMSO-d_6): **3c** δ 2.5 (s, 3H, *p*-tolyl protons), 6.5-6.7 (d, 2H, vinyl protons), 7.1-7.4 (m, 8H, aromatic protons), 7.7-7.9 (d, 2H, furan protons). MS: m/z 359 (M^+), 313 ($M-NO_2$).

Acknowledgement

The authors are thankful to Head, RSIC, CDRI, Lucknow and Director, SIF, IISc., Bangalore for providing nitrogen analyses, mass and ^1H NMR spectral data. They are also thankful to Prof. M V Ramana, N.G.S.M. College of Pharmacy, Deralakatte for his help in carrying out the antibacterial activities of the compounds reported herein. Two of them (M K S and M T P) are grateful to CSIR, New Delhi and Plama Laboratories Ltd., respectively for research fellowships.

References

1 Srivastava V K, Singh S, Gulati A & Shanker K, *Indian J Chem*, 26B, **1987**, 652.
2 Gupta D P, Ahmad S, Kumar A & Shanker K, *Indian J Chem*, 27B, **1988**, 1060.
3 Chaurasia M R & Sharma A K, *J Indian Chem Soc*, 52, **1985**, 308.
4 Joshi V & Chaudhari R P, *Indian J Chem*, 26B, **1987**, 602.
5 Ram V J, Srimal R C, Kushwaha D S & Mishra L J, *J Prakt Chem*, 332, **1990**, 629.
6 Kumar A, Singh S, Saxena A K & Shanker K, *Indian J Chem*, 27B, **1988**, 443.
7 Husain M I & Jamali M R, *Indian J Chem*, 27B, **1988**, 43.
8 Ram V J & Verma M, *Indian J Chem*, 30B, **1991**, 1119.
9 Abdel-Alim M, Abdel Alim, Abdel-Nasser, AEL-Shorbagi, Hosny A H, El-Sharief Mahmoud, AEL-Gendy & Monir Amin, *Indian J Chem*, 33B, **1994**, 260.
10 Dodd M C & Stillman W B, *J Pharmacol Exp Therap*, 82, **1944**, 11.
11 Nardi D, Massarani E, Tajana A, Degen L & Magistretti M J, *J Med Chem*, 10, **1967**, 530.
12 Holla B S, Kalluraya B, Sridhar K R, Drake E, Thomas L M, Bhandary K K & Levine M J, *Eur J Med Chem*, 29, **1994**, 301.
13 Holla B S, Udupa K V & Sridhar K R, *Bull Chem Soc Japan*, 65, **1988**, 524.
14 Holla B S & Kalluraya B, *Indian J Chem*, 27B, **1988**, 683.
15 Klosa J, *J Prakt Chem*, 14, **1961**, 84; *Chem Abstr*, 56, **1962**, 2449.
16 Gillman H & Wright G F, *J Am Chem Soc*, 52, **1936**, 2553.