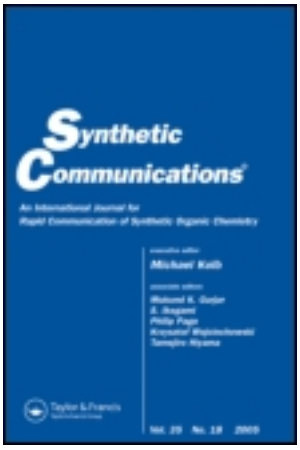


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Microwave-Assisted Synthesis of Quinoline Derivatives from Isatin

El Sayed H. El Ashry [a], El Sayed Ramadan [a], Hamida Abdel Hamid [a] & Mohamed Hagar [a]
[a] Department of Chemistry, Faculty of Science, Alexandria University, Alexandria, Egypt
Version of record first published: 18 Aug 2006.

To cite this article: El Sayed H. El Ashry , El Sayed Ramadan , Hamida Abdel Hamid & Mohamed Hagar (2005): Microwave-Assisted Synthesis of Quinoline Derivatives from Isatin, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 35:17, 2243-2250

To link to this article: http://dx.doi.org/10.1080/00397910500184719

Synthetic Communications®, 35: 2243–2250, 2005

ISSN 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910500184719

Taylor & Francis
Taylor & Francis Group

Microwave-Assisted Synthesis of Quinoline Derivatives from Isatin

El Sayed H. El Ashry, El Sayed Ramadan, Hamida Abdel Hamid, and Mohamed Hagar
Department of Chemistry, Faculty of Science, Alexandria University, Alexandria, Egypt

Abstract: Microwave irradiation has been used for a rapid and efficient synthesis of quinoline-4-carboxylic acids **5a–g** and 1,2,3,4-tetrahydroacridine-9-carboxylic acid **(6)** from the reaction of isatins **1–3** with acyclic and cyclic ketones in basic medium. 2-Hydroxyquinoline-4-carboxylic acid **(11)** was also obtained by irradiating a mixture of isatin **1** and malonic acid in AcOH. The esters of **5f** and **11** and their respective hydrazides **8** and **13** were also prepared under MWI.

Keywords: Hydrazide, isatin, ketone, microwave, quinoline

INTRODUCTION

The synthesis of quinolines and their derivatives has been of considerable interest because a large number of natural products and drugs contain this heterocyclic unit.[1–5] Quinoline-4-carboxylic acids and their analogs have a wide variety of medicinal applications including antitumor, antiviral, and antibacterial activities.[6,7] 2-(4-Bromophenyl)-quinoline-4-carboxylic acid selectively inhibited *C. albicans* prolyl-tRNA synthetase and 2-phenylquinoline-4-carboxamides are used as analgesic, tranquillizer, antitumor, and antitubercular agents.[8–11]

Received in the U.K. November 12, 2004
Address correspondence to El Sayed H. El Ashry, Department of Chemistry, Faculty of Science, Alexandria University, Alexandria, Egypt. Fax: +20-3-4271360; E-mail: eelashry60@link.net; eelashry60@hotmail.com

In a continuation of our studies on microwave-assisted reactions,[12–15] we report a versatile approach for the formation of quinoline-4-carboxylic acids, esters, and hydrazides using microwave irradiation (MWI).

