Organic Chemistry
Current Research

Agnimonhan et al., Organic Chem Curr Res 2017, 6:2
DOI: 10.4172/2161-0401.1000180

Research Article Open Access

Willgerodt-Kindler Reaction's Microwave-Enhanced Synthesis of Thiobenzamides Derivatives in Heterogeneous Acid Catalysis with Montmorillonite K-10

Hyacinthe F. Agnimonhan[1]*, Léon A. Ahoussi[1], Bienvenu Glinma[1], Justin M. Kohoudé[2], Fernand A. Gbaguidi[1], Salomé D. S. Kpoviessi[1], Jacques Poupaert[3] and Georges C. Accrombessi[1]

[1]*Laboratory of Physics and Synthesis Organic Chemistry (LaCOPS), Faculty of Sciences and Techniques (FAST), University of Abomey-Calavi, BP: 4521 Cotonou, Benin*
[2]*Laboratory of Molecular Interactions and Reactivity Chemical and Photochemical, University Paul Sabatier of Toulouse, France*
[3]*Louvain Drug Research Institute (LDRI), School of Pharmacy, University Catholique of Louvain, B1 7203 Av. E. Mounier 72, B-1200 Brussels, Belgium*

Abstract

The Willgerodt-Kindler (WK) reaction of is one of most synthesis methods used to access the thioamides. The known to thioamides have made this reaction more attractive in catalytic synthesis methods. Heterogeneous catalysis acid with the montmorillonite K-10 applied to this reaction under activation microwave for the synthesis of phenyl (morpholino) methanethiones derivatives shows that the mixture (aldehyde, sulfur, morpholine and K-10) is not only appropriate, but optimizes the reaction. This solid catalyst was easily separated from the reaction mixture and was recycled at least twice (02) without any loss of activity. Operational simplicity, short reaction times, excellent yields and benign environmental conditions are other advantages of this protocol, thus respecting the principles of green chemistry. Among the thioamides synthesized, 4-(morpholine-4-carbonothioyl)benzoic acid (**h**) is a novel molecule which to our knowledge has never before been synthesized. We obtained it with a yield of 68%. In summary, we can be concluded that the heterogeneous catalysis acid conditions with the montmorillonite K - 10 favourable to the Willgerodt-Kindler reaction for carbonyl compounds. The structures of thioamides synthesized were characterized and confirmed by high-resolution mass spectrometry (HRMS) and nuclear magnetic resonance (NMR) 1D and 2D (COSY, HSQC, HMBC).

Keywords: Green chemistry; Microwave irradiation; Montmorillonite; K-10; Thiobenzamides; Willgerodt-Kindler

Introduction

In recent years, the thioamides are often appeared in the literature as intermediates in medicinal chemistry and biological [1,2], but also in organic synthesis for the preparation of heterocycles containing sulphur [3,4]. The synthesis of thioamides derivatives has attracted so much attention among many researchers and several synthesis methods have been developed which validated is the Willgerodt-Kindler's reaction (WK). The Willgerodt-Kindler's reaction is a method that is well known for the synthesis of thioamides [5]. It consists the condensation of the carbonyl compound with an amine in the presence of sulfur. This WK reaction has found in the past a bad reputation because of long reaction time, difficult conditions of reaction and formation of hydrogen sulfide (gas) toxic to humans and the environment. In the quest to find methods of catalytic synthesis responding to the new requirements of green chemistry, optimization conditions have made the WK reaction more attractive [6]. The application of the catalyst montmorillonite K-10 to this reaction for the synthesis of 1-morpholino-2- (naphthalen-1-yl) ethanethione, concluded that acid-base catalysis conditions ameliorate the WK's reaction of ketone compounds [7]. Our working group are employed this catalyst K-10 in Willgerodt-Kindler's reaction under microwave assistance of aryl aldehyde compounds. We reported recently a study which the synthesis by reaction of Willgerodt-Kindler in acid catalysis with K-10 and DMF as solvent of phenyl (morpholino) methanethione and dimethylaminophenyl (morpholino) methanethione was discussed [8]. It is noted that the use of an aprotic polar solvent such as DMF optimizes this reaction under microwave assistance in reducing the reaction time, decreased formation of hydrogen sulfide, reduction of secondary reactions [6] In extension of our work for a green synthesis of phenyl (morpholino) methanethione derivatives and evaluating the effect of the solid catalyst Montmorillonite K-10 in this reaction, we reported the synthesis and characterization of others phenyl (morpholino) methathione derivatives. We have sought to establish a relationship substrate-reactivity of this protocol for the synthesis of these phenyl (morpholino)methathiones derivatives.

