ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 5, Issue, 05, pp.1046-1048, May, 2013

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

RECENT APPROACHE TO THE SYNTHESIS OF 3-FORMYLQUINOLIN-2(1*H*)-ONES

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ARTICLE INFO

Article History:
Received 19th February, 2013
Received in revised form
14th March, 2013
Accepted 18th April, 2013
Published online 12th May, 2013

Key words:
Microwave,
Quinoline,
Acetic acid,
Dechlorination

ABSTRACT

3-Formylquinolin-2(1*H*)-ones have been synthesized efficiently by dechlorination of 2-chloro-3-formylquinolines with acetic acid and sodium acetate in just 1.5 to 2.5 min. under microwave irradiation. Consequently, microwave irradiation significantly reduced reaction times compared to traditional heating methods. Particularly synthesis by solvent-free solid supported microwave irradiation was found more eco-friendly and had higher reaction efficiency. The purity of the synthesized compounds was confirmed by their C, H and N analysis and the structure was analyzed on the basics of Mass, FT-IR and ^{1}H NMR.

INTRODUCTION

In recent year, the application of microwave irradiation for promotion of organic reactions has received increasing attention (Abramovitch, 1991) (Majetich and Elec, 1995). The technique has been used to assist in transfer hydrogenation, oxidation, aromatic substitution pericyclic reactions and many other process of significance to organic chemistry. In addition, (Kidawi, 2001) the technique has also found application in the areas of inorganic and solid state synthesis (Loupy, 1998). The application of (Caddick, 1995) microwave irradiation to chemical reaction has been shown to enhance significantly the rate of many processes (Strauss and Trainor, 1995). In some cases, (nadaraj *et al*., 2009, 2011) the technique has been used to promote reaction previously not observed under conventional thermal activation. Microwave induced organic reactions are gaining popularity over conventional technique for rapid organic synthesis. The main features are short reaction time and increased purity of resulting product (nadaraj *et al*., 2006). The synthesis of nitrogen heterocycles has been of considerable interest to organic and medicinal chemistry for many years as large number of natural product and drugs contain this hetero atom. Among them, (Kalsow and Marsh, 1947, Ukrainets *et al*., 1997)) the nitrogen heterocyclic compounds, quinolines find valuable applications in medicinal field. Several quinolones like ciprofloxacin, pefloxacin, levofloxacin, spafloxacin are released in the clinical world. Synthesis of various substituted quinolone intermediate compounds is of current interest because of their therapeutically potential in the area of human and animal health.

The quinolines skeleton is a common structural motif in a broad range of biologically active compounds. Quinoline derivatives are utilised as anti-malarial (Bernard, 1969) antibacterial (Mitsos *et al.*, 2003), antifungal (Patel *et al*, 2007), anti-inflammatory (Dillard *et al.*, 1973) and antitumour (Sukhova *et al*., 1989). Due to their importance, the synthesis of quinolines attracted widespread attention.3-Formylquinolin-2 (1*H*)-ones occupy a prominent position, as they are key intermediates for further [*b*]-annelation of a wide variety of rings and for various functional group interconversions. It is well known that, (Sekar and Prasad, 1998) the major synthetic routes leading to the formation of pyrano-, pyrido-pyrimidioquinolines (Sumpathkumar *et al.*, 2004) and acridines(Selvi and Mohan, 1999) invariably involved some common intermediates. Several methods such as skraup, Doebner-Miller, Friedlander and Combes synthesis were developed which provide quinolines derivatives efficiently, but so in multiple steps and using harmful reagents and harsh conditions. However many of these methods suffer from the needs of high temperature prolonged reaction time (Manandhar *et al.*, 1985) and drastic reaction conditions (Bhudevi *et al.*, 2009) and also the unsatisfied yields (Vidya *et al*., 2003). Therefore, the design of improved and environmentally benign approaches for their preparation is great demand. Hence we felt that it is worthwhile to synthesis a few substituted-3-formylquinolin-2(1*H*)-ones compounds in a convenient, efficient approach, the structure and characterization of these compounds are confirmed by Mass, FT-IR and ^{1}H NMR.

