

**Solvent free, Microwave-Assisted Synthesis of Aromatic Nitriles and Oximes
Using Solid Acids as Catalysts**

Ousama Dabbit*, Mohammed Nasouh Alaya and Anas Makansi

Department of Chemistry, Faculty of Science, University of Aleppo, Syria

Abstract: Microwave-Assisted organic synthesis of aromatic nitriles and oximes was performed using aromatic aldehydes in the presence of hydroxylamine hydrochloride $\text{NH}_2\text{OH}\cdot\text{HCl}$ and solid acids as catalysts to give good yields in short reaction times. The effect of the heterogeneous catalysts such as mixed oxides and TiO_2 were discussed. This efficient method enabled us to synthesize a variety of useful nitriles and oximes.

Keywords: Microwave, Nitrile, Oxime, Aldehyde, Catalyst, Mixed oxides.

1- Introduction:

Recently, the application of microwave-assisted solvent-free synthesis in organic reaction has been of growing interest as an efficient, economic and clean procedure (green chemistry) [1-5]. Over the past few years, a considerable number of reactions have been developed in which inorganic solid supports such as alumina, silica gel and montmorillonite and others appeared to be useful in terms of mildness of conditions, yield and convenience [6-8]. Heterogeneous catalyst such as titanium dioxide TiO_2 has attracted attention of synthetic organic chemists due to its application as heterogeneous catalyst and as photo catalyst. In addition, TiO_2 is inexpensive, non-toxic and safe [9].

Tanabe classified acid and base solid catalysts [10]. He found that SnO_2 possesses both acidic and basic properties [10]. It was noticed that the formation of mixed oxides accompanied by increasing both their acidic and basic properties, catalytic activity and mechanical stability. Loading of some metal oxides with sulfate ion produced very active catalysts (super acid) for various acidic catalytic reactions like polymerization, acylation and esterification etc.... These superacid solids possess both Lewis and Bronsted acid sites and are environmentally friendly and noncorrosive reactors, compared to the corrosive properties observed with known liquid acids like HF and H_2SO_4 [11-13].

Microwave-assisted solvent free organic synthesis is currently gaining ground in synthetic chemistry largely due to the dramatic reduction in reaction time (from days or hours to minutes or even seconds) [14,15].

Sharghi and Sarvari converted aldehydes into the respective amides in the presence of $\text{NH}_2\text{OH.HCl}$ and TiO_2 in a one-pot solvent free procedure with long reaction times [16]. TiO_2 may form a complex with the carbonyl oxygen atoms of aldehydes, therefore it may activate the carbonyl group for nucleophilic attack [17].

Lucas and Co-Workers converted aldehydes into nitriles and oximes in the presence of $\text{NH}_2\text{OH.HCl}$ and TiO_2 without using solvent and in good yields [18]. Varma and Co-Workers also converted aldehydes into nitriles by using $\text{NH}_2\text{OH.HCl}$ and Na_2CO_3 in solvent free conditions with good yields [19].

In this paper. we tried to compare different kinds of catalysts in the synthetic reactions of aromatic nitriles and oximes from the corresponding aldehydes under microwave irradiation. The transformation of aldehydes into nitriles and oximes are a highly valued reaction, due to the versatility of the latter as starting materials in organic synthesis [20]. These compounds have a potential use in perfumery industry due to their higher stability when compared to their corresponding aldehydes, while retaining a pleasant odor [21]. The aldehydes used in this research have already been prepared by us in a previous research by the oxidation of the appropriate alkyl

halides also in a solvent-free conditions using new catalysts such as pure zeolite, organo zeolite and montmorillonite k_{10} supported by iodic acid as oxidant [22,23].

Based on these facts, we decided to evaluate the conversion of aromatic aldehydes into aromatic nitriles and oximes under microwave irradiation by FT-IR Spectrometry and by GC-MS. The spectroscopic data of the products were compared to those available in the literature.

2-Experimental:

2.1.Measurement methods:

The HR GC/MS analyses were carried out on Agilent-5975C operating in electron ionization mode at 70 eV. Helium was used as carrier gas and the injection split ratio was 1:100. Separation was achieved on DB-5 capillary column (30 m \times 0.25 mm \times 0.25 μ m) using the following temperature program: 1 min at 60°C, 20°C/min until 260°C, then 10 min at 260°C. Ion source and injection temperature were at 260°C. The FT-IR spectrum was recorded on Jasco 4100 spectrometer (KBr pellets). The spectroscopic data and the melting point of products were compared to those available in the literature.