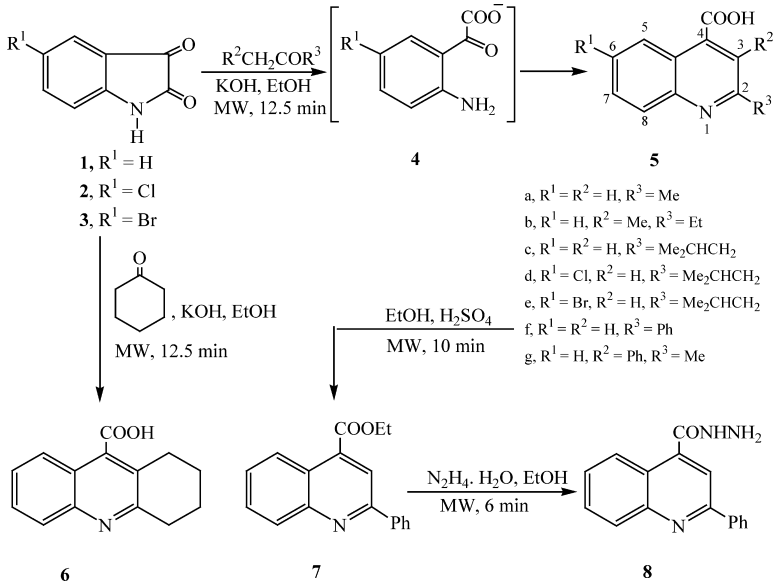
RESULTS AND DISCUSSION

Recently, efficient procedures for the synthesis of various quinoline derivatives were achieved using microwave irradiation.[16–24] However, the role of MWI on the performance of the Pfitzinger reaction[25] for the synthesis of quinoline-4-carboxylic acids has not been reported yet. The reaction between isatin and dialkyl ketones, in basic medium, required heating for about 70–96 h to give a considerable yield.[26] However, it did not give appreciable amounts of the products when a strong steric hindrance was present in the ketone.[27] Moreover, employing aqueous acid conditions required heating in an oil bath for 16 h.[28]

However, we found that MWI has successfully accelerated the condensation of isatins **1–3** with a number of ketones, such as acetone, diethyl ketone, isobutyl methyl ketone, acetophenone, and benzyl methyl ketone, in alcoholic potassium hydroxide solution, whereby the corresponding quinoline-4-carboxylic acids **5a–g** were obtained in 12.5 min; the reactions were carried out in a closed Teflon vessel and the yield of products ranged between 50 and 96%. The highest yield observed in the cases of acetophenone (95%) and benzyl methyl ketone (96%) can be attributed to the stability of their carbanions, whose attack on the carbonyl group of the presumably formed isatic acid derivative **4** resulted from the ring opening of the isatin derivatives **1–3** and subsequent cyclization (Scheme 1).

Esterification of 2-phenylquinoline-4-carboxylic acid **(5f)** with ethanol in the presence of a catalytic amount of concentrated sulphuric acid under MWI in a closed Teflon vessel required 10 min to afford ethyl 2-phenylcinchoninate **(7)** in 94% yield; under the conventional conditions the reaction required heating under reflux for 22 h to give a comparable yield.[29] Under MWI activation, the ester **7** was transformed into the corresponding acid hydrazide **8** in a much shorter time (6 min) compared with conventional heating (15.5 h). Furthermore, the yield of **8** was improved to 80% compared with 61%.[29] When isatin **1** was reacted with cyclohexanone as the ketonic reagent under MWI, 1,2,3,4-tetrahydroacridine-9-carboxylic acid **(6)** was produced in 95% yield within 12.5 min, but under conventional heating, the reaction required 72 h and gave only a 55% yield.[30]

Conventionally, isatin **(1)** was acetylated by heating with acetic anhydride for 2 h to give 75–80% yield of *N*-acetylisatin **(10)**.[31] However, when the reaction was conducted under MWI, the reaction time was dramatically reduced to 5 min to give 70% yield of **10**. When a mixture of **10** and aqueous sodium hydroxide was irradiated by MW for 3 min, 2-hydroxyquinoline-4-carboxylic acid **(11)** was produced in 65% yield; the reaction required 1 h of conventional heating to give a comparable yield.[32] Another route for



Scheme 1.

the preparation of **11** involved heating a mixture of isatin **1** and malonic acid in the presence of acetic acid for 2 days,[33] but when the reaction was carried out under MWI in a closed Teflon vessel, it required only 15 min to give a 68% yield (Scheme 2).