Experimental Section

General experimental methods

The synthesis was made under microwave irradiation in a domestic microwave oven "Brandt type MB 18 T (940 W, 2450 MHz)" without any modification. The evolution of the reagents to products is assessed using a thin layer chromatography (TLC). This TLC was realized on the plates of silica (silica gel 60 F254 Merck TCL) with mobile phase which is a mixture of hexane and ethyl acetate in proportion (v/v, 6/4) and then revealed to the ultraviolet (UV) light of wavelength λ=254 nm. All compounds reported here were purified on column chromatography with mobile phase which is a mixture of hexane and ethyl acetate in proportion (v/v, 6/4) and phase stationary silica (Silica gel 63-160 µm). The melting point of synthesized and purified thioamides is made on a fusion meter, of type electrothermal 1A 9000, before the characterization and confirmation of their structure by the spectral analysis methods (MS, NMR-1D and 2D-NMR) The mass spectra to determine the molecular molar mass and the fragments that result has made by high-resolution mass spectrometry (HRMS) in electrospray ionization (ESI) on positive

---

***Corresponding author:** Hyacinthe FA, Laboratory of Physics and Synthesis Organic Chemistry (LaCOPS), Faculty of Sciences and Techniques (FAST), University of Abomey-Calavi, BP: 4521 Cotonou, Benin, Tel: +22995407273; E-mail: agninegre@yahoo.fr

Received: April 08, 2016; **Accepted:** April 29, 2017; **Published:** May 10, 2017

Citation: Agnimonhan HF, . Ahoussi LA, Glinma B, Kohoudé JM, Gbaguidi FA, et al. (2017) Willgerodt-Kindler Reaction's Microwave-Enhanced Synthesis of Thiobenzamides Derivatives in Heterogeneous Acid Catalysis with Montmorillonite K-10. Organic Chem Curr Res 6: 180. doi: 10.4172/2161-0401.1000180

mode (ES+) of system XEVO-G2QTOF#YCA210 on spectrometer TOF. Fragmentation is made out under a tension of the cone to 30 V. The domain of mass analysis extends to m/z 100 to 700 uma. The NMR spectra were carried out in the solvent of analysis DMSO-d_6 (deuterie dimethylsulfoxide) at 298.16 K, using Brüker Avance 400 spectrometer. The spectra for the proton ^1H are made at 300.132 MHz and 75.478 MHz for the carbon ^{13}C. It is the same for COSY; HSQC; HMBC spectra. All reagents were purchased from Sigma/Aldrich, PROLABO and Acros Organics.

Catalyst K-10: Montmorillonite K-10 also known as Terre de Sommières Montmorillonite K-10 is a commercial clay obtained by acidification of the natural Montmorillonite belonging to smectite group of the family of phylosilicates of the formula $(Na, Ca)_{0.3} (Al, Mg)_2Si_4O_{10} (OH)_2 \bullet nH_2O$ [9,10]. It obtained from Sigma Chemical Corporation.

General procedure

The reaction mixture of methods A and B in a domestic microwave oven has been irradiated during 10-15 minutes at 940 W according to the following scheme: 10 or 15 irradiations of 1 min spaced out by 20 seconds for agitation, eventually to cool and return to oven, in order to better control a boiling too marked. The method B is similar method described by Agnimonhan et al. [8]. The temperature of this reaction mixture is comprised to 138 -143°C.

Method A: Without catalysis: In a mixture (5 mmol) aldehyde and morpholine (0.63 mL, 7.5 mmol) put under agitation, 15 mL of DMF (the solvent) are added. To the mixing under agitation, we are added sulphur (0.26 g, 8 mmol). The agitation continues until the obtaining a mixture of Brown colour which will be placed on the rotating plateau of microwave oven to be irradiated. After cooling to room temperature, the mixture is then poured in a solution of ethyl acetate for allowing the elimination of sulphur by simple filtration. The filtrate obtained is treated with 100 mL of hydrochloric acid (0.1 M) to protonate the amine in excess, then with 100 mL of saturated NH_4Cl solution and finally washed with 2 × 100 ml of distilled water. The organic phase after drying over $MgSO_4$ is concentrated by evaporation. The organic phase after drying over $MgSO_4$ is concentrated by evaporation. The crystals formed were recrystallized from ethyl alcohol 95°. To eliminate any traces of sulfur in the product, despite the recrystallization, the washing of thioamide is done with hexane if this thioamide is insoluble; otherwise, a chromatography column is made. The mobile phase used is a mixture of hexane and ethyl acetate (v/v, 6/4) to afford the pure products in 18-26% yields.