2.2. Preparation of novel WO_3/SnO_2 catalysts:

(i) Preparation of SnO_2 : pure tin oxide hydrogel was prepared by a dropwise addition of ammonia solution (10 wt%) to 0.5 M solution of $SnCl_4 \cdot 5H_2O$ with continuous vigorous stirring for 4 h. The pH of the hydrogel was adjusted to 8. The gel was left overnight then washed by decantation with 1% ammonium acetate solution, until all Cl^- ions were eliminated. Then, the product was washed with bi-distilled water (WTHG), then the resulting SnO_2 gel was dried at 120°C for 4 h.

(ii) Preparation of 15% SO_4^{2-}/SnO_2 or (S. Sn) support: the catalyst (S. Sn) was prepared by vigorous mixing of appropriate amount of 1 M H_2SO_4 with SnO_2 gel for 4 h, the percent loading of sulfate ions was 15% wt that was then dried at 120°C for 24 h.

(iii) Preparation of $xWO_3/SO_4^{2-}/SnO_2$: the support S. Sn was impregnated with appropriate amount of ammonium paratungstate $[(NH_4)_{10}W_{12}O_{41} \cdot 5H_2O]$ solution to obtain percentage ratios of x loading of 15 and 45% wt of WO_3 , with vigorous stirring for 4 h, then dried at 120°C for 24 h. All prepared catalysts 15%W-S. Sn and 45% W-S. Sn were calcined in air at 500°C for 4h. The specific surface areas, S_{BET} , were determined from nitrogen adsorption at 77K and the total surface acidity was measured by potentiometric titration method in a non-aqueous solution [13]. Table 1 summarises the surface properties of the used catalysts.

Table (1). The textural properties of (15-WSS, 45-WSS)

Catalyst	S_{BET} (m^2/g)	Total acidity(mmol/g)	Density acidity(N/m^2)
15-WSS	101	0.0575	3.429
45-WSS	66.4	0.0600	5.442

2.3. Microwave assisted conversion of aldehydes into Nitriles and Oximes:

A 25 ml reaction flask was charged with a ground mixture of an aldehyde (1 mmol), one of the catalysts 15-WSS, 45-WSS or TiO_2 (0.4 g), and hydroxylamine hydrochloride (5 mmol, 0.35 g). The reaction mixture was taken in a microwave reactor and irradiated at the power settings and reaction times specified in Tables 2 and 3. After cooling to room temperature, the reaction mixture was extracted with dichloromethane (10 ml \times 2). The progress of the reaction was monitored by thin layer chromatography (40% ethyl acetate in hexane), filtered and the sample was submitted to GC-MS analysis. In our research, we used a microwave irradiator with a power that can reach 1400 W and frequency of 2450 MHz.

3. Results and discussion:

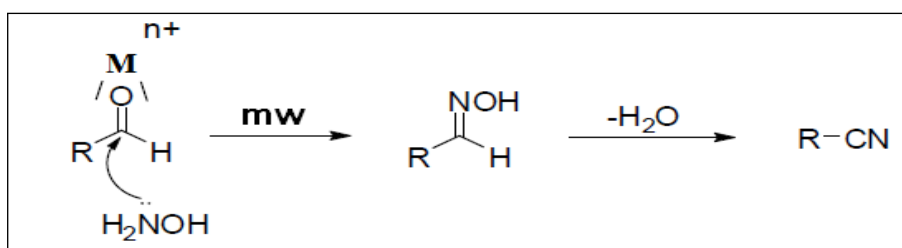
We studied the conversion of some useful and interesting aldehydes, namely, 4-hydroxy benzaldehyde, 4-hydroxy 3-methoxy benzaldehyde and 2-nitro benzaldehyde, to the corresponding nitriles and oximes over different catalysts 15-WSS, 45-WSS and TiO_2 , in the presence of $\text{NH}_2\text{OH.HCl}$ under microwave irradiation at power 840 W for 3 min. The results which we obtained are summarized in Table (2).

Table (2). Microwave-assisted conversion of aldehydes to the corresponding nitriles and oximes over different catalysts 15-WSS, 45-WSS and TiO_2 , in the presence $\text{NH}_2\text{OH.HCl}$.