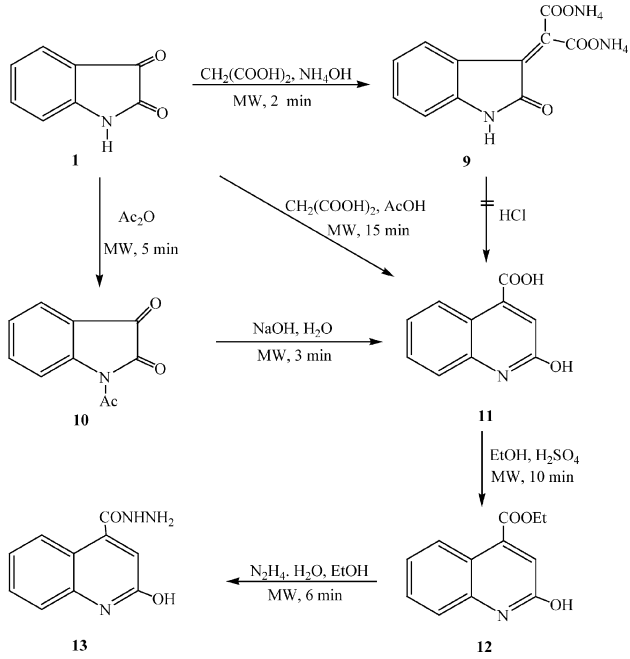
Isatin **(1)** has also been condensed with malonic acid in ammonia solution under MWI to give 94% yield of ammonium-3-(methylene di-acid)-oxindole **9** in a much shorter time (2 min) than under classical heating conditions (1 h).[34] However, in our hands the treatment of **9** with hydrochloric acid at room temperature did not give **11** as previously reported.[34] Esterification of **11** to the ethyl ester **12** and its subsequent transformation to the acid hydrazide **13** were carried out under MWI within 6–10 min to give 99 and 92% yields, respectively.

In conclusion, the use of MWI provides an efficient, clean, and quick methodology for the synthesis of quinoline-4-carboxylic acids as well as their esters and hydrazides with greater yields than the previously reported conventional methods.

EXPERIMENTAL

General Methods

Melting points were determined with a Mel-Temp apparatus and are uncorrected. TLC was performed on Baker-Flex silica gel 1B-F plates using ethyl



Scheme 2.

acetate–petroleum ether (3 : 2) and ethyl acetate–methanol (4 : 1) as eluents; the compounds were detected by UV light absorption. Irradiation was achieved using a domestic microwave oven EM-230M (800-W output power). IR spectra were recorded on Perkin-Elmer 1430 spectrometer. ^{1}H NMR spectra were recoded on Jeol spectrometer (500 MHz). Chemical shifts (δ) are given in ppm relative to TMS as internal standard.

General Procedure

Quinoline-4-carboxylic acids (5a–g): A mixture of isatin, 5-chloro, or 5-bromoisatin **1–3** (3.4 mmol), ketone (8.6 mmol), and potassium hydroxide (0.63 g, 11 mmol) in 20% aqueous ethanol (2 ml) was placed in a closed Teflon vessel and irradiated by MWI for 12.5 min. The reaction mixture was acidified with acetic acid and the product was recrystallized from EtOH or MeOH–$CHCl_3$.

2-Methylquinoline-4-carboxylic acid (5a): Yield 0.318 g, 50%; mp 244–245°C, lit.[35] mp 242°C.

2-Ethyl-3-methylquinoline-4-carboxylic acid[36] **(5b):** Yield 0.373 g, 51%; mp 287–288°C; IR (KBr): 2940 cm^{-1} (OH), 1708 cm^{-1} (C=O); ^{1}H NMR

($CDCl_3$): δ 1.47 (t, 3H, $J = 7.7$ Hz, CH_3CH_2), 2.69 (s, 3H, CH_3), 3.33 (q, 2H, CH_2CH_3), 7.92 (t, 1H, $J_{7,6} = 7.7$ Hz, $J_{7,8} = 8.6$ Hz, H-7), 8.05–8.08 (m, 2H, H-6, H-8), 8.21 (d, 1H, $J_{5,6} = 8.6$ Hz, H-5), 14.58 (s, 1H, COOH).