Method B: Catalysis with K-10: To a mixture (5 mmol) aldehyde and morpholine (0.63 mL, 7.5 mmol) put under agitation, 15 mL of DMF (the solvent), Then 0.35 g of K-10 and sulphur (0.26 g, 8 mmol) are added. The agitation continues until the obtaining a mixture of Brown colour which will be placed on the rotating plateau of microwave oven to be irradiated. After cooling to room temperature, the mixture is then poured in a solution of ethyl acetate for allowing the elimination of sulphur and K-10 by simple filtration. The same workup procedure followed by purification as described in the procedure A furnished the pure products in 34-68% yields.

phenyl(morpholin-4-yl)methanethione (a): Aldehyde used is benzaldehyde (0.53 g; 5 mmol). The pure product (compound **a**), yellow solid is obtained with a final weigh 0.27 g (Yield=26%) and weigh 0.69 g (yield=67%) following methods A and B respectively.

mp: 137-138 °C**. Rf (Hex/ AcOEt, v/v, 6/4):** 0.71. **HRMS** (ESI/TOF-MS ES+) m/z: $[M+H]^+$ Calcd for $C_{11}H_{14}NOS$ 208.0796; Found 208.0795. **NMR ^{1}H (**DMSO-d_6**,** δ ppm**):** 7.27 (1H, d, C^2,C^6 aromatic); 7.39 (1H, m, C^3, C^5aromatic); 7.37 (1H, m, C^4aromatic); 4.30 (2H, t, $C^{1'}H_2$); 3.56 (2H, t, $C^{2'}H_2$); 3.76 (2H, t, $C^{3'}H_2$); 3.50 (2H, t, $C^{4'}H_2$). **NMR ^{13}C (**DMSO-d_6**,** δ ppm): 198.6 (C thioamide); 142.3 (C^1 aromatic); 128.5 (C^2, C^6 aromatic); 125.8 (C^3, C^5 aromatic); 128.2 (C^4 arom); 49.2 ($C^{1'}$); 65.7 ($C^{2'}$); 65.9 ($C^{3'}$); 52.2 ($C^{4'}$).

(3-nitrophenyl)(morpholin-4-yl) methanethione (b): 3-nitrobenzaldehyde (0.76 g; 5 mmol) is used to obtain the compound **b**, yellow powder with a final weigh 0.29 g (Yield=23%) and weigh 0.81 g (yield=64%) following methods A and B respectively.

mp: 150-151°C**. Rf (Hex/ AcOEt, v/v, 6/4):** 0.63. **HRMS** (ESI/TOF-MS ES+) m/z: $[M+H]^+$ Calcd for $C_{11}H_{13}N_2O_3S$ 253.0647; Found 253.0646. **NMR ^{1}H (**DMSO-d^6**,** δ ppm**):** 7.68 (1H, s, C^2aromatic); 8.20 (1H, m, C^4aromatic); 7.73 (1H, d, C^5aromatic); 8.12 (1H, d, C^6aromatic); 4.31 (2H, t, $C^{1'}H_2$); 3.80 (2H, t, $C^{2'}H_2$); 3.590 (2H, t, $C^{3'}H_2$); 3.54 (2H, t, $C^{4'}H_2$). **NMR ^{13}C (**DMSO-d_6, δ ppm**):** 195.1 (C thioamide); 143.4 (C^1 aromatic); 129.9 (C^2aromatic); 147.4 (C^3aromatic); 123.0 (C^4 aromatic); 132.0 (C^5 aromatic); 120.6 (C^6 aromatic); 49.1 ($C^{1'}$); 65.4 ($C^{2'}$); 65.7 ($C^{3'}$); 52.3 ($C^{4'}$).