Substrate	Catalyst	%Nitrile	%Oxime	%Others
4-hydroxy benzaldehyde	15-WSS	83	10	7
	45-WSS	77	9	14
	TiO_2	80	11	9
4-hydroxy 3-methoxy benzaldehyde	15-WSS	86	9	5
	45-WSS	80	9	11
	TiO_2	84	10	6
2-nitro benzaldehyde	15-WSS	18	79	3
	45-WSS	15	76	9
	TiO_2	17	78	5

* Condition: 1 mmol aldehyde, 0.4 g 15WSS, 5 mmol $\text{NH}_2\text{OH.HCl}$.

The results show that the best conversion percentage was obtained by irradiating the solid mixture for three minutes at 840 W by using 15-WSS catalyst. The aldehydes bearing electron donating groups were readily converted into the corresponding nitriles in satisfactory conversion percentage (77-86%), whereas the substrate bearing electron withdrawing group afforded the respective oximes more than nitriles. The proposed mechanism for these reactions is given in Scheme 1. The conversion of the aldehyde into the respective nitrile occurs at the expense of the oxime through acid catalyzed dehydration.



Scheme (1). Proposed sequence of transformation during catalyst- promoted conversion of aldehydes to nitriles.

We have also explored the effects of the amounts of catalyst and $\text{NH}_2\text{OH.HCl}$ in the reaction mixture on the yield of the resulting products. Reducing the amount of the reagent from 5 mmols to 2.5 mmols for $\text{NH}_2\text{OH.HCl}$ and from 0.4 g to 0.2 g for catalyst that led to incomplete conversion of aldehyde and enhanced yield of undesired products. Table (3) summarizes the results obtained for the conversion of 4-hydroxy benzaldehyde to the corresponding products as an example of our study.

Table (3). Microwave-assisted conversion of 4-hydroxy benzaldehyde to the corresponding nitriles and oximes over different amounts of catalyst 15-WSS, and different amounts of $\text{NH}_2\text{OH.HCl}$.

substrate	Catalyst 15-WSS	%Nitrile	%Oxime	%Others
4-hydroxy benzaldehyde	0.4 g	83	10	7
	0.2 g	69	12	19
	$\text{NH}_2\text{OH.HCl}$	%Nitrile	%Oxime	%Others
	5 mmols	83	10	7
	2.5 mmols	65	11	24

* Condition: 1 mmol aldehyde, 840 W, 3 min.

To confirm the best reaction conditions, we have studied the effects of time and irradiation potency on the conversion of 4-hydroxy benzaldehyde to oxime and nitrile using 15-WSS as catalyst under microwave irradiation. The results obtained are summarized in Table (4).

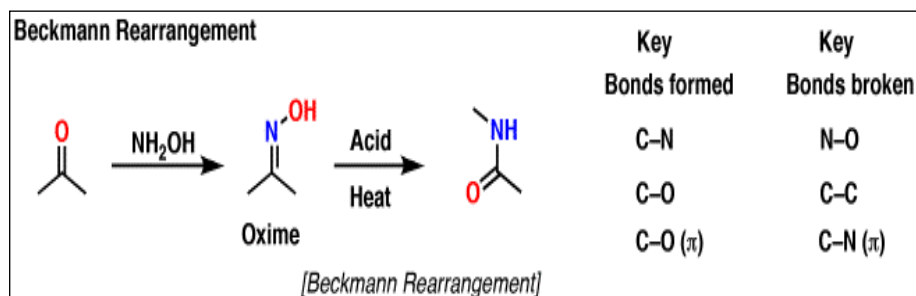
Table (4). Time and potency effects on the conversion of 4-hydroxy benzaldehyde to 4-hydroxybenzoxime and 4-hydroxybenzoxime.

Entry	Time(min)	Power(W)	%Nitrile	%Oxime	%Others
1	2	840	40	60	0
2	3	840	83	10	7
3	4	840	56	17	27
4	3	700	69	28	3
5	3	980	78	14	8

* Condition: 1 mmol aldehyde, 0.4 g 15WSS, 5 mmol NH₂OH.HCl.

The results show that the best conversion percentage was obtained by irradiating the solid mixture for three minutes at 840 W. Upon increasing the reaction time, higher yields of undesired products (such as the amide and degradation products) are obtained. When we reduced the reaction time, higher amounts of the oxime were formed.