2-Isobutylquinoline-4-carboxylic acid (5c): Yield 0.467 g, 60%; mp 156–158°C, lit.[27] mp 192°C; IR (KBr): 2729 cm^{-1} (OH), 1692 cm^{-1} (C═O); ^1H NMR (DMSO-d_6): δ 0.89 (d, 6H, $J = 6.9$ Hz, $(CH_3)_2CH$), 2.10–2.18 [m, 1H, $CH(CH_3)_2$], 2.81 (d, 2H, $J = 7.7$ Hz, CH_2CH), 7.61 (t, 1H, $J_{7,6} = 6.9$ Hz, $J_{7,8} = 8.4$ Hz, H-7), 7.75 (ddd, 1H, $J_{6,5} = 8.4$ Hz, $J_{6,7} = 6.9$ Hz, $J_{6,8} = 1.5$ Hz, H-6), 7.78 (s, 1H, H-3), 8.01 (d, 1H, $J_{8,7} = 8.4$ Hz, H-8), 8.61 (d, 1H, $J_{5,6} = 8.4$ Hz, H-5).

6-Chloro-2-isobutylquinoline-4-carboxylic acid (5d): Yield 0.538 g, 60%; mp 182–184°C; IR (KBr): 2758 cm^{-1} (OH), 1705 cm^{-1} (C═O); ^1H NMR ($CDCl_3$): δ 1.02 (d, 6H, $J = 6.1$ Hz, $(CH_3)_2CH$), 2.27–2.29 [m, 1H, $CH(CH_3)_2$], 3.06 (d, 2H, $J = 7.7$ Hz, CH_2CH), 7.77 (dd, 1H, $J_{7,8} = 8.4$ Hz, $J_{7,5} = 1.5$ Hz, H-7), 8.00 (s, 1H, H-3), 8.31 (d, 1H, $J_{8,7} = 8.4$ Hz, H-8), 8.93 (s, 1H, H-5), 9.75 (s, 1H, COOH). Anal. calcd. for $C_{14}H_{14}NO_2Cl$: C, 63.76; H, 5.31; N, 5.31. Found: C, 63.84; H, 5.19; N, 5.22.

6-Bromo-2-isobutylquinoline-4-carboxylic acid (5e): Yield 0.627 g, 60%; mp 186–188°C, lit.[27] mp 189°C.

2-Phenylquinoline-4-carboxylic acid (5f): Yield 0.805 g, 95%; mp 212–214°C, lit.[37] mp 209–210°C, lit.[38] mp 210–212°C.

2-Methyl-3-phenylquinoline-4-carboxylic acid[26] (5 g): Yield 0.859 g, 96%; mp > 300°C; IR (KBr): 2735 cm^{-1} (OH), 1644 cm^{-1} (C═O); ^1H NMR ($CDCl_3$): δ 2.4 (s, 3H, CH_3), 7.35 (d, 2H, $J = 6.9$ Hz, Ph-H), 7.40–7.48 (m, 3H, Ph-H), 7.62 (t, 1H, $J_{7,8} = 6.9$ Hz, $J_{7,6} = 7.7$ Hz, H-7), 7.76 (t, 1H, $J_{6,7} = 7.7$ Hz, $J_{6,5} = 7.7$ Hz, H-6), 7.79 (d, 1H, $J_{8,7} = 6.9$ Hz, H-8), 8.02 (d, 1H, $J_{5,6} = 7.7$ Hz, H-5).

1,2,3,4-Tetrahydroacridine-9-carboxylic acid (6): A mixture of isatin **1** (0.5 g, 3.4 mmol), cyclohexanone (0.9 ml, 8.7 mmol), and potassium hydroxide (0.63 g, 11 mmol) in 20% aqueous ethanol (2 ml) was placed in a closed Teflon vessel and irradiated by MWI for 12.5 min. The reaction mixture was processed as previously described to give **6**; yield 0.734 g, 95%; mp 284°C (dec.), lit.[30] mp 285–286°C.

Ammonium 3-(methylene di-acid)-oxindole (9): A mixture of isatin **1** (1.0 g, 6.8 mmol) and malonic acid (0.8 g, 7.7 mmol) in 10% absolute ethanolic ammonia (3 ml) was placed in an Erlenmeyer flask (250 ml) and irradiated by MWI for 2 min. The product was filtered and washed with hot $CHCl_3$; yield 1.707 g, 94%; mp 168–170°C; mp was not determined in lit.[34] IR (KBr): 3581–2633 cm^{-1} (NH_4, NH), 1725 cm^{-1} (C═O).

