Microwave-assisted synthesis of 2-pyridone and 2-pyridone-based compounds

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Abstract

2-Pyridones are important heterocyclic compounds that are widely used in medical chemistry, and their various derivatives have significant biological and medical applications. In this paper, the synthesis of 2-pyridones as well as 2-pyridone-based compounds, such as 2-quinolones, using microwave assisted organic chemistry is reviewed. The review is divided in three parts. In the first part, microwave synthesis of 2-pyridones according to the type of condensation is discussed. In the second part, microwave assisted synthesis of 2-quionolones is listed. At the end of the review several examples of microwave synthesis of other 2-pyridone based compounds (ring fused *N*-substituted 2-pyridones) are given.

Keywords: heterocyclic compounds, medical chemistry, microwave assisted organic chemistry, 2-quinolone ring fused *N*-substituted 2-pyridones.

Available online at the Journal website: http://www.ache.org.rs/HI/

REVIEW PAPER

UDC 61:54]:547.7/.8:547.824

Hem. Ind. **68** (1) 1–14 (2014)

doi: 10.2298/HEMIND121204021M

Aromatic heterocyclic compounds represent an important group of compounds due to their biological and medical applications. The six-member heterocyclic rings containing nitrogen (*e.g.*, pyridine, pyridone, pyrimidine, piperidine and piperazine) are used in medicine since they possess certain pharmacological properties. Among them, 2-pyridone compounds are particularly significant (Figure 1).

2-Pyridone derivatives are especially interesting because the 2-pyridone structure is present in many compounds of natural origin [1], many of which possess biological activity. Most of these compounds possess antibacterial [2,3], antifungal [4], anti-inflammatory [5], antiviral [6,7], antitumor [8] and antiplatelet [9,10] properties. 2-Pyridone derivatives are used in the manufacturing of paints [11], pigments, additives for fuels and lubricants, acid-base indicators, stabilizers for polymers and coatings [12]. Due to a variety of pharmacological properties, the 2-pyridone structure is important in the pharmaceutical industry [13]. Many medications contain 2-pyridone structure: cardiotonics (milrinone (Figure 1a) and amrinone (Figure 1b) used for the treatment of heart failure [14,15]; and antibiotics (pilicides (Figure 1c) and curlicides) which treat bacterial infections caused by Gram-negative bacteria [16,17]. A derivative of *N*-phenyl-2-pyridone, perampanel (Figure 1d), acts as a non-competitive and selective antagonist of α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor, and improves motor symptoms in animal models of Parkinson's disease [18].

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Paper received: 4 December, 2012

Paper accepted: 25 January, 2013

It should be noted that 4-pyridone, isomer of 2-pyridone, due to mesogenic properties, is used in the synthesis of liquid crystals [19]. It has antioxidant properties and is used in the treatment of hyperglycemia [20]. 4-pyridone also has the capability of complexation and can be used for the preparation of supramolecular structures [21]. Methylated *N*-4-pyridone derivatives are used as intermediates for the synthesis of pharmaceuticals, pesticides, insecticides, fungicides, etc. *N*-Methyl-4-pyridone is used in the production of compounds that are used to produce images [22].

Due to the many applications of the compounds that contain 2-pyridone structure, a number of procedures for their synthesis was developed [23,24]. A general procedure for obtaining substituted 2-pyridones is the Guareschi-Thorpe condensation reaction of 1,3-dicarbonyl compounds with cyanoacetamide [25,26], which was used for the synthesis of large number of pyridones [27–29]. Cyclization of cyanoacetamide with 1,3-dicarbonyl compounds belongs to the 3-2 type of condensation that leads to the formation of pyridone ring. The mechanism of the reaction is complex and involves Knoevenagel reaction, addition of Michael or Perkin reaction, whereby the degree of enolyzation of dioxo compounds determines the participation of Michael addition [30,31]. Also, this type of reaction is used to obtain arylazo pyridone dyes [32–37]. Unlike conventional conditions (high temperature, polar organic solvents), the newer approach, enzymatically catalyzed synthesis of 2-pyridones, carried under mild reaction conditions, is characterized by high regio- and stereo-selectivity, high purity and final yield of the obtained products [38,39].

The conventional way of performing organic synthesis involves heating by external heat sources (*e.g.*, oil bath). In this way, heat is transferred by conduction,

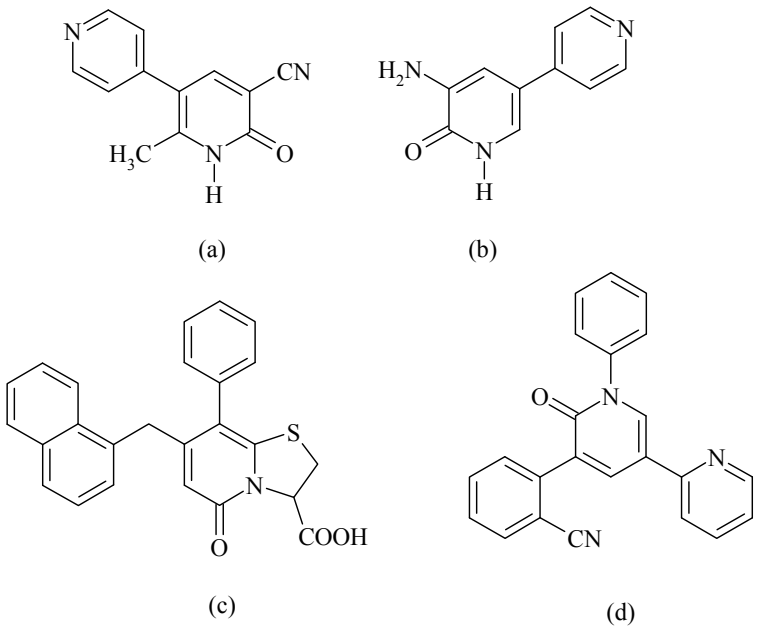


Figure 1. 2-Pyridone compounds which possess physiological activity: a) milrinone, b) amrinone, c) ring fused pyridone with pilicide activity and d) perampanel.

which is a slow and inefficient method of energy transfer, because it depends on the thermal conductivity of the materials and the reactor temperature is higher than the temperature of the reaction mixture. On the other hand, microwave irradiation is an efficient way of heating where energy is transmitted directly through interaction with polar molecules present in the reaction mixture [40,41].

Microwave irradiation is not ionizing and does not belong to harmful radiation. Microwaves have a frequency between 0.3 GHz and 300 GHz, corresponding to wavelengths between 1 cm and 1 m [42]. The main advantages of microwave-assisted organic chemistry are the increase of product yields and the reduction of reaction time [43,44]. The short reaction time and the increasing number of microwave assisted reactions lead to the application of this technique in the various fields of industry. For example, the modern pharmaceutical industry requires the creation of a growing number of new molecules, forcing chemists to conduct a number of experiments in a short period of time [45]. Also, the microwave technique is used in the food industry as well as in the pyrolysis of waste materials [46], the preparation of samples for analysis [47], extraction of natural products [48] and hydrolysis of proteins and peptides [49].

Microwave synthesis is among methods that respect the principles of the so-called "green chemistry" which is one more reason for performing this type of synthesis [50].

In this paper, the synthesis of the certain 2-pyridones and 2-pyridone based compounds using microwave irradiation will be discussed. We will point out the advantages of microwave assisted synthesis in comparison to conventional heating. First, we will discuss the microwave synthesis of 2-pyridones. In the second part, microwave assisted synthesis of 2-quionolones will be given. At the end of the review, examples of microwave synthesis of ring fused *N*-substituted 2-pyridones will be discussed.

MICROWAVE SYNTHESIS OF 2-PYRIDONE

The application of microwave techniques in the synthesis of organic compounds has inevitably led to the microwave synthesis of compounds with the 2-pyridone ring. In the beginning, the synthesis was performed using conventional microwave ovens. Due to the problems associated with the use of these ovens in the synthesis (reproducibility, controllability and safety), dedicated microwave reactors were introduced. The basic principles of synthesis of heterocyclic molecules used in conventional synthesis were applied to microwave synthesis [51]. Thus conducted synthetic route yield pyridone ring from fragments containing different numbers of carbon atoms. Different combinations of fragments were used: 4-1, 3-2, 1-3-1, 2-2-1 and 2-1-2. Condensation of type 4-1 means that the condensation involves two acyclic systems one of which has four and the other only one carbon atom. Nitrogen can be a part of one of the fragments, or be introduced as a separate fragment.

A good example of such a combination is given in a paper by Gorobets *et al.* [1], in which different carbonyl building blocks were reacted with *N*,*N*-dimethyl-

formamide dimethyl acetal (DMFDMA) to obtain enaminones in high yields (the reaction is carried out in the absence of solvent and at elevated temperature). The obtained enaminones, without purification, react with different methylene nitriles at 100 °C for 5 min in 2-propanol and in the presence of a catalytic amount of piperidine (base). In this way, the authors were able to isolate 18 different 2-pyridones of 80 possible with yields varying from 27 to 96%, while some products were obtained in pure form after simple filtration. This synthesis is given in Figure 2.