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MATERIALS AND METHODS

Melting points (mp) were determined using Boetieus micro heating table and are uncorrected. IR (KBr, cm^{-1}) spectra were obtained on Shimadzu-8201 spectrophotometer. ^{1}H NMR spectra were recorded on Bruker AMX-400 (400 MHz) spectrometer using TMS as an internal reference (Chemical shifts in δ, ppm). Elemental analyses were performed on Perkin Elmer CHN-analyzer. Mass spectra were recorded on Shimadzu GCMS-QP5050A (70 ev) mass spectrometer. For microwave irradiation a Kenstar (OM-20ESP, 2450 MHz) domestic microwave oven was used.

General procedure for synthesis of 3-formylquinolin-2(1*H*)-ones (2a-j)

A mixture of 2-chloro-3-formylquinoline/ substituted 2-chloro-3-formylquinolines (0.5 mmol), glacial acetic acid (87.5 mmol) and sodium acetate (25 mmol) was taken in a open Teflon vessel and irradiated in a microwave oven at power 320 W for the specified time. After irradiation, the reaction mixture waspoured intocrushed

ice. The precipitated product was filtered, washed with water, dried and recrytallized from aqueous acetic acid afford the desired substituted

3-formylquinolin-2(1*H*)-ones (2a-j)

3-Formylquinolin-2(1H)-one (2a): Time-2.00 min., Yield 98% mp. 305 °C, IR (KBr): ν=1550 cm^{-1}, 1680 cm^{-1} (C=O), 3200 cm^{-1}(NH); H NMR (DMSO-d_6): δ=7.25 (t, 1H; C_7-H,) 7.35 (d, 1H; C_8-H), 7.66 (t, 1H; C_6-H), 7.92 (d, 1H; C_5-H), 8.52 (s, 1H; C_4-H), 10.24 (s, 1H; CHO), 12.25 (s, 1H; NH); ^{13}C NMR (DMSO-d_6): δ=118.2, 120.1, 126.3, 132.5, 134.3, 138.2, 142.8, 144.3, 164.3, 191.2; MS m/z: 173 [M^+]; elemental analysis calcd (%) for $C_{10}H_7NO_2$; C 69.36, H 4.07, N 8.09; found: C 69.33, H 4.05, N 8.06.

6-Methyl-3-formylquinolin-2(1H)-one (2b): Time-2.00 min., Yield 94% mp. 273 °C, IR (KBr): ν=1560 cm^{-1}, 1680 cm^{-1}(C=O), 3200 cm^{-1}(NH); ^{1}H NMR (DMSO-d_6): δ=2.57 (s, 3H; C_6-CH_3), 7.46-7.98 (m, 2H; C_7-H & C_8-H,) 8.42 (s, 1H; C_5-H,), 8.68 (s, 1H; C_4-H), 10.34 (s, 1H; CHO), 10.56 (s, 1H; NH).

7-Methyl-3-formylquinolin-2(1H)-one (2c): Time-2.20 min., Yield 93% mp. 297 °C, IR (KBr): ν=1555 cm^{-1}, 1675 cm^{-1}(C=O), 3200 cm^{-1}(NH); ^{1}H NMR (DMSO-d_6): δ=2.55 (s, 3H; C_7-CH_3), 7.79 (d, 1H; C_6-H) 7.84 (s, 1H; C_8-H), 8.40 (d, 1H; C_5-H), 8.92 (s, 1H; C_4-H), 10.48 (s, 1H; CHO), 11.01 (s, 1H; NH).

8-Methyl-3-formylquinolin-2(1H)-one (2d): Time-1.80 min., Yield 96% mp. 285 °C, IR (KBr): ν=1550 cm^{-1}, 1683 cm^{-1}(C=O), 3250 cm^{-1}(NH); ^{1}H NMR (DMSO-d_6): δ=2.50 (s, 3H; C_8-CH_3), 7.45-8.40 (m, 3H; C_5-H, C_6-H & C_7-H) 8.65 (s, 1H; C_4-H), 10.24 (s, 1H; CHO), 11.04 (s, 1H; NH).