***N*-Acetylisatin (10):** A mixture of isatin **1** (0.5 g, 3.4 mmol) and acetic anhydride (10 ml) was placed in an Erlenmeyer flask (250 ml) and irradiated

by MWI for 5 min. The product was filtered, washed with ether, and recrystallized from benzene; yield 0.45 g, 70%; mp 144–145°C, lit.[31] mp 143–144°C.

2-Hydroxyquinoline-4-carboxylic acid (11): Method (a): A mixture of *N*-acetylisatin **(10)** (0.5 g, 2.6 mmol) and sodium hydroxide (0.26 g, 6.5 mmol) in water (10 ml) was placed in an Erlenmeyer flask (250 ml) and irradiated by MWI for 3 min; the reaction mixture was acidified with acetic acid and the product was recrystallized from EtOH; yield 0.325 g, 65%; mp 332–336°C, lit.[31] mp 335–338°C.

Method (b): A mixture of isatin **1** (1.0 g, 6.8 mmol) and malonic acid (1.07 g, 10.3 mmol) in acetic acid (3 ml) was placed in a closed Teflon vessel and irradiated by MWI for 15 min. The product (0.874 g, 68%), was found to be identical with that obtained from the previous method.

Ethyl 2-substituted quinoline-4-carboxylate (7) and (12): A mixture of compound **5f** or **11** (2.02 mmol), ethyl alcohol (3 ml), and concentrated sulfuric acid (0.5 ml) was placed in a closed Teflon vessel and irradiated by MWI for 10 min. The mixture was neutralized with sodium bicarbonate solution and the products were recrystallized from EtOH.

Ethyl 2-phenylquinoline-4-carboxylate (7): Yield 0.523 g, 94%; mp 56–58°C, lit.[29] mp 58–59°C.

Ethyl 2-hydroxyquinoline-4-carboxylate (12): Yield 0.432 g, 99%; mp 210–212°C, lit.[32] mp 206°C.

2-Substituted quinoline-4-carboxylic acid hydrazides (8) and (13): A mixture of the ethyl ester **7** or **12** (1.38 mmol) in ethyl alcohol (3 ml) was treated with hydrazine hydrate (4.6 mmol) and then irradiated by MWI for 6 min in a closed Teflon vessel. The products were recrystallized from EtOH.

2-Phenylquinoline-4-carboxylic acid hydrazide (8): Yield 0.29 g, 80%; mp 222–224°C, lit.[29] mp 224°C.

2-Hydroxyquinoline-4-carboxylic acid hydrazide (13): Yield 0.257 g, 92%; mp 288–290°C, lit.[39] mp 287–288°C.

REFERENCES

1. Morimoto, Y.; Matsuda, F.; Shirahama, H. Total synthesis of (±) virantmycin and determination of its stereochemistry. *Synlett.* **1991**, 202–203.
2. Isobe, M.; Nishikawa, T.; Yamamoto, N.; Tsukiyama, T.; Ino, A.; Okita, T. Methodologies for synthesis of heterocyclic compounds. *J. Heterocycl. Chem.* **1992**, *29*, 619–625.
3. Markees, D. G.; Dewey, V. C.; Kidder, G. W. Antimalarials. 4,4′-Diaminodiphenyl sulfone-type compounds. *J. Med. Chem.* **1970**, *13*, 324–326.
4. Alhaider, A. A.; Abdelkader, M. A.; Lien, E. J. Design, synthesis, and pharmacological activities of 2-substituted 4-phenyl quinolines as potential antidepressant drugs. *J. Med. Chem.* **1985**, *28*, 1394–1398.