An example of 3-2 type condensation of 3-cyano-2--pyridones is shown in Figure 3 [28]. *N*-substituted 4,6--dimethyl-3-cyano-2-pyridones were obtained from acetylacetone and the corresponding *N*-substituted cyanoacetamide using conventional and microwave synthesis in the presence of piperidine as a catalyst. Conventional synthesis was performed by heating the reaction mixture under reflux (solvent mixture water/ /ethanol). Microwave synthesis was performed using a conventional microwave oven in the absence of solvent. The products were obtained in high yields and in a short reaction time (up to 7 min), while the conventional method of synthesis required up to 4 h with lower yields (Figure 4).

6-Hydroxy-3-cyano-4-methyl-2-pyridone was also synthesized using microwave technique (condensation type 3-2). The first microwave synthesis was reported in 1994 in the German patent [52]. Compared to the conventional synthesis which takes 16.5 h with a yield of 80%, microwave synthesis is carried out for 5 min with a yield of 96%. In this synthesis, product was obtained starting from cyanoacetamide, ethyl cyanoacetate and ethylamine. This pyridone can also be

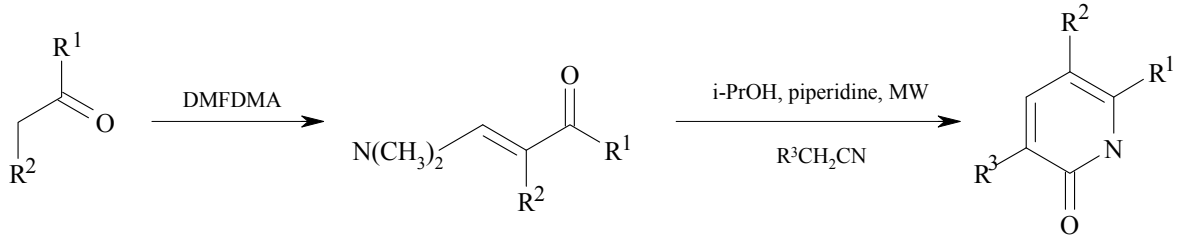


Figure 2. Microwave synthesis of substituted 2-pyridones from enaminones.

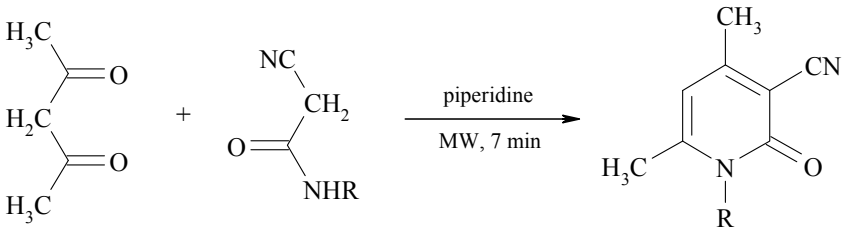


Figure 3. Synthesis of N-substituted 4,6-dimethyl-3-cyano-2-pyridones.

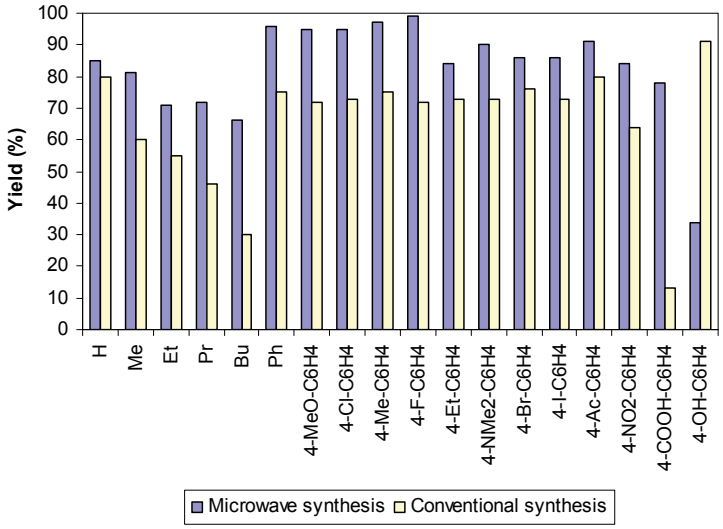


Figure 4. N-Substituted 4,6-dimethyl-3-cyano-2-pyridones yields obtained by microwave and conventional synthesis.

obtained using conventional synthesis with potassium hydroxide as a catalyst [27,53]. Reaction times varied from 1 to 8 h, with yields ranging from 40–60%. Recently, a synthesis of this pyridone was published, using microwave irradiation in a conventional microwave oven, in the absence of solvent starting from ethyl cyanoacetate and cyanoacetamide, using powdered potassium hydroxide as a catalyst (Figure 5). The isolated yield was 60%, after only 4 min of irradiation [54].

Dave *et al*. reported on microwave synthesis of 4,6-diaryl-3-cyano-2-pyridones starting from cyanoacetamide and 1,3-diarylpropen-1-ones in the presence of powdered potassium hydroxide, with phenyl or substituted phenyl groups in positions 4 and 6 [55]. The authors have reported yields that ranged from 74 to 81% with high purity of compounds after only 1–2 min of irradiation (Figure 6).

Microwave synthesis of arylazo pyridone dyes [56] is based on the previously described 3-2 type of condensation. This type of synthesis involves the reaction of phenylazo carbonyl compounds and cyanoacetamide using KOH as base and ethanol as solvent in a dedicated microwave reactor. Synthesis of 5-phenylazo-4,6-dimethyl-3-cyano-2-pyridones and 5-phenylazo-4,6-diphenyl-3-cyano-2-pyridone are shown in Figure 7. The synthesized derivatives of 4,6-dimethyl-3-cyano-2-pyridone (Table 1, entries 1–6) were obtained in nearly quantitative yield, while the derivatives of 4,6-diphenyl-3-cyano-2-pyridones (Table 1, entries 7–9) were obtained in lower yields. Synthesis of 5-phenylazo-4,6-dimethyl-3-cyano-2-pyridone in the conventional manner [35] also takes place in the presence of a base in ethanol, except that this synthesis lasted for 3 h with somewhat lower yields (70–80%).

Similarly, the synthesis of the 5-phenylazo-2-hydroxy-4-methyl-3-cyano-2-pyridones starting from β-phenylazo ketoesters under the same conditions was performed (Figure 7, Table 1, entries 10–13). In addition to these products a derivative of 2-hydroxy-4-phenyl-3-cyano-2-pyridones was also obtained (Table 1, entry 14). In comparison to derivatives of dialkyl 2-pyridone, lower yields were obtained as a result of lower reactivity of β-keto esters compared to 1,3-diketones [56], in which is still higher yield compared to conventional synthesis (30–60%) [32].

Synthesis of substituted 3-cyano-2-pyridones at positions 4 and 6 was also carried out using microwave irradiation (1-2-2 type condensation) [57], and under conventional conditions [58] (Figure 8). By applying microwave irradiation (dedicated microwave reactor) yields of 90–95% over 5–7 min were obtained, while

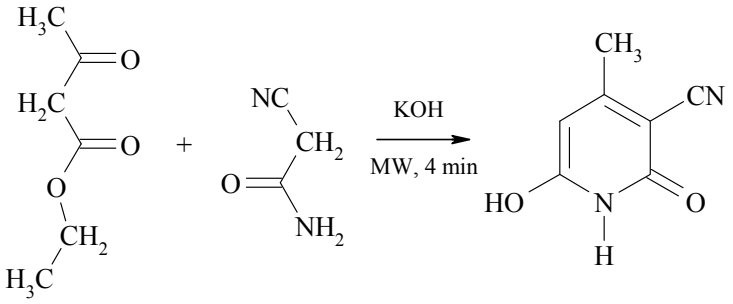


Figure 5. Synthesis of 4-methyl-6-hydroxy-3-cyano-2-pyridones.

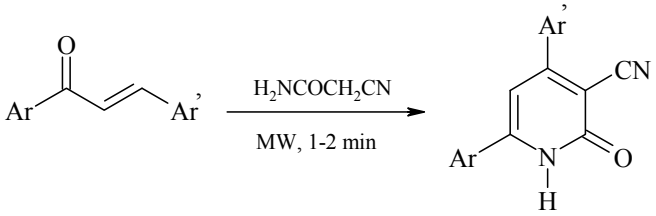


Figure 6. Synthesis of 4,6-diaryl-3-cyano-2-pyridones.