6-Methoxy-3-formylquinolin-2(1H)-one (2e): Time-1.50 min., Yield 98% mp. 276 °C, IR (KBr): ν=1545 cm^{-1}, 1675 cm^{-1}(C=O), 3200 cm^{-1}(NH); ^{1}H NMR (DMSO-d_6): δ=3.91 (s, 3H; C_6-OCH_3), 7.35 (d, 1H; C_8-H), 7.59 (d, 1H; C_7-H), 8.04 (s, 1H; C_5-H), 8.35 (s, 1H; C_4-H), 10.41 (s, 1H; CHO), 11.52 (s, 1H; NH); ^{13}C NMR (DMSO-d_6): δ=56.5, 118.2, 120.9, 126.4, 132.6, 134.2, 138.1, 142.9, 144.2, 164.2, 191.1; MS m/z: 203 [M^+]; elemental analysis calcd (%) for $C_{11}H_9NO_3$: C 65.02, H 4.46, N 6.89; found: C 65.05, H 4.44, N 6.86.

7-Methoxy-3-formylquinolin-2(1H)-one (2f): Time-1.70 min., Yield 97% mp. 266 °C, IR (KBr): ν=1555 cm^{-1}, 1680 cm^{-1}(C=O), 3250 cm^{-1}(NH); ^{1}H NMR (DMSO-d_6): δ=3.93 (s, 3H; C_7-OCH_3), 7.81 (d, 1H; C_6-H), 7.85 (d, 1H; C_8-H), 8.45 (d, 1H; C_5-H), 9.01 (s, 1H; C_4-H), 10.46 (s, 1H; CHO), 11.03 (s, 1H; NH).

8-Methoxy-3-formylquinolin-2(1H)-one (3g): Time-1.50 min., Yield 97% mp. 262 °C, IR (KBr): ν=1550 cm^{-1}, 1685 cm^{-1}(C=O), 3200 cm^{-1}(NH); ^{1}H NMR (DMSO-d_6): δ=3.92 (s, 3H; C_8-OCH_3), 7.39-7.60 (m, 2H; C_6-& C_7-H), 8.05 (d, 1H; C_5-H), 8.38 (s, 1H; C_4-H), 10.39 (s, 1H; CHO), 11.52 (s, 1H; NH); ^{13}C NMR (DMSO-d_6): δ=56.7, 119, 121.0, 126.5, 132.2, 135.1, 138.6, 143.1, 144.6, 164.2, 190.9; MS m/z: 203 [M^+]; elemental analysis calcd (%) for $C_{11}H_9NO_3$: C 65.02, H 4.46, N 6.89; found: C 65.07 ,H 4.42, N 6.90.

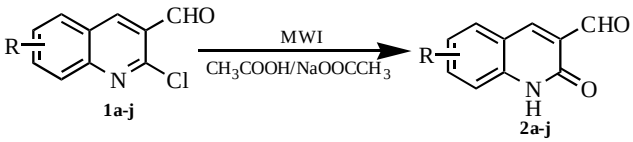
6-Bromo-3-formylquinolin-2(1H)-one (2h): Time-2.20 min., Yield 72% mp. >300 °C, IR (KBr): ν=1545 cm^{-1}, 1680 cm^{-1}(C=O), 3200 cm^{-1}(NH); ^{1}H NMR (DMSO-d_6): δ=7.25-7.65 (m, 2H; C_7-H & C_8-H), 8.20 (s, 1H; C_5-H), 8.45 (s, 1H; C_4-H), 10.25 (s, 1H; CHO), 11.01 (s, 1H; NH).