5. Campbell, S. F.; Hardstone, J. D.; Palmer, M. J. Diamino-6,7-dimethoxyquinoline derivatives as α_1-adrenoceptor antagonists and antihypertensive agents. *J. Med. Chem.* **1988**, *31*, 1031–1035.
6. David, H. P. (du Pont de Nemours, E.I., and Co.). Preparation of 2-phenyl-4-quinoline carboxylates as antitumer agents. U. S. Pat. 1987 4,680,299; Chem. Abstr. **1988**, *109*, 54674k.
7. Yu, X. Y.; Hill, J. M.; Yu, G.; Yang, Y.; Kluge, A. F.; Keith, D.; Finn, J.; Gallant, P.; Silverman, J.; Lim, A. A series of quinoline analogues as potent inhibitors of *C. albicans* prolyl tRNA synthetase. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 541–544.
8. Kar, A. Structure of the isonicotinyl hydrazone of norethindrone. *J. Pharm. Sci.* **1983**, *72*, 1082–1084.
9. Dubroeucq, M. C.; Lefur, G.; Renault, C. 4-Quinoline carboxamide derivatives. Eur. Pat. 1884 112776; Chem. Abstr. **1984**, *101*, 191716.
10. Atwell, G. J.; Bos, C. D.; Baguley, B. C.; Denny, W. A. Potential antitumor agents. 56. "Minimal" DNA-intercelating ligands as antitumor drugs: Phenylquinoline-8-carboxamides. *J. Med. Chem.* **1988**, *31*, 1048–1052.
11. Medvecky, R.; Hornackova, M.; Odlerova, Z. Research of new antituberculotics. III. Preparation and antimycobacterial effect of halogen-substituted thioamides of 4-quinolinecarboxylic acid. *Acta Fac. Pharm. Univ. Comenianae* **1991**, *43*, 15–31; *Chem. Abstr.* **1991**, *115*, 228126.
12. Abdel-Rahman, A. A. H.; El Ashry, E. S. H. Efficient synthesis of 5-hydroxymethyl pyrimidines and their nucleosides using microwave irradiation. *Synlett* **2002**, 2043–2044.
13. Abdel Hamid, H.; Ramadan, E.; Hagar, M.; El Ashry, E. S. H. Synthesis of aryloxyacetic acids, esters and hydrazides assisted by microwave irradiation. *Synth. Commun.* **2004**, *34*, 377–382.
14. El Ashry, E. S. H.; Ramadan, E.; Abdel Hamid, H.; Hagar, M. Microwave irradiation for accelerating each step for the synthesis of 1,2,4-triazino[5,6-*b*]indole-3-thiols and their derivatives from isatin and 5-chloroisatin. *Synlett* **2004**, 723–725.
15. El Ashry, E. S. H.; Ramadan, E.; Abdel Hamid, H.; Hagar, M. Synthesis of azlactones, phenylpyruvic acid, and 1,2,4-triazine derivatives under microwave irradiation. *Lett. Org. Chem.* **2005**, *2*, 136–139.
16. Tu, S.; Wei, Q.; Ma, H.; Shi, D.; Gao, Y.; Cui, G. The synthesis of novel substituted 2,5-dioxo-1,2,3,4,5,6,7,8-octahydroquinolines without solvent under microwave irradiation. *Synth. Commun.* **2001**, *31*, 2657–2661.
17. Tu, S.; Gao, Y.; Miao, C.; ;, Li; TZhang, X.; Zhu, S.; Fang, F.; Shi, D. A novel reaction of aldoxime with dimedone under microwave irradiation. *Synth. Commun.* **2004**, *34*, 1289–1294.
18. Ahluwalia, V. K.; Goyal, B.; Das, U. One-pot syntheses of 5-oxo-1,4,5,6,7,8-hexahydroquinolines and pyrimido[5,6-*b*]quinolines using microwave irradiation and ultrasound. *J. Chem. Res., Synop.* **1997**, 266.
19. Wang, J. X.; Zhang, M.; Hu, Y. Synthesis of 8-quinolinyl ethers under microwave irradiation. *Synth. Commun.* **1998**, *28*, 2407–2413.
20. Sabitha, G.; Satheesh Babu, R.; Subba Reddy, B. V.; Yadav, J. S. Microwave-assisted Friedländer condensation catalyzed by clay. *Synth. Commun.* **1999**, *29*, 4403–4408.
21. Mojtahedi, M. M.; Sharifi, A.; Mohsenzadeh, F.; Saidi, M. R. Microwave-assisted aminomethylation of electron-rich compounds under solvent-free condition. *Synth. Commun.* **2000**, *30*, 69–72.