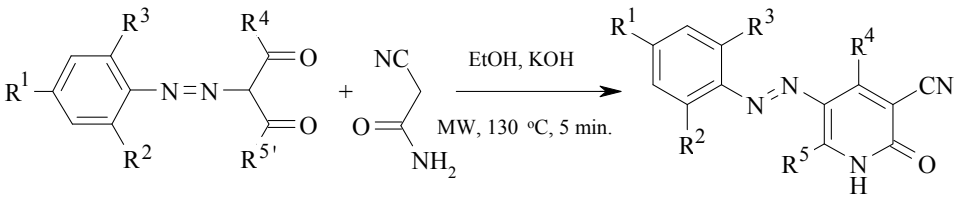
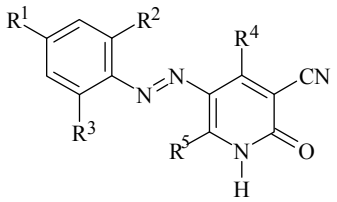


Figure 7. Microwave synthesis of arylazo 4,6-dimethyl- and 4,6-diphenyl-3-cyano-2-pyridone dyes.

Table 1. Synthesized arylazo 4,6-dimethyl- and 4,6-diphenyl-3-cyano-2-pyridone dyes with their yields



Entry	R^1	R^2	R^3	R^4	R^5	Yield, %
1	H	H	H	Me	Me	99
2	H	H	NO_2	Me	Me	100
3	Br	H	H	Me	Me	92
4	Br	Me	Me	Me	Me	100
5	H	Me	Me	Me	Me	100
6	H	H	I	Me	Me	100
7	H	H	H	Ph	Ph	72
8	Br	Me	Me	Ph	Ph	72
9	H	Me	Me	Ph	Ph	83
10	H	H	H	Me	OH	47
11	Br	H	H	Me	OH	93
12	Br	Me	Me	Me	OH	80
13	H	Me	Me	Me	OH	50
14	H	H	H	Ph	OH	78

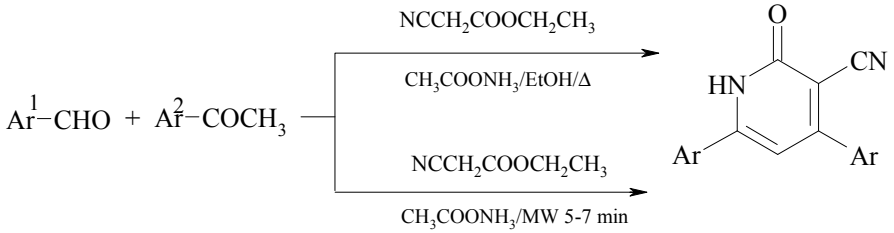


Figure 8. Conventional and microwave synthesis of substituted 3-cyano-2-pyridones.

the conventional method of synthesis lasted for 6 h and gave lower yields (67–85%).

Another example of microwave synthesis of 2-2-1 condensing type of 2-pyridones is shown in Figure 9 [59]. The synthesis of 3,5-dicyano-2-pyridone is carried out in aqueous solution starting from aldehydes and malononitrile in the presence of sodium hydroxide as a base. The advantage of this synthesis is short reaction time, efficiency and use of water instead of organic solvents which have a favorable impact on the environment. The method is applicable not only to aromatic aldehydes with electron-donor and electron-acceptor groups, but also to heterocyclic and aliphatic aldehydes.

Syntheses were performed at 100 °C both in the conventional and the microwave method. The reaction time of microwave synthesis was 2–3 min while conventional synthesis took 2–3 h. On the other hand, reaction yields increased from 25–37% (conventional) to 40–49% (microwave synthesis).

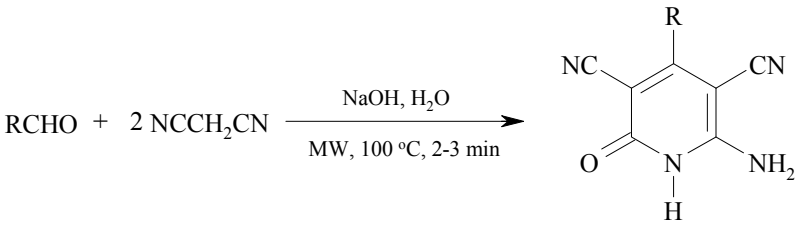


Figure 9. Synthesis of 4-substituted 6-amino-3,5-dicyano-2-pyridones in aqueous media under microwave irradiation.

4-Aryl substituted 5-alkoxycarbonyl-6-methyl-3,4--dihydropyridones were prepared by the reaction of Meldrum's acid, methyl acetoacetate and appropriate benzaldehyde in the presence of ammonium acetate (2-2-1 condensation type, Figure 10) [60–62]. Microwave assisted synthesis, performed in a dedicated microwave reactor, produced pure products in high yields (81–91%), while the conventional synthesis gave yields lower by 17–28%.

Synthesis of 2-pyridone based bifunctional compounds (1,4-dihydropyridines) by the condensation of dialdehyde, Meldrum's acid, acetoacetic acid and ammonium acetate is another example of 2-2-1 type condensation of pyridones (Figure 11) [63]. This synthesis was achieved by heating the reaction mixture in a conventional microwave oven for 8 min using small amounts of glycol as an energy transfer reagent (yield 83%).

MICROWAVE SYNTHESIS OF RING FUSED 2-PYRIDONE DERIVATIVES

Synthesis of 2-quinolones

The most widely used procedure for the synthesis of 2-quinolones is the reaction of aniline with malonic acid esters. However, this reaction is conducted at high temperatures (250–350 °C) that are difficult to achieve by conventional heating methods. The reaction of aniline with malonic acid esters produces two moles of ethanol, which affect the equilibrium between the reactants and the reaction products (Figure 12). There-

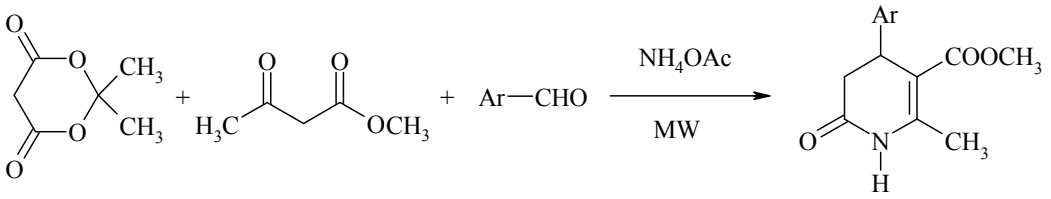


Figure 10. Synthesis of 4-aryl substituted 5-alkoxycarbonyl-6-methyl-3,4-dihydropyridones.

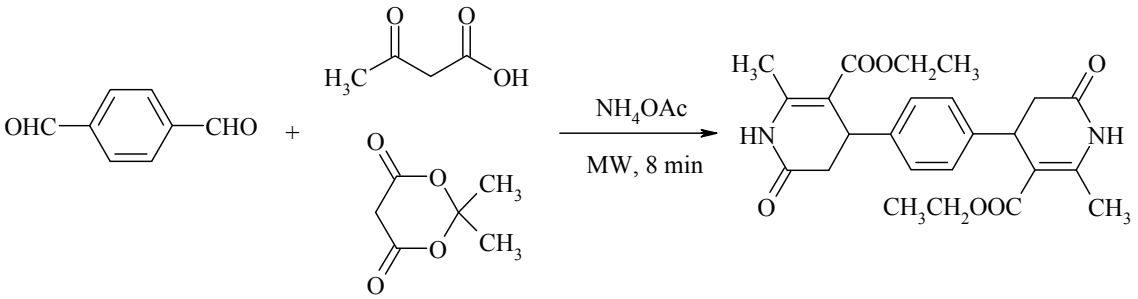


Figure 11. Synthesis of bifuncional 2-pyridone.

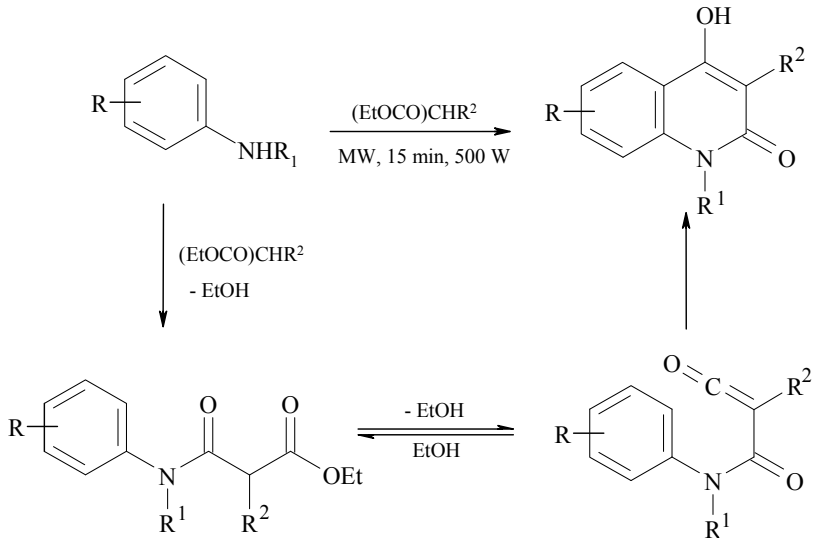


Figure 12. Formation of 3-substituted 4-hydroxy-2-quinolones in the reaction between anilines and substituted malonic esters.

fore, it is essential, if the reaction is carried out in a closed reactor, to maintain the volume and concentration of reactants low, in order to shift the equilibrium towards the products. On the other hand, the reaction can be carried out in an open vessel even on a larger scale without such demands [64]. It was found that the synthesis of 4-hydroxy-2-quinolones proceeds best when an electron-donor group (R) is substituent in aniline. The nucleophilicity of the nitrogen is increased and therefore both reactions, the condensation with the malonic ester and the ring closing acylation proceed faster (Figure 5). The presence of R^2-aryl group provides additional conjugation and stability of the product, which is reflected in the high product yield (up to 94%) [64].