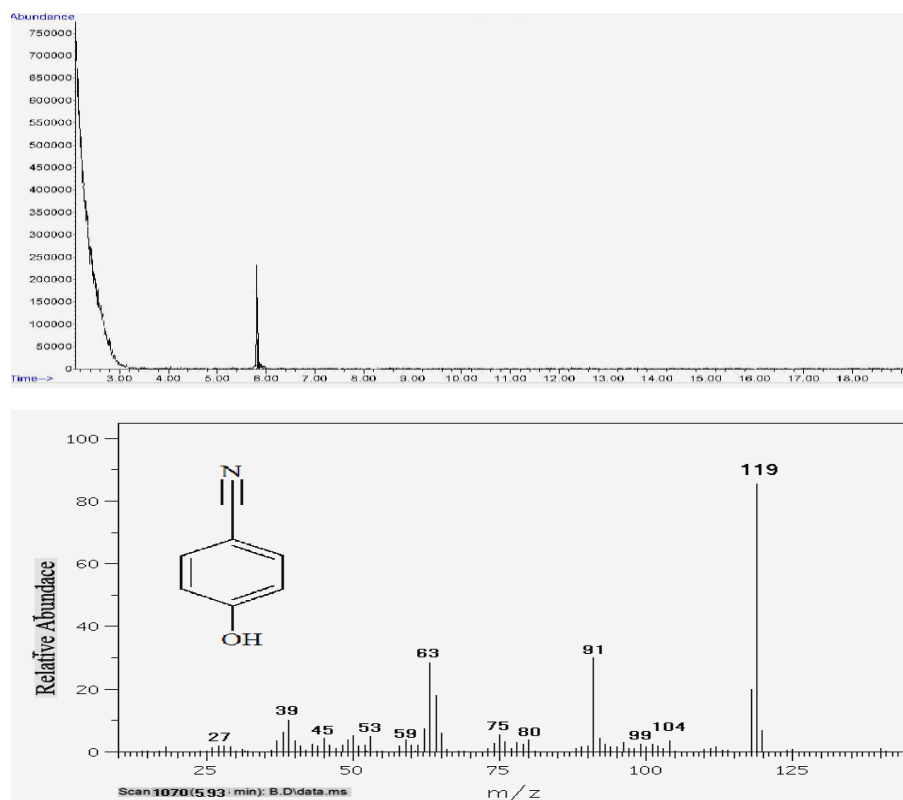
It can also be observed that increasing the power led to higher yields of undesired products, and when we reduced the power, there was incomplete conversion of the aldehyde to corresponding nitrile. In addition, we can write the proposed mechanistic of amide formation as we increase the reaction time and irradiation potency as given in Scheme 2.



Scheme 2. Proposed sequence of transformations during increasing the reaction time and power with formation of amides.

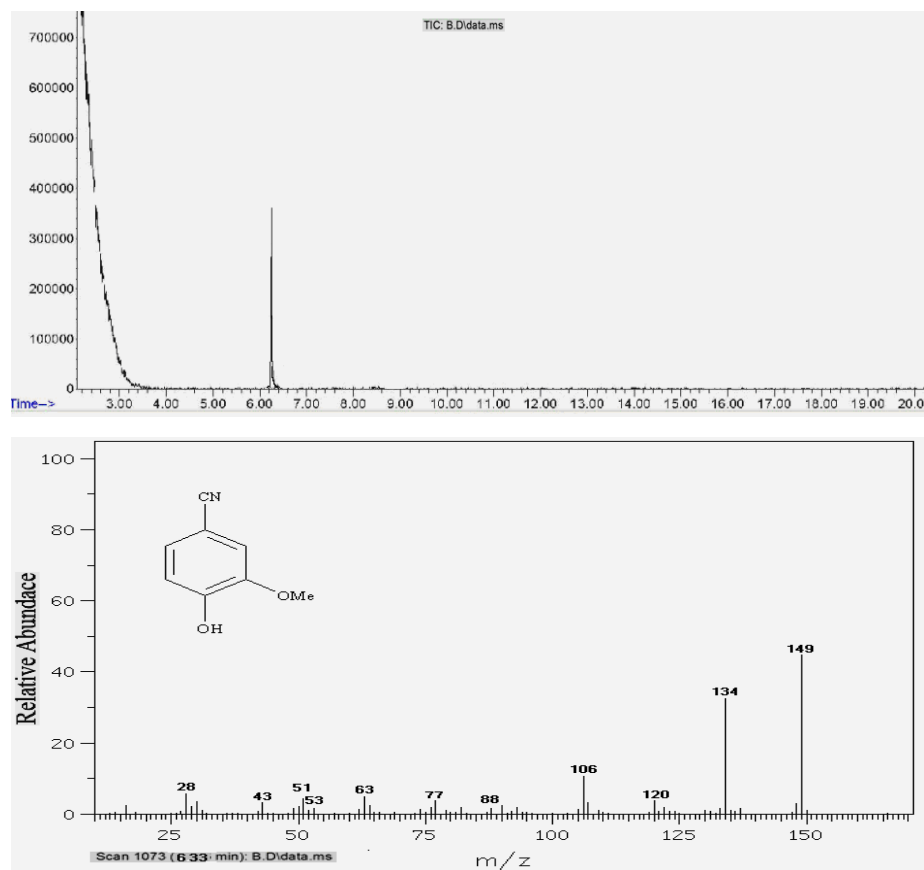
The isolated products were re-crystallised in ethanol and identified by FT-IR and GC-MS. The results are shown in Figures 1-3.