(4-nitrophenyl)(morpholin-4-yl)methanethione (c): 4-nitrobenzaldehyde (0.76 g; 5 mmol) is used to obtain the compound **c**, yellow orange powder with a final weigh 0.29 g (Yield=23%) and weigh 0.82 g (yield=65%) following methods A and B respectively.

mp: 199 - 200°C**. Rf (Hex/ AcOEt, v/v, 6/4):** 0.67**. HRMS** (ESI/TOF-MS ES+) m/z: $[M+H]^+$ Calcd for $C_{11}H_{13}N_2O_3S$ 253.0647; Found 253.0654. **NMR ^{1}H (**DMSO-d_6, δ ppm**):** 7.53 (1H, d, C^2aromatic); 8.22 (1H, d, C^3aromatic); 8.25 (1H, d, C^5aromatic); 7.55 (1H, d, C^6aromatic); 4.30 (2H, t, $C^{1'}H_2$); 3.70 (2H, t, $C^{2'}H_2$); 3.590 (2H, t, $C^{3'}H_2$); 3.50 (2H, t, $C^{4'}H_2$). **NMR ^{13}C (**DMSO-d_6**,** δ ppm**):** 195.4 (C, thioamide); 146.7 (C^1 aromatic); 126.8 (C^2, C^6 aromatic); 123.7 (C^3, C^5 aromatic); 147.9 (C^4 aromatic); 48.8 ($C^{1'}$); 65.5 ($C^{2'}$); 65.7 ($C^{3'}$); 52.2 ($C^{4'}$).

(3-hydroxyphenyl)(morpholin-4-yl)methanethione (d): The aldehyde reagent: 3-hydroxybenzaldehyde (0.61 g; 5 mmol) has given the compound **d**, brown powder with a final weigh 0.20 g (Yield=18%) and weigh 0.41 g (yield=37%) following methods A and B respectively.

mp: 162-163°C**. Rf (Hex/ AcOEt, v/v, 6/4):** 0.54. **HRMS** (ESI/TOF-MS ES+) m/z: $[M+H]^+$ Calcd for $C_{11}H_{14}NO_2S$ 224.0745; Found 224.0743. **NMR ^{1}H (**DMSO-d_6, δ ppm**):** 9.68 (OH); 7.17 (1H, t, C^5aromatic); 6.74 (1H, d, C^4aromatic); 6.65 (2H, m, C^2,C^6aromatic); 4.28 (2H, t, $C^{1'}H_2$); 3.55 (2H, t, $C^{2'}H_2$); 3.75 (2H, t, $C^{3'}H_2$); 3.55 (2H, t, $C^{4'}H_2$). **RMN ^{13}C (**DMSO-d_6**,** δ ppm**):** 198.6 (C, thioamide); 143.5 (C^1 aromatic); 112.8 (C^2aromatic); 157.0 (C^3aromatic); 115.4 (C^4 aromatic); 129.3 (C^5 aromatic); 116.1 (C^6 aromatic); 49.5 ($C^{1'}$); 65.6 ($C^{2'}$); 66.0 ($C^{3'}$); 52.1 ($C^{4'}$).

(4-hydroxyphenyl)(morpholin-4-yl)methanethione (e): 4-hydroxybenzaldehyde (0.61 g; 5 mmol) is used to obtain the compound **e**, yellow orange Pink powder with a final weigh 0.22 g (Yield=20%) and weigh 0.44 g (yield=39%) following methods A and B respectively.

mp: 204-205°C**. Rf (Hex/ AcOEt, v/v, 6/4):** 0.51. **HRMS** (ESI/TOF-MS ES+) m/z: $[M+H]^+$ Calcd for $C_{11}H_{14}NO_2S$ 224.0745; Found 224.0741. **NMR ^{1}H (**DMSO-d_6, δ ppm**):** 7.16 (1H, d, C^2aromatic); 6.74 (1H, d, C^3aromatic); 6.74 (1H, d, C^5aromatic); 7.16 (1H, d, C^6aromatic); 4.27 (2H, t, $C^{1'}H_2$); 3.74 (2H, t, $C^{2'}H_2$); 3.40 (2H, t, $C^{3'}H_2$); 3.40 (2H, t, $C^{4'}H_2$). **NMR ^{13}C (**DMSO-d_6, δ ppm**):** 199.9 (C, thioamide); 133.6 (C^1 aromatic); 128.8 (C^2, C^6 aromatic); 115.1 (C^3, C^5 aromatic); 158.6 