This method cannot be applied in cases where an electron-acceptor group (*e.g.*, trifluoromethyl group) is substituent in aniline. In this case, malondianilide was treated with Eaton's reagent (7.7% phosphorus pentoxide in methanesulfonic acid) and resulted in high yield products (80–90%, Figure 13) [65,66].

In addition to Eaton's reagent, *p*-toluenesulfonic acid can be used in the microwave synthesis of 2-quinolones. 2-Quinolones can be obtained from substituted aniline and diethyl malonate with a yield of 89––96% in only 6 min [67]. Instead of *p*-toluenesulfonic acid, silica gel or aluminum oxide can be used, but yields were lower with longer reaction times. Also, malonic acid can be used. Microwave synthesis of 2-quinolones can be achieved in a conventional microwave oven by irradiation of a mixture of aniline and malonic acid in the presence of dimethylformamide for 3–5 min (yield 85–94%) [68].

Instead of diethyl malonate/malonic acid, acetoacetic ester can be used. In this manner, carbostyril analogues can be synthesized (Figure 14). The synthesis is favored by electron-donor groups in the aniline ring and electron-acceptor groups in electrophilic compounds [69]. Microwave synthesis reduces the reaction time from 18–58 h to just 80 min giving products of high purity and in higher yield (58%).

In a similar way, 2-quinolones can be obtained from *o*-aminoarylketones and acetoacetic ester using microwave synthesis (4–6 min at 160 °C in the presence of a catalyst ($CeCl_3 \cdot 7H_2O$) – yields 85–95%) (Figure 15) [70]. In comparison to conventional synthesis, microwave reactor synthesis shows that the reaction is 5 or more times faster using microwave technique.

2-Quinolones can also be obtained by intramolecular Heck cyclizations of heteroarylamide [71]. Conventionally Heck cyclizations are achieved with *N*,*N*-dimethylacetamide (DMA) as a solvent, potassium acetate and $Pd(PPh_3)_4$ as a catalyst at 120 °C for 24 h with yields from 56 to 89%. Microwave irradiation often has a positive effect on the metal-catalyzed reactions [72–75] and in this case 2-quinolones were

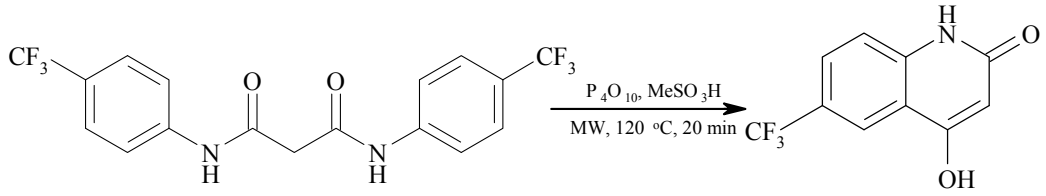


Figure 13. Synthesis of 2-quinolones from 1,3-dicarbonyl compounds.

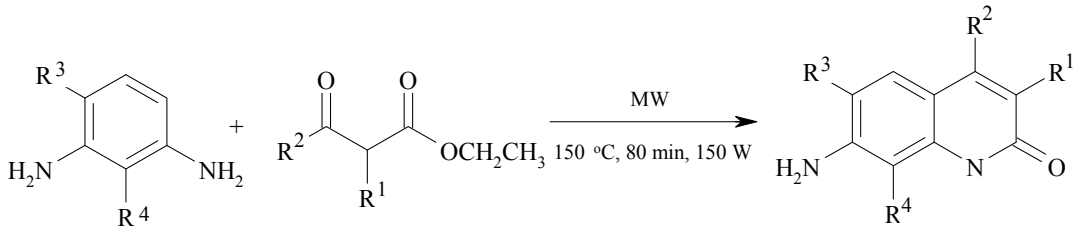


Figure 14. Synthesis of carbostyril analogues of 2-quinolones from 1,3-dicarbonyl compounds.

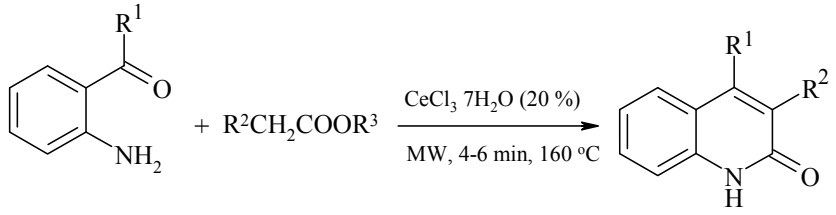


Figure 15. Synthesis of 2-quinolones by the $CeCl_3$-catalysed reaction.

obtained in 90–96% yields during 12-30 min in DMA (Figure 16).

Stadler *et al*. [76] applied successfully the microwave technique in the synthesis of 4-hydroxy-2-quinolone (Figure 17). The reaction was performed in 1,2--dichlorobenzene, in which the reactants are soluble, but the product of the reaction is not. The product, of high purity, can be obtained from the reaction mixture by simple filtration. The reaction can be also performed by applying solvent-free microwave irradiation conditions.

2-Quinolone derivative, needed for the synthesis of cryptotackieine and cryptosanguinolentine, compounds which display various biological properties, can also be obtained from *o*-vinylsubstituted isocyanate by microwave heating [77]. 3-Aryl substituted 2-quinolones were synthesized in yields of 80% by heating the reaction mixture in a dedicated microwave reactor at 150 °C for 12 min in nitrobenzene as a solvent (Figure 18).

It should be noted that 4-quinolones can be obtained from substituted aniline and diethyl (etoxymethylene) malonate in a conventional microwave oven. Although the synthesized compounds (ethyl esters of 4-oxo-1,4-dihydroquiniline-3-carboxylic acid) were obtained in a yield of about 50%, the reaction times were from 0.4 to 5 min [78].

Synthesis of other ring fused 2-pyridone derivatives

In the last part of this review, the synthesis of condensed derivatives of 2-pyridone (ring fused *N*-sub-

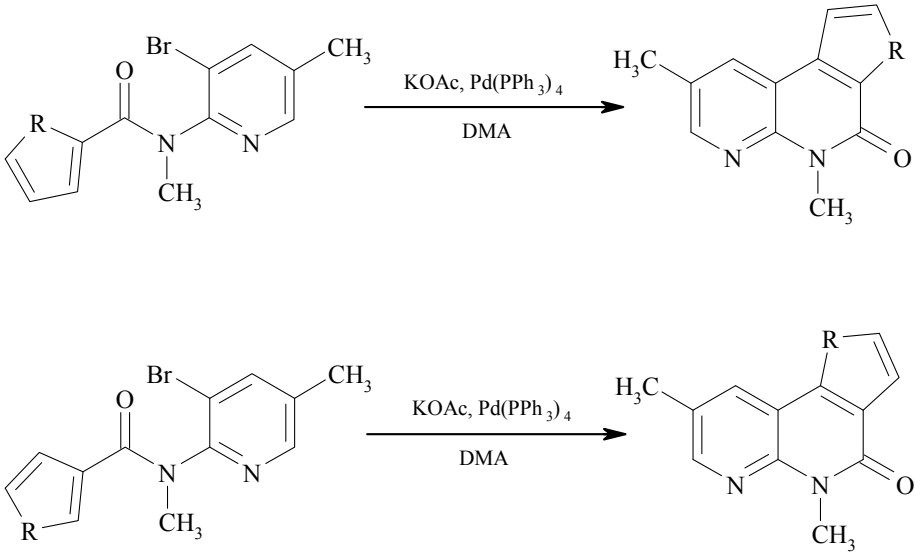


Figure 16. Synthesis of heterocyclic derivatives of 2-quinolones using intramolecular Heck coupling.

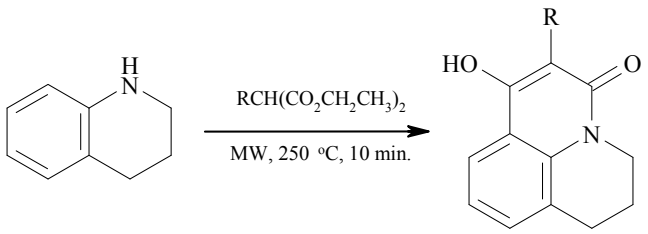


Figure 17. Microwave synthesis of 2-quinolones.