Figure (1). GC chromatogram of scaled- up conversion of 4-hydroxy benzaldehyde into 4-hydroxybenzoxime and MS of the major compound ($t_R = 5.93$ min).



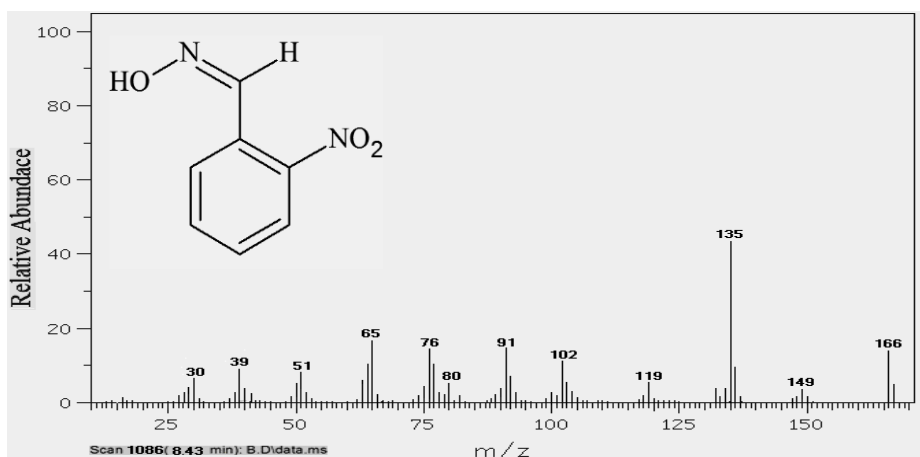
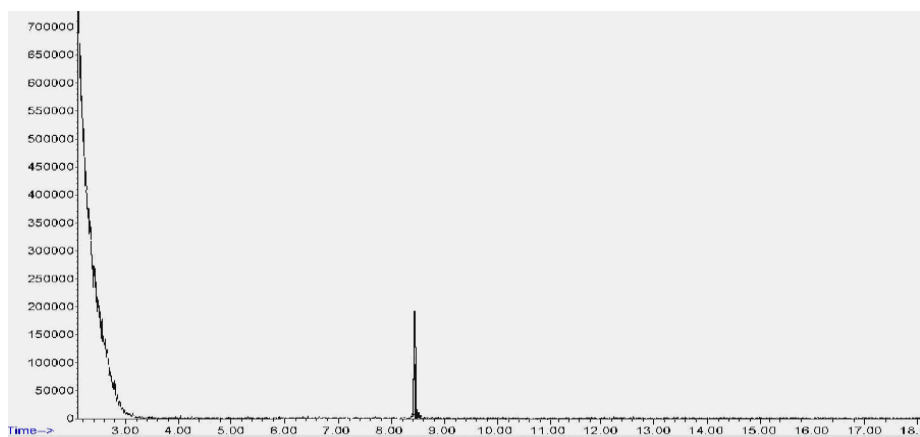
4-hydroxybenzointrile: mp = (109 - 112°C, lit. 110-113°C); FT-IR (KBr): 2227 cm^{-1} ($\text{C}\equiv\text{N}$), 1520, 1600 cm^{-1} ($\text{C}=\text{C}$) in aromatic ring, 3596 cm^{-1} (O-H); GC-MS: t_{R} =5.93 min, m/z = 119 (M^+).