22. Varma, R. S.; Saini, R. K. Microwave-assisted isomerization of 2′-aminochalcones on clay: An easy route to 2-aryl-1,2,3,4-tetrahydro-4-quinolines. *Synlett* **1997**, 857.
23. Longhmani-Khouzani, H.; Sadeghi, M. M.; Safari, J.; Minaeifar, A. A novel method for the synthesis of 2-ketomethyl quinolines under solvent-free conditions using microwave irradiation. *Tetrahedron Lett.* **2001**, *42*, 4363–4364.
24. Suarez, M.; Loupy, A.; Salfran, E.; Moran, L.; Rolando, E. Synthesis of decahydroacridines under microwaves using ammonium acetate supported on alumina. *Heterocycles* **1999**, *51*, 21–27.
25. Lindwall, H. G.; Maclennan, J. S. A condensation of acetophenone with isatin by the Knoevenagel method. *J. Am. Chem. Soc.* **1932**, *54*, 4739–4744.
26. Henze, H. R.; Carroll, D. W. Utilization of n-alkyl methyl ketones in the Pfitzinger reaction. *J. Am. Chem. Soc.* **1954**, *76*, 4580–4584.
27. Buu-Hoi, N. P.; Royer, R. The application of Pfitzinger reactions of the synthesis of quinoline derivatives: A novel route to 4-hydroxyquinolines. *J. Chem. Soc.* **1948**, 106–110.
28. Lackey, K.; Sternbach, D. D. Synthesis of substituted quinoline-4-carboxylic acids. *Synthesis* **1993**, 993–997.
29. Gansser, C.; Rumpf, P. Contribution á la chimiothérapie de la tuberculose I influence exercée sur l'activité des hydrazides par l'introduction de groupements lipophiles ou hydrophiles et par une extension du systéme conjugué. *Helv. Chim. Acta* **1953**, *36*, 1423–1432.
30. Al-Tai, F. A.; Sarkis, G. Y. Further utilization of cyclic ketones in the Pfitzinger reaction. *Bull. Coll. Sci.* **1963**, *7*, 11–15; *Chem. Abstr.* **1964**, *61*, 10657b.
31. Campbell, K. N.; Kerwin, J. F. Studies in the quinoline series. II. The preparation of some dialkylaminomethyl-4-quinoline methanols. *J. Am. Chem. Soc.* **1946**, *68*, 1837–1840.
32. Kondo, H.; Nozoe, T. K. Transformation of α-ethoxycinchoninic acid to ethyl-α-hydroxycinchoninate. *J. Pharm. Soc. Japan* **1936**, *56*, 10–16.
33. Borsche, W.; Jacobs, W. Untersuchungen über isatin und verwandte verbindungen. *I. Ber.* **1914**, *47*, 354–363.
34. Lindwall, H. G.; Hill, A. J. Condensation reactions of cyclic ketones. III. Oxindolemalonic acid derivatives. *J. Am. Chem. Soc.* **1935**, *57*, 735–737.
35. Pandalai, K. M. Synthesis of substituted cinchoninic acids by the use of weak bases as condensation agents. *Ann.* **1935**, *515*, 302–306; *Chem. Abstr.* **1935**, *29*, 2172.
36. Koelsch, C. F. Steric factors in the thermochromism of spiropyrans and in reactivities of certain methylene groups. *J. Org. Chem.* **1951**, *16*, 1362–1370.
37. DuPuis, R. N.; Lindwall, H. G. A synthesis of 1,4-dihydrocinchophens from 3-phenacyloxindoles. *J. Am. Chem. Soc.* **1934**, *56*, 2716–2719.
38. DuPuis, R. N.; Lindwall, H. G. A synthesis of cinchophens from phenacylideneoxindoles. *J. Am. Chem. Soc.* **1934**, *56*, 471–472.
39. Toldy, L.; Nogradi, T.; Vargha, L.; Ivanovics, G.; Koczka, I. Antituberculous agents. I. Thiosemicarbazones and hydrazides. *Acta Chim. Acad. Sci. Hung.* **1954**, *4*, 303–313; *Chem. Abstr.* **1956**, *50*, 362.