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Organic Chemistry

Elixir Org. Chem. 47 (2012) 9131-9133

ISSN: 2229-712X

Effective microwave synthesis of some ring fused quinolines

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ARTICLE INFO

Article history:

Received: 30 April 2012;

Received in revised form:

15 June 2012;

Accepted: 27 June 2012;

Keywords

Acetic acid,
Microwave,
Pyranoquinoline,
Quinolines,
Solvent free synthesis.

ABSTRACT

Pyrano[2,3-*b*]quinolin-2-ones was synthesized by cyclic condensation of 2-chloro-3-formylquinolines with sodium acetate and acetic acid in microwave reactor. Microwave reactions are very inexpensive, operational simplicity, eco-friendly method and good yield in a very short reaction time. Unexpectedly, 3-formylquinolin-2(1*H*)-ones were exclusively formed in very high yield by changing the molar ratio of acetic acid and sodium acetate in just 1.5 to 2.5 min. The synthesized compounds were characterised by IR, NMR, and Mass Spectra.

Introduction

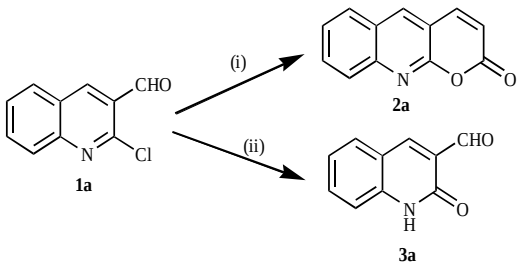
MICROWAVE irradiation using commercial domestic oven has been recently used to accelerate organic reactions, the high heating efficiency giving remarkable rate enhancement and dramatic reduction in reaction time.[1]-]2] As a part of a research project to develop environmentally benign organic reactions, we have recently reported the synthesis of simple quinolines, pyrimido- and pyrazoloquinolines under microwaves.[3]-[5] Hence, our new approach reported herein involves the use of microwave irradiation in the synthesis of pyrano[2,3-*b*]quinolin-2ones under mild conditions and unexpected formation of 3-formylquinolin-2(1*H*)-ones as intermediates.

The preparation of pyranoquinolines has received significant attention[6]-[8] in previous years because of the broad spectrum of their biological properties such as psychotropic, antiallergic, anti-inflammatory and estrogenic activities.[9] In addition, pyranoquinoline derivatives are found to possess a wide range of pharmacological activity.[10] Further, several bioactive alkaloids which are widely distributed in nature contain a pyranoquinoline moiety.[11] Among the pyranoquinolines, pyrano[2,3-*b*]quinolin-2-one systems are of interest because they are linear benzaza analogues of coumarins and they constitute the parent ring structures of pyranoquinoline alkaloids such as khaplofoline, which occurs in the *rutaceae* plant family.[12]

So far, only a few methods have been reported [13]-[18] for the construction of pyrano[2,3-*b*]quinolin-2-ones, which generally involve 2-chloro-3-formylquinolines (**1**) as starting materials. However, these methods have some disadvantages, which include multiple steps, longer reaction time, and use of toxic organic solvents, harsh reaction conditions and requirement of excess of reagents such as HCl, acetic anhydride and PPA.

Result and discussion

To identify an efficient reagent for the synthesis of pyrano[2,3-*b*]quinolin-2-one derivatives, from 2-chloro-3-formylquinolines. We initially examined the reaction of 2-chloro-3-formylquinoline (**1**) with acetic acid under microwave irradiation for 10 min. But unfortunately we got mixture of product, such as target compound pyrano[2,3-*b*]quinoline (**2a**, 30%) and unknown compound 3a in 58% (Scheme 1). IR spectrum of 3a showed absorption at 1680 cm^{-1} corresponding to free aldehyde group. The spectral [19] (^{1}H-NMR & Mass) and analytical data attested the compound 3a to be 3-formylquinolin-2(1*H*)-one, which is also a good intermediate in the synthesis of other quinoline heterocycles. [20], [21]



Scheme1. (i) Method 3 and (ii) Method 4

Table 1

Microwave irradiation of 2-chloro-3-formylquinoline (1a) with acetic acid and sodium acetate under different conditions

Methods	Reagent / Catalyst	Molar ratio (mmol)	Irradiation Power (W)	Time (min)	Product formed	Yield (%)
1	Acetic acid	175	480	10	2a & 3a	30 & 58
2	Acetic acid and sodium acetate	87.5 and 25	320	10.00	2a & 3a	48 & 45
3	Acetic acid and sodium acetate	123 and 50	320	5.00	2a	92
4	Sodium acetate	50	480	2.20	3a	98

a - Microwave irradiations were carried out using Kenstar, OM-20ESP, 2450 MHz, domestic microwave oven with adjustable irradiation power.