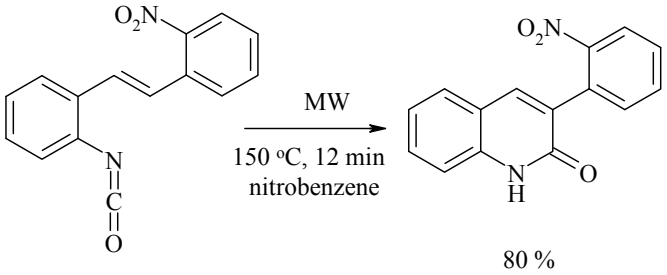


Figure 18. Microwave synthesis of 2-quinolones from o-vinyl substituted isocyanates.

stituted 2-pyridones) will be presented. The optically active bicyclo-2-pyridone was obtained by the reaction of acyl-ketenes with substituted Δ^2-thiazolines by microwave heating at 140 °C for 2 min with the yield of 73 to 95% (Figure 19). The thiazolines were prepared from iminoethers and cysteine while the acyl-ketenes were generated *in situ* from acyl Meldrum's acid derivatives [79]. This type of synthesis leads to the preparation of pilicide and curlicide compounds, based on the same peptidomimetic scaffold, that target bacterial virulence factors in Gram-negative bacteria [16,17].

It was demonstrated that the sulfur in the pilicide scaffold could be exchanged for oxygen with an almost retained pilicide activity. Dihydrooxazolo and dihydrothiazolo ring fused 2-pyridones were prepared using microwave assisted organic synthesis in good yields and high enantiomeric purity. Trifluoro acetic acid (TFA), tosic acid and pyridinium *p*-toluenesulfonate were used to optimize reaction conditions. Reactions were performed in 1,2-dichloroethane (DCE) at 120 °C for 140 s [80].

The above mentioned reactions were carried out in the presence of solvents [81] and in the solid state [82] using the conventional synthesis. However, the use of microwave irradiation has a number of advantages over both conventional methods: the reaction is carried out in two steps by reducing the reaction time from 2 days (conventional method) to 8±2 min with yields up to 79%. Microwave synthesis requires less acid which results in milder reaction conditions. Instead of Δ^2-thiazoline, imines can be used, thus making possible synthesis of multiple ring fused 2-pyridones (Figure 20) [83]. TFA was used as a proton source reducing the formation of byproducts and increasing the isolated yields.

Condensed 2-pyridone derivatives can also be obtained from aminopropenoate obtained from dimethylformamide diethyl acetal (DMFDEA) and CH-acidic carbonyl compounds. Microwave technology is used in both synthetic steps. Disubstituted quinalozines were obtained by reaction of intermediates (aminopropenoate) with bident C,N nucleophiles (Figure 21) in yields of up to 92% [84]. Synthesis can be also performed in the solid phase.

In addition, condensed 2-pyridone can be obtained by the reaction of 1,3-dicarbonyl compounds and substituted benzaldehydes or phenylendialdehide in the presence of ammonium acetate using microwave irradiation in the absence of a solvent, as previously described for the synthesis of 2-pyridones [61–63].

It should be pointed out that a significant number of papers on the reactions of functionalization of 2-pyridone ring exist. One such review was published by Pemberton *et al*. which summarized papers published until 2006 [85]. This issue requires special attention and is beyond the scope of this paper.

CONCLUSION

2-Pyridone and 2-pyridone-based compounds, such as 2-quinolones, are known for having specific pharmacological properties and are widely used in medicine. Because of the various applications of compounds that contain 2-pyridone structure a number of procedures for their synthesis was developed. Besides the conventional synthesis, microwave assisted syntheses were also developed. Synthesis of 2-pyridone and compounds based on 2-pyridones under microwave irradiation has certain advantages over conventional methods of synthesis primarily in terms of higher

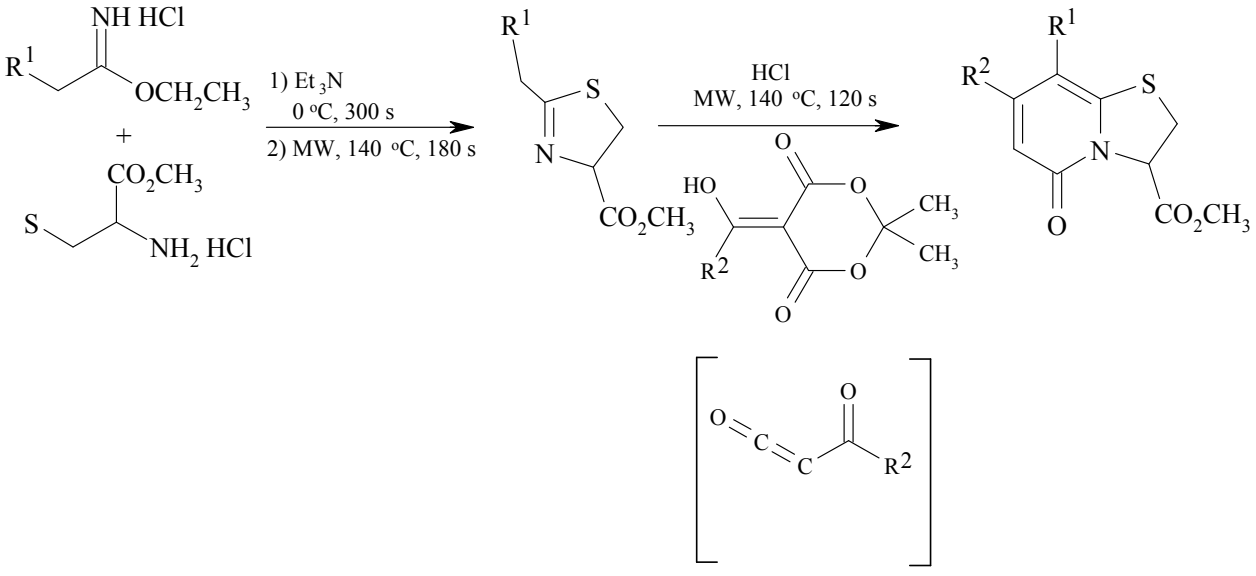


Figure 19. Synthesis of chiral bicyclic 2-pyridones via acyl-ketenes and Δ^2-thiazolines.

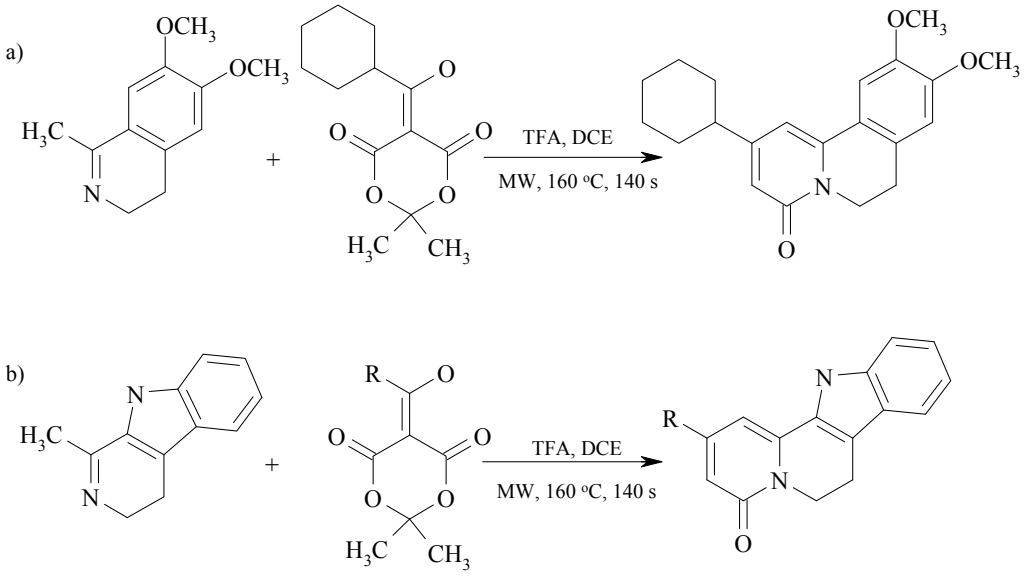


Figure 20. 2-Pyridone synthesis from the reaction of acyl-ketenes and imines.