6-Chloro-3-formylquinolin-2(1H)-one (2i): Time-2.20 min., Yield 87% mp. >300 °C, IR (KBr): ν=1550 cm^{-1}, 1680 cm^{-1}(C=O), 3200 cm^{-1}(NH); ^{1}H NMR (DMSO-d_6): δ=7.30-7.55 (m, 2H; C_7-H & C_8-H), 8.15 (s, 1H; C_5-H), 8.36 (s, 1H; C_4-H), 10.31 (s, 1H; CHO), 11.20 (s, 1H; NH); MS m/z: 207 [M^+]; elemental analysis calcd (%) for $C_{10}H_6NO_2Cl$; C 57.79, H 2.92, N 6.76; found: C 57.76, H 2.90, N 6.74.

7-Chloro-3-formylquinolin-2(1H)-one (2j): Time-2.50 min., Yield 75% mp. >300 °C, IR (KBr): ν=1550 cm^{-1}, 1680 cm^{-1}(C=O), 3250 cm^{-1}(NH); ^{1}H NMR (DMSO-d_6): δ=7.25-7.95 (m, 3H; C_5-H, C_6-H & C_8-H), 8.35 (s, 1H; C_4-H), 10.25 (s, 1H; CHO), 11.21 (s, 1H; NH).

RESULTS AND DISCUSSION

Dechlorination of 2-chloro-3-formylquinoline with mixture of acetic acid and sodium acetate under microwave reactor at 320 W to give 3-formylquinolin-2(1*H*)-one. We found that the best yield of 2a, 98% was obtained after only just 2 min. The reaction proceeds efficiently in good yields at ambient pressure within a few minutes. The experimental procedure is very simple. The high yield transformation did not form any undesirable by-products. Structure from obtained compounds (2a-j) was determined from spectral analysis IR, ^{1}H-NMR, mass spectroscopy and elementary analysis.



2a R=H, **2b** R=6-CH_3, **2c** R=7-CH_3, **2d** R=8-CH_3, **2e** R=6-OCH_3, **2f** R=7-OCH_3, **2g** R=8-OCH_3, **2h** R=6-Br, **2i** R=6-Cl, **2j** R=7-Cl

Scheme 1. Synthesis of substituted 3-formyl-quinolin-2(1*H*)-one

The 3-formyl-quinolin-2(1*H*)-one (2a) solid showed absorption bands at 800-700 (CH-bend), 880 (-C-N-Stretch), 1250 (-C-O-C Stretch), 1550 cm^{-1}, 1680 cm^{-1}, 2950-2853 (CH-Stretch), 3200 cm^{-1}, attributable to 2-quinolone and NH stretching vibrations. The ^{1}H NMR spectrum represented two triplets at δ 7.25 and δ 7.66 for the C_7-H and C_6-H protons, two doublets registered at δ 7.35 and δ 7.92 for C_8-H and C_5-H protons respectively. Spectrum also showed three singlets at δ 8.52, δ 10.24 and δ 12.25 for the C_4-H, CHO, NH protons respectively. The ^{13}C NMR spectrum showed the peak at δ 118.2, 120.1, 126.3, 132.5, 134.3, 138.2, 142.8, 144.3, 164.3, 191.2; Mass spectrum showed molecular ion peak at *m/z* 173 [M^+]; Elemental analysis corroborated the proposed molecular formula; C 69.36, H 4.07, N 8.09; found: C 69.33, H 4.05, N 8.06. To establish the generality and applicability of these methods, various substituted 2-chloro-3-formylquinolines (1b-j) were subjected to the same reaction conditions to furnish the corresponding quinolines 2b-j in good yields. The spectroscopic properties of our synthetic material agreed well with those reported in literature (Meth-Cohn *et al.*, 1981).

Conclusion

The present study was aimed at synthesis of characterization of 3-formyl-quinolin-2(1*H*)-one derivatives. In this paper, we reported a procedure where the dechlorinations are performed in microwave irradiation, in order to improve the conditions and to prevent problems connected with conventional conditions (cost, handling, safety and pollution).

Acknowledgment

The authors would like to thank the NMR Research centre, Indian Institute of Science, Bangalore, INDIA for providing ^{1}H NMR spectral data. The author VN is grateful to Director of Collegiate Education, Govt. of Tamilnadu, India, for financial support.

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