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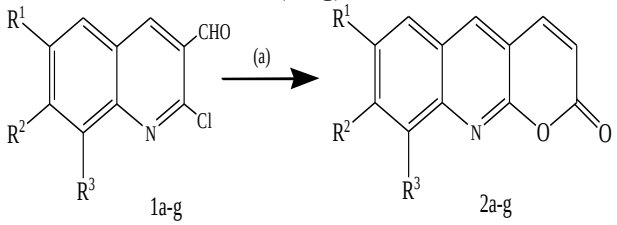
Next we improve the yield of target product using sodium acetate in the reaction sequence. When we irradiated of 2-chloro-3-formylquinoline (1a) with acetic acid/ sodium acetate using various parameters such as different molar ratio of acetic acid/ sodium acetate, irradiation power and time were studied and optimized (Table 1, Methods 1-4).

From the results obtained by using different parameters, it is obvious that method 3 [22] is the most suitable for the synthesis of pyrano[2,3-*b*]quinolin-2-one 2a, as it reduces the reaction time to minimum and increases the yield of the product to maximum (Table 1). The solid-state condition was also checked for the reaction, unexpectedly, 3-formylquinolin-2(1*H*)-ones were exclusively formed in very high yields by changing the molar ratio of acetic acid and sodium acetate in just 1.5 to 2.5 min (Method 4, Table I).

To establish the generality and applicability of these methods, various substituted 2-chloro-3-formylquinolines (1b-g) were subjected to the same reaction conditions (Method 3) to furnish the corresponding quinolines 2b-g and in good yields (Table II).

Table II.
Microwave Synthesis of 2-oxo-2H-pyrano[2,3-b]quinolines (2a-g)



(a) acetic acid (123 mmol), sodium acetate (50 mmol), mw, 320W

Entry	Product	R^1	R^2	R^3	Time (min)	Yield (%)	mp (Lit.mp)°C
1	2a	H	H	H	5.00	92	243-244 (243)
2	2b	CH_3	H	H	6.20	95	245-247 (240)
3	2c	H	H	CH_3	6.40	86	231-232 (230)
4	2d	OCH_3	H	H	5.00	78	224-225
5	2e	H	H	OCH_3	6.00	89	260-262
6	2f	Br	H	H	9.00	70	262-264
7	2g	Cl	H	H	8.20	75	210-212 (215)

All the yields were calculated from crystallized products and the products were identified by comparison of analytical data (mp, mmp, IR, NMR, and Mass) with those reported or with authentic samples prepared by the conventional methods. Some new derivatives were also prepared and reported.

Conclusion

The procedures described above provide a useful, clean, fast and efficient alternative for the preparation of both pyrano[2,3-*b*]quinolin-2(1*H*)-ones and 3-formylquinolin-2(1*H*)-ones. Prominent among the advantages of these new methods are operational simplicity, good yield in a very short reaction time, solvent-free conditions, very inexpensive, easily available reagent and catalyst and easy workup procedure employed.

Acknowledgment

The author VN is grateful to Director of Collegiate Education, Govt. of Tamilnadu, India, for financial support. Author thank to Research centre, Indian Institute of Science, Bangalore, INDIA for providing 1HNMR spectral data.

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[19]. Spectral data of 3-formylquinolin-2(1*H*)-one (3a): IR (KBr): ν=1550 cm^{-1}, 1680 cm^{-1} (C=O), 3200 cm^{-1};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.

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[22]. Spectral data of pyrano[2,3-*b*]quinolin-2-one (2a): IR (KBr): ν=1621 cm^{-1}, 1740 cm^{-1} (C=O); ^{1}H NMR (DMSO-d_6): δ=6.56 (d, ^3J (H,H) = 9 Hz, 1H; C_3-H), 7.50-7.85 (m, 3H; C_7-H, C_8-H & C_9-H), 7.95 (d, ^3J (H,H)= 8.3 Hz, 1H; C_6-H), 8.10 (d, ^3J (H,H) = 9 Hz, 1H; C_4-H), 8.41 (s, 1H; C_5-H); ^{13}C NMR (DMSO-d_6): δ=117.5, 122.5, 126.5, 132.3, 134.2, 136.8, 137.9, 140.5, 143.2, 146.2, 156.3, 162.3; MS *m/z*: 197 [M^+]; elemental analysis calcd (%) for $C_{12}H_7NO_2$; C 73.09, H 3.58, N 7.10; found: C 73.07, H 3.58, N 7.06.

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