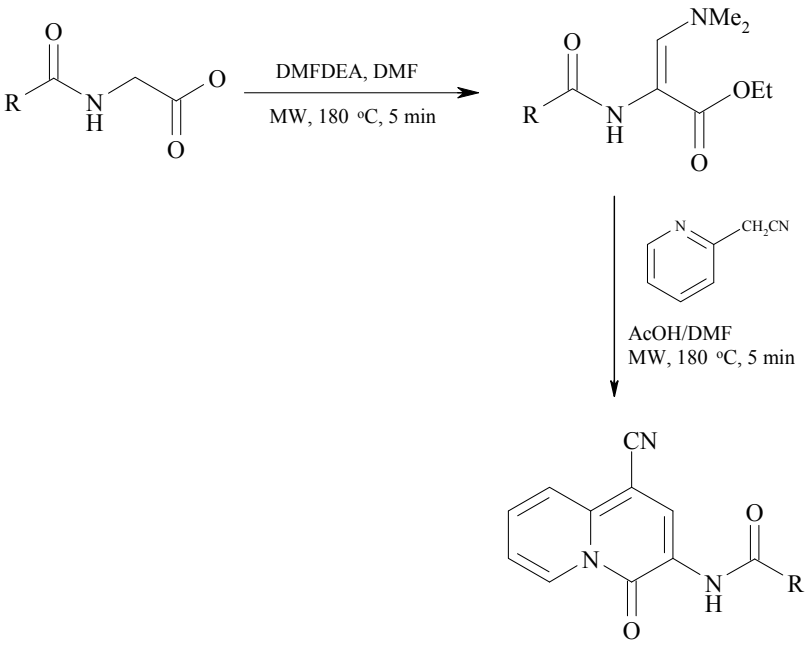


Figure 21. Synthesis of ring fused 2-pyridones via aminopropenoates.

yields and shorter reaction time. Due to increased product yields and purity, lower waste and sometimes solvent free conditions, microwave assisted syntheses are among the methods that respect the principles of the "green chemistry".

Acknowledgement

The authors would like to thank the Ministry of Education, Science and Technological Development of the Republic of Serbia for the financial support (project 172013).

REFERENCES

[1] N.Y. Gorobets, B.H. Yousefi, F. Belaj, C.O. Kappe, Rapid microwave-assisted solution phase synthesis of substituted 2-pyridone libraries, Tetrahedron **60** (2004) 8633––8644.

[2] Q. Li, L.A. Mitscher, L.L. Shen, The 2-pyridone antibacterial agents: bacterial topoisomerase inhibitors, Med. Res. Rev. **20** (2000) 231–293.

[3] Y. Fujita, H. Oguri, H. Oikawa, Biosynthetic studies on the antibiotics PF1140: a novel pathway for a 2-pyridone framework, Tetrahedron Lett. **46** (2005) 5885–5888.

[4] A. Fassihi, D. Abedi, L. Saghaie, R. Sabet, H. Fazeli, G. Bostaki, O. Deilami, H. Sadinpou, Synthesis, antimicrobial evaluation and QSAR study of some 3-hydroxypyridine-4-one and 3-hydroxypyran-4-one derivatives, Eur. J. Med. Chem. **44** (2009) 2145–2157.

[5] G. Semple, B.M. Andersson, V. Chhajlani, J. Georgsson, M.J. Johansson, Å. Rosenquist, L. Swanson, Synthesis and Biological activity of kappa opioid receptor agonists. Part 2: Preparation of 3-aryl-2-pyridone analogues generated by solution- and solid-phase parallel synthesis methods, Bioorg. Med. Chem. Lett. **13** (2003) 1141––1145.

[6] R.L.T. Parreira, O. Abrahão Jr., S.E. Galembeck, Conformational preferences of non-nucleoside HIV-1 reverse transcriptase inhibitors, Tetrahedron **57** (2001) 3243–3253.

[7] P.S. Dragovich, T.J. Prins, R. Zhou, E.L. Brown, F.C. Maldonado, S.A. Fuhrman, L.S. Zalman, T. Tuntland, C.A. Lee, A.K. Patick, D.A. Matthews, T.F. Hendrickson, M.B. Kosa, B. Liu, M.R. Batugo, J.P.R. Gleeson, S.K. Sakata, L. Chen, M.C. Guzman, J.W. Meador, R.A. Ferre, S.T. Worland, Structure-Based Design, Synthesis, and Biological Evaluation of Irreversible Human Rhinovirus 3C Protease Inhibitors. 6. Structure−Activity Studies of Orally Bioavailable, 2-Pyridone-Containing Peptidomimetics, J. Med. Chem. **45** (2002) 1607–1623.

[8] L.A. Hasvold, W. Wang, S.L. Gwaltney, T.W. Rockway, L.T.J. Nelson, R.A. Mantei, S.A. Fakhoury, G.M. Sullivan, Q. Li, N.H. Lin, L. Wang, H. Zhang, J. Cohen, W.Z. Gu, K. Marsh, J. Bauch, S. Rosenberg, H.L. Sham, Pyridone-containing farnesyltransferase inhibitors: synthesis and biological evaluation, Bioorg. Med. Chem. Lett. **13** (2003) 4001–4005.

[9] J.J. Parlow, R.G. Kurumbail, R.A. Stegeman, A.M. Stevens, W.C. Stallings, M.S. South, Design, Synthesis, and Crystal Structure of Selective 2-Pyridone Tissue Factor VIIa Inhibitors, J. Med. Chem. **46** (2003) 4696–4701.

[10] J.J. Parlow, M.S. South, Synthesis of 2-pyridones as tissue factor VIIa inhibitors, Tetrahedron **59** (2003) 7695––7701.

[11] D.Ž. Mijin, G.S. Ušćumlić, N.V. Valentić, A.D. Marinković, Sinteza arilazo piridonskih boja, Hem. Ind. **65** (2011) 517–532.

[12] V.P. Litvinov, S.G. Krivokolysko, V.D. Dyachenko, Synthesis and properties of 3-cyanopyridine-2(1H)-chalcogenones. Review, Chem. Heterocyclic Comp. **35** (1999) 509–540.

[13] N. Pemberton, E. Chorell, F. Almqvist, Microwave-Assisted Synthesis and Functionalization of 2-Pyridones, 2-Quinolones and Other Ring-Fused 2-Pyridones, Top. Heterocycl. Chem. **1** (2006) 1–30.

[14] G. Pastelin, R. Mendez, E. Kabela, A. Farah, The search for a digitalis substitute II milrinone (Win 47203) its action on the heart-lung preparation of the dog, Life Sci. **33** (1983) 1787–1796.

[15] J.M. Mirković, D.Ž. Mijin, S.D. Petrović, Milrinon-svojstva i sinteza, Hem. ind. **67** (2012) 17–25

[16] V. Åberg, F. Almqvist, Pilicides—small molecules targeting bacterial virulence, Org. Biomol. Chem. **5** (2007) 1827–1834.

[17] L. Cegelski, J.S. Pinkner, N.D. Hammer, C.K. Cusumano, C.S. Hung, E. Chorell, V. Åberg, J.N. Walker, P.C. Seed, F. Almqvist, M.R. Chapman, S.J. Hultgren, Small-molecule inhibitors target Escherichia coli amyloid biogenesis and biofilm formation, Nat. Chem. Biol. **5** (2009) 913–919.

[18] K. Eggert, D. Squillacote, P. Barone, R. Dodel, R. Katzenschlager, M. Emre, A. J. Lees, O. Rascol, W. Poewe, E. Tolosa, C. Trenkwalder, M. Onofrj, F. Stocchi, G. Nappi, V. Kostic, J. Potic, E. Ruzicka, W. Oertel, Safety and efficacy of perampanel in advanced Parkinson's disease: A randomized, placebo-controlled study, Movement Disord. **25** (2010) 896–905.

[19] D.J. Dyer, V.Y. Lee, R.J. Twieg, The forgotten liquid crystals of Daniel Vorlander: A new look at mesogenic 4-pyridones, Liquid Cryst. **23** (1997) 551–560.

[20] V. Štětinová, V. Grossmann, Effects of known and potential antioxidants on animal models of pathological processes (diabetes, gastric lesions, allergic bronchospasm), Exp. Toxicol. Pathol. **52** (2000) 473–479.

[21] F. You, R.J. Twieg, Aromatic nucleophilic substitution with 4-hydroxypyridine, Tetrahedron Lett. **40** (1999) 8759–8762.

[22] D. Gibson, D. Clarke, Ch. Winscom, Photographic elements containing a de-aggregating compound and dye-forming coupler, (Eastman Kodak Co. US) US 6841344 (2005).

[23] G. Jones, Pyridines and their benzo derivatives: synthesis. In: A. McKillop (Ed.), Comprehensive heterocyclic chemistry II, Pergamon Press, Oxford, 1996, p. 167.

[24] G. Jones, Pyridines and their benzo derivatives: synthesis. In: Boulton A, A. McKillop (Ed.), Comprehensive heterocyclic chemistry, Pergamon Press, Oxford, 1984, p. 395.

[25] I. Guareschi, Oxypiridine aus β-diketonen, Chem. Zentr. **1** (1899) 289–290.

[26] A.O. Fitton, R.K. Smalley, Practical Heterocyclic Chemistry, Academic Press, London, 1968, p. 71.

[27] D.Ž. Mijin, G.S. Ušćumlić, N.V. Valentić, Synthesis and investigation of solvent effects on the ultraviolet absorption spectra of 5-substituted-4-methyl-3-cyano-6--hydroxy-2-pyridones, J. Serb. Chem. Soc. **66** (2001) 507–516.