Figure (2). GC chromatogram of scaled- up conversion of 4-hydroxy-3-methoxy benzaldehyde into 4-hydroxy 3-methoxy benzonitrile and MS of the major compound (t_{R} = 6.33 min).



4-hydroxy-3-methoxybenzonitrile: mp = (84-88°C, lit. 85-87°C), FT-IR (KBr): 2240 cm^{-1} (C \equiv N), 2966 cm^{-1} (C-H), 3082 cm^{-1} (C=C-H), 1510, 1586 cm^{-1} (C=C) in aromatic ring, 3379 cm^{-1} (O-H); GC-MS: t_R =6.33 min, m/z = 149 (M^+).

Figure (3). GC chromatogram of scaled- up conversion of 2-nitro benzaldehyde into 2-nitro benzaldoxime and MS of the major compound (t_R =8.43 min).



2-nitrobenzaldehyde oxime: mp = (91-94°C, lit. 89-93°C); FT-IR (KBr): 3256 (hydrogen bonded) cm^{-1} , 3561 (free OH) cm^{-1} , 910 cm^{-1} ,

1306 cm^{-1} (N-O-H), 1615 cm^{-1} (C=N), 1542 cm^{-1} (C=C) in aromatic ring, 3093 (C=C-H) cm^{-1} , GC-MS: t_R = 8,43 min, m/z = 166 (M^+).

4. Conclusions:

Mixed oxides 15WSS, 45WSS and titanium oxide TiO_2 are useful catalysts for a fast and convenient procedure to synthesize nitriles and oximes from the appropriate aldehydes using $\text{NH}_2\text{OH}\cdot\text{HCl}$ under microwave irradiation without solvent. This method offers some advantages in terms of simplicity of performance, solvent-free conditions, short reaction time and also to synthesize a wide range of

aromatic nitriles and oximes by converting the corresponding aromatic aldehydes under microwave irradiation. On the other hand, the catalysts 15WSS, 45WSS and TiO₂ may be recycled after activation.

5. References

- [1] R.S. Varma, Clay and clay- supported reagent in organic synthesis. *Tetrahedron*, 58: 1235-1255 (2002).
- [2] R.S. Varma, Water mediated condensation reaction of aldehydes and amines. *Pure Appl.Chem*,73: 193-198 (2001).
- [3] L. Perreux, A. Loupy, A tentative rationalization of microwave effects in organic synthesis according to the reaction medium, and mechanistic considerations. *Tetrahedron*, 57: 9199-9223 (2001).
- [4] R.S. Varma, Solvent-free organic synthesis using supported reagents and microwave irradiation. *Green Chemistry*, 1:43-55 (1999).
- [5] P. Lidstom, J. Tierney, B. Wathey, J. Westman, Microwave assisted organic synthesis - a review. *Tetrahedron*, 57: 9225-9283 (2001).
- [6] M. Jeselnik, R.S. Varma, S. Polanc, M. Kocivar, Solid –state synthesis of heterocyclic hydrazones using microwave under catalyst-free conditions. *Green Chem*,4, 35-38 (2002).
- [7] A. Mckillop, D.W. Young, Organic synthesis using supported reagents-part II. *Synthesis*, 481-500 (1979).
- [8] G.W. Kabalka, R.M. Ragni, Benign approaches for the microwave-assisted synthesis of quinoxalines. *Tetrahedron*, 53, 7999-8016 (1997).
- [9] E. Diebold, The surface science of titanium dioxide. *Surf. Sci. Rep.* 48: 53-229 (2003).
- [10] K. Tanabe, "Solid acid and Base Catalysts", in: *Catalysis Science and Technology*. Ed. J.R. Anderson and M. Boudart, Springer-Verlag, New York , Vol.2,Ch-5,pp.231-273 (1981).
- [11] M.N. Alaya, M.A. Rabah, Some physico-chemical properties and catalytic activity of sulfate ion supported on WO₃/SnO₂ Catalyst. *Arabian J.Chem.*, (on line 15 Oct 2012 in Elsevier), In Press (2012).
- [12] M.N. Alaya, M.A. Rabah, Textural and catalytic properties of WO₃/SnO₂ mixed oxide catalysts, this submitted for Ph. Degree in chemistry.