[28] D. Mijin, A. Marinković, Synthesis of N-Substituted 4,6-Dimethyl-3-cyano-2-pyridones Under Microwave Irradiation, Synthetic Commun. **36** (2006) 193–198.

[29] M. Mišić-Vuković, D. Mijin, M. Radojković-Veličković, N.Valentić, V. Krstić, Condensation of 1,3-diketones with cyanoacetamide: 4,6-disubstituted-3-cyano-2-pyridones, J. Serb. Chem. Soc. **63** (1998) 585–599.

[30] M. Berson, J.P. Calmon, Effect of substituents on the keto-enol equilibriums of aromatic β-diketones in aqueous solution, C.R. Chim. **273** (1971) 181–184.

[31] R.M. Silverstain, G.C. Bassler, T.C. Morill, Spectrophotometric Indentification of Organic Compounds, Wiley, New York, 1981, pp. 195, 316.

[32] J. Dostanić, N. Valentić, G. Uščumlić, D. Mijin, Synthesis of 5-(substituted phenylazo)-6-hydroxy-4-methyl-3--cyano-2-pyridones from ethyl 3-oxo-2-(substituted phenylazo)butanoates, J. Serb. Chem. Soc. **76** (2011) 499––504.

[33] A.S. Alimmari, A.D. Marinković, D.Ž. Mijin, N.V. Valentić, N. Todorović, G.S. Uščumlić, Synthesis, structure and solvatochromic properties of 3-cyano-4,6-diphenyl-5-(3- and 4-substituted phenylazo)-2-pyridones, J. Serb. Chem. Soc. **75** (2010) 1019–1032.

[34] N.V. Valentić, Ž.J. Vitnik, D.Ž. Mijin, G.S. Uščumlić, N. Todorović, I.O. Juranić, Linear Free Energy Relationships of the ^{13}C NMR chemical shifts in 5-(3- and 4-substituted arylazo)-4,6-dimethyl-3-cyano-2-pyridones, ARKIVOC (2009) 227–240.

[35] D. Mijin, G. Uščumlić, N. Perišić-Janjić, I. Trkulja, M. Radetić, P. Jovančić, Synthesis, properties and colour assessment of some new 5-(3- and 4-substituted phenylazo)-4,6-dimethyl-3-cyano-2-pyridones, J. Serb. Chem. Soc. **71** (2006) 435–444.

[36] D.Ž. Mijin, G.S. Uščumlić, N.U. Perišić-Janjić, N.V. Valentić, Substituent and solvent effects on the UV/Vis absorption spectra of 5-(3- and 4-substituted arylazo)--4,6-dimethyl-3-cyano-2-pyridones, Chem. Phys. Lett. **418** (2006) 223–229.

[37] G.S. Uščumlić, D.Ž. Mijin, N.V. Valentić, V.V. Vajs, B.M. Sušić, Substituent and solvent effects on the UV/Vis absorption spectra of 5-(4-substituted arylazo)-6-hydroxy-4-methyl-3-cyano-2-pyridones, Chem. Phys. Lett. **397** (2004) 148–153.

[38] N.Ž. Prlainović, D.I. Bezbradica, Z.D. Knežević-Jugović, R.T. Kozlowska, D.Ž. Mijin, A Kinetic study of *Candida rugosa* lipase-catalyzed synthesis of 4,6-dimethyl-3-cyano-2-pyridone, J. Braz. Chem. Soc. **21** (2010) 2285––2293.

[39] D.Ž. Mijin, B.D. Milić, M.M. Mišić-Vuković, Synthesis of substituted 3-cyano-2-pyridones: Part IV Influence of 3-alkyl-2,4-pentanedione and *N*-alkyl cyanoacetamide structure on the enzyme catalyzed synthesis of substituted 3-cyano-2-pyridones, Indian J. Chem., B **45** (2006) 993–1003.

[40] C.O. Kappe, Controlled microwave heating in modern organic synthesis, Angew. Chem. Int. Ed. **43** (2004) 6250–6284.

[41] C.O. Kappe, D. Dallinger, The impact of microwave synthesis on drug discovery, Nat. Rev. Drug Discov. **5** (2006) 51–63.

[42] D. Stuerga, M. Delmotte, in: A. Loupy (Ed.), Microwaves in Organic Synthesis, Wiley-VCH, Weinheim, 2002.

[43] C.O. Kappe, D. Dallinger, S.S. Murphree, Practical Microwave Synthesis for Organic Chemists - Strategies, Instruments, and Protocols, Wiley-VCH, Weinheim, 2009.

[44] D.Ž. Mijin, S.D. Petrović, Primena mikrotalasne tehnike u organskoj hemiji i organskoj hemijskoj tehnologiji, Hem. Ind. **59** (2005) 224–229.

[45] B. Wathey, J. Tirney, P. Lindstrom, J. Westman, The impact of microwave-assisted organic chemistry on drug discovery, Drug Discov. Today **7** (2002) 373–380.

[46] Y. Fernández, A. Arenillas, J. Ángel Menéndez, in: S. Grundas (Ed.), Advances in Induction and Microwave Heating of Mineral and Organic Materials, InTech, Rijeka, 2011, pp. 723–752.

[47] P.J. Walter, S. Chalk, H.M. Kingston, in: H.M. Kingston, S.J. Haswell (Eds.), Microwave-Enchanced Chemistry, Fundamentals, Sample Preparations and Applications, American Chemical Society, Washington DC, 1997, pp. 55–222.

[48] L. Jassie, R. Savesz, T. Kierstead, E. H. Asty, S. Matz in: H.M. Kingston, S.J. Haswell (Eds.), Microwave-Enhanced Chemistry, Fundamentals, Sample Preparations and Applications, American Chemical Society, Washington DC, 1997, pp. 569–611.

[49] W. G. Engelhart, in: H.M. Kingston, S.J. Haswell (Eds.), Microwave-Enchanced Chemistry, Fundamentals, Sample Preparations and Applications, American Chemical Society, Washington DC, 1997, pp. 613–638.

[50] S. Ravichandran, E.Karthikeyan, Microwave Synthesis - A Potential Tool for Green Chemistry, Int. J. ChemTech. Res. **3** (2011) 466–470.

[51] E. Klingsberg, Pyridine and its Derivitives, Part I, Interescience, New York, 1960, pp. 272–273, 362–364.

[52] H. Schmid, Process for the preparation of pyridone compounds, (Sandoz AG), DE 4314430 (1994).

[53] J.M. Bobbit, D.A. Scola, Synthesis of Isoquinoline Alkaloids. II. The Synthesis and Reactions of 4-Methyl-3-pyridinecarboxaldehyde and Other 4-Methyl-3-Substituted Pyridines, J. Org. Chem. **25** (1960) 560–564.

[54] J.M. Dostanić, D.R. Lončarević, P.T. Banković, O.G. Cvetković, D.M. Jovanović, D.Ž. Mijin, Influence of process parameters on the photodegradation of synthesized azo pyridone dye in TiO_2 water suspension under simulated sunligh**,** J. Environ. Sci. Health, A **46** (2011) 70–79.

[55] C. Dave, G. Chaitanya, D.A. Shah, Y.K. Agrawal, A simple and convient synthesis of 4,6-disubstituted 3-cyanopyridin-2(1H)-ones under solvent-free microwave conditions, Indian J. Chem., B **43** (2004) 885–887.

[56] D.Z. Mijin, M. Baghbanzadeh, C. Reidlinger, C.O. Kappe, The microwave-assisted synthesis of 5-arylazo-4,6--disubstituted-3-cyano-2-pyridone dyes, Dyes Pigm. **85** (2010) 73–78.

[57] S.S. Al-Neyadi, A.H. Hassan, I.M. Abdou, Microwave-assisted synthesis of 2(1*H*)-pyridones and their glucosides as cell proliferation inhibitors, Nucleos. Nucleot. Nucl. **30** (2011) 120–134.

[58] A. Abadi, O. Al-Deeb, A. Al-Afify, H. El-Kashef, Synthesis of 4-alkyl (aryl)-6-aryl-3-cyano-2(1*H*)-pyridinones and their 2-imino isosteres as nonsteroidal cardiotonic agents, Farmaco **54** (1999) 195–201.

[59] R. Jia, S. Tu, Y. Zhang, B. Jiang, J. Zhang, C. Yao, F. Shi, An efficient and greener approach to the synthesis of 3,5-dicyanopyridin-2(1H)-one derivatives in aqueous media under microwave irradiation conditions, J. Heterocyclic Chem. **44** (2007) 1177–1180.

[60] H. Rodriguez, M. Suarez, R. Perez, A. Petit,; A. Loupy, Solvent-free synthesis of 4-aryl substituted 5-alkoxycar-

bonyl-6-methyl-3,4-dihydropyridones under microwave irradiation, Tetrahedron Lett. **44** (2003) 3709–3712.