University of Aleppo, Syria. 226 page (2013).

- [13] M.N. Alaya, M.A. Rabah, Surface acidity and catalytic activity of aged $\text{SO}_4^{2-}/\text{SnO}_2$ catalyst supported with WO_3 . *J. Allays Comp* 575: 285-291 (2013).
- [14] C.O. Kappe, D. Dallinger, The impact of microwave synthesis on drug discovery. *Nature Reviews Discovery*, vol.5, no. 1: 51-63, (2006).
- [15] C.O. Kappe, Controlled microwave heating in modern organic synthesis, *Angewandte Chemie International Edition*, vol.43, no. 46: 6250-6284 (2004).
- [16] H. Sharghi, M.H. Sarvari, Titanium Oxide catalysed one-Step Beckman rearrangement of aldehydes and ketones in solvent free conditions. *J. Chem. Res*, 3: 176-178.(2003).
- [17] G. Lu, A. Linsebliger, J.T. Yates, Ti^{3+} defect sites on TiO_2 production and chemical-detection of active- sites. *J. Phys. Chem.* 98: 11733-11738 (1994).
- [18] L. Villas-Boas Hoelz, B.T. Gonçalves, J.C. Barros and J.F. Mendes da Silva, Solvent Free, Microwave Assisted Conversion of Aldehydes into Nitriles and Oximes in the Presence of $\text{NH}_2\text{OH HCl}$ and TiO_2 . *Molecules*; 15 Issue 1, p94 (2010).
- [19] R.S. Varma, K.P. Naicker, D. Kumar, R. Dahiya and P.J. Liesen, Solvent-free organic transformations using supported reagents and microwave irradiation. *Journal of Microwave Power and Electromagnetic Energy*, 34, Vol. 34 no 2 (1999).
- [20] N.D. Arote, D.S. Bhalero, K.G. Akamanchi, Direct oxidative conversion of aldehydes to nitriles using IBX in aqueous ammonia. *Tetrahedron*, 48: 3651-3653 (2007).
- [21] I.W. Ouedraogo, M. Boulvin, R. flammang, P. Gerbaux, Y.L. Bonzi-Coulibaly, Conversion of natural aldehydes from *Eucalyptus citriodora*, *Cymbopogon citrates*, and *Lippia multiflora* into oxime: GC-MS and FT-IR analysis. *Molecules*, 14: 3275-3285 (2009).
- [22] O. Dabbit, A. Makansi, The Effect of Microwave in Organic Synthesis"Oxidation of Aromatic Alkyl Halides and Conversion it to Aldehydes and ketones". *Research Journal of Aleppo University*, 97: (in press) (2014).
- [23] O. Dabbit, A. Makansi, The synthesis of some aldehydes from the appropriate raw materials, in the Presence of different Catalysts and under the effect of microwave. *Research Journal of Aleppo University*, 105: (in press) (2015).

اصطناع النتريلات والأوكسيمات العطرية تحت تأثير الأمواج المكروية باستخدام حموض صلبة كحفازات وبدون مُحل

أسامة ضبيط* ، محمد نصوح علايا، أنس مكانسي

قسم الكيمياء، كلية العلوم، جامعة حلب، سوريا

ملخص البحث. تم الاستفادة من تأثير الأمواج المكروية في بعض تفاعلات الاصطناع العضوي حيث قمنا بتحضير بعض النتريلات والأوكسيمات العطرية إنطلاقاً من الألدهيدات العطرية الموافقة وبوجود الهيدروكسيل أمين هيدروكلوريد $\text{NH}_2\text{OH}\cdot\text{HCl}$ ، كما تم استخدام حموض صلبة كحفازات وتم الحصول على مراديد جيدة للنواتج ويزمن تفاعل قليل. تم مناقشة تأثير بعض الحفازات غير المتجانسة كالأكاسيد المشتركة **15-WSS, 45-WSS** وثنائي أكسيد التيتانيوم TiO_2 على مردود التفاعل، إن هذه الطريقة الفعالة مكنتنا من اصطناع العديد من النتريلات والأوكسيمات المفيدة.