[61] Y. Xiang, W.-J. Zhu, One-pot synthesis of pyridones and related compounds under microwave irradiation in water, Jiamusi Daxue Xuebao (Ziran Kexueban) **28** (2010) 753–755. [C.A. 154\2010 109398].

[62] S.-J. Tu, X. Deng, D.-Q. Shi, Y. Gao, J.-C. Feng, Microwave assisted synthesis of pyridone derivatives, Chin. J. Chem. **19** (2001) 714–715. [C.A. 135\2001 303753].

[63] S. Tu, C. Miao, F. Fang, Y. Feng, T.Li, Q. Zhuang, X. Zhang, S. Zhu, D. Shi, New potential calcium channel modulators: design and synthesis of compounds containing two pyridine, pyrimidine, pyridone, quinoline and acridine units under microwave irradiation, Bioorg. Med. Chem. Lett. **14** (2004) 1533–1536.

[64] J.H.M. Lange, P.C. Verveer, S.J.M. Osnabrug, G.M. Visser, Rapid microwave-enhanced synthesis of 4-hydroxyquinolinones under solvent-free conditions, Tetrahedron Lett. **42** (2001) 1367–1369.

[65] T.N. Glasnov, W. Stadlbauer, C.O. Kappe, Microwave-Assisted Multistep Synthesis of Functionalized 4-Arylquinolin-2(1*H*)-ones Using Palladium-Catalyzed Cross-Coupling Chemistry, J. Org. Chem. **70** (2005) 3864–3870.

[66] T. Kappe, A.S. Karem, W. Stadlbauer, Synthesis of benzohalogenated 4-hydroxy-2(1*H*)-quinolones, J. Heterocycl. Chem. **25** (1988) 857–862.

[67] N. Vetrivel, S.T. Selvi, R. Sasi, Microwave-assisted synthesis of quinoline alkaloids: 4-methoxy-1-methyl-2-quinolinone and its analogs, ARKIVOC **10** (2006) 82–89.

[68] K. Arya, M. Agarwal, Microwave prompted multigram synthesis, structural determination, and photo-antiproliferative activity of fluorinated 4-hydroxyquinolinones, Bioorg. Med. Chem. Lett. **17** (2007) 86–93.

[69] H.K. Lee, H. Cao, T.M. Rana, Design, Microwave-Assisted Synthesis, and Photophysical Properties of Small Molecule Organic Antennas for Luminescence Resonance Energy Transfer, J. Comb. Chem. **7** (2005) 279–284.

[70] C-S. Jia, Y-W. Dong, S-J. Tu, G-W. Wang, Microwave-assisted solvent-free synthesis of substituted 2-quinolones, Tetrahedron **63** (2007) 892–897.

[71] P.W. Anzalone, A.R. Baru, E.M. Danielson, P.D. Hayes, M.P. Nguyen, A.F. Panico, R.C. Smith, R.S. Mohan, Bismuth Compounds in Organic Synthesis. A One-Pot Synthesis of Homoallyl Ethers and Homoallyl Acetates from Aldehydes Catalyzed by Bismuth Triflate, J. Org. Chem. **70** (2005) 2091–2096.

[72] M. Larhed, A. Hallberg, Microwave-Promoted Palladium-Catalyzed Coupling Reactions, J. Org. Chem. **61** (1996) 9582–9584.

[73] J. Li, A.W.H. Mau, C.R. Strauss, The use of palladium on porous glass for catalytic coupling reactions, Chem. Commun. **1997** (1997) 1275–1276.

[74] N. Garg, M. Larhed, A. Hallberg, Heck Arylation of 1,2-Cyclohexanedione and 2-Ethoxy-2-cyclohexenone, J. Org. Chem. **63** (1998) 4158–4162.

[75] K. Olofsson, M. Larhed, A. Hallberg, Highly Regioselective Palladium-Catalyzed Internal Arylation of Allyltrimethylsilane with Aryl Triflates, J. Org. Chem. **63** (1998) 5076–5079.

[76] A. Stadler, S. Pichler, G. Horeis, C.O. Kappe, Microwave-enhanced reactions under open and closed vessel conditions. A case study, Tetrahedron **58** (2002) 3177–3183.

[77] P.M. Fresneda, P. Molina, S. Delgado, A novel approach to the indoloquinoline alkaloids cryptotackieine and cryptosanguinolentine by application of cyclization of o-vinylsubstituted arylheterocumulenes, Tetrahedron **57** (2001) 6197–6202.

[78] B.V. Suma, A.K. Rochani, C.H.S. Venkataramana, J. Jays, V. Madhavan, Synthesis, Characterization, invitro Antibacterial, Anti-inflammatory Evaluations of Novel 4-Quinolone containing Pyrazolidinedione derivatives, Int. J. ChemTech. Res. **2** (2010) 2156–2162.

[79] H. Emtenäs, C. Taflin, F. Almqvist, Efficient microwave assisted synthesis of optically active bicyclic 2-pyridinones *via* Δ^2-thiazolines, Mol. Div. **7** (2003) 165–169.

[80] E. Chorell, S. Edvinsson, F. Almqvist, Improved procedure for the enantioselective synthesis of dihydrooxazolo and dihydrothiazolo ring-fused 2-pyridones, Tetrahedron Letters **51** (2010) 2461–2463.

[81] H. Emtenäs, L. Alderin, F. Almqvist, An Enantioselective Ketene−Imine Cycloaddition Method for Synthesis of Substituted Ring-Fused 2-Pyridinones, J. Org. Chem. **66** (2011) 6756–6761.

[82] H. Emtenäs, K. Åhlin, J. S. Pinkner, S. J. Hultgren, F. Almqvist, Design and Parallel Solid-Phase Synthesis of Ring-Fused 2-Pyridinones That Target Pilus Biogenesis in Pathogenic Bacteria, J. Comb. Chem. **4** (2002) 630–639.

[83] N. Pemberton, L. Jakobsson, F. Almqvist, Synthesis of Multi Ring-Fused 2-Pyridones via an Acyl-Ketene Imine Cyclocondensation, Org. Lett. **8** (2006) 935–938.

[84] J. Westman, R. Lundin, J. Stalberg, M. Ostbye, A. Franzen, A. Hurynowicz, Alkylaminopropenones and Alkylamino-Propenoates as Efficient and Versatile Synthons in Microwave-Assisted Combinatorial Synthesis, Comb. Chem. High T. Scr. **5** (2002) 565–571.

[85] N. Pemberton, E. Chorell, F. Almqvist, Microwave-assisted synthesis and functionalization of 2-pyridones, 2-quinolones and other ring-fused 2- pyridones, Top. Heterocycl. Chem. **1** (2006) 1–30.

IZVOD

MIKROTALASNA TEHNIKA U SINTEZI 2-PIRIDONA I JEDINJENJA NA BAZI 2-PIRIDONA

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(Pregledni rad)

Aromatična heterociklična jedinjenja predstavljaju veoma značajnu grupu jedinjenja zbog svoje biološke i medicinske primene. Šestočlana heterociklična jedinjenja koja sadrže azot (npr. piridini, piridoni, pirimidini, piperidini, piperazini) se puno koriste u medicini jer poseduju određena farmakološka svojstva, a poseban značaj imaju 2-piridoni i 4-piridoni. Derivati 2-piridona su posebno interesantni jer je 2-piridonska struktura prisutna u mnogim jedinjenjima prirodnog porekla od kojih mnoga poseduju biološku aktivnost. Zbog široke primene jedinjenja koja u sebi sadrže piridonsku strukturu razvijen je veliki broj postupaka za njihovu sintezu. Konvencionalni način izvođenja organskih sinteza podrazumeva zagrevanje spoljašnjim izvorima toplote pri čemu se toplota prenosi kondukcijom, što predstavlja spor i neefikasan metod prenosa energije, jer zavisi od toplotne provodljivosti materijala, pa je temperatura reaktora veća od temperature reakcione smeše. Nasuprot tome, mikrotalasno zračenje je efikasan izvor zagrevanja koji direktno prenosi energiju kroz interakciju sa polarnim molekulima prisutnim u reakcionoj smeši. Mikrotalasne sinteze se ubrajaju među metode koje poštuju principe takozvane „zelene hemije" što predstavlja razlog više za ovakvo izvodjenje sinteza. U okviru rada dat je pregled sinteza 2-piridona i jedinjenja koja sadrže 2-piridonsko jezgro primenom mikrotalasne tehnike. Pregled obuhvata sinteze koje su izvršene kako u savremenim laboratorijskim mikrotalasnim reaktorima tako i one koje su izvršene u komercijalnim mikrotalasnim pećnicama za domaćinstvo. Takođe je ukazano na prednosti mikrotalasne sinteze u odnosu na konvencionalni način zagrevanja.

Ključne reči: Heterociklična jedinjenja • Medicinska hemija • Mikrotalasna organska hemija • 2-Hinolon • Kondenzovani *N*-supstituisani 2-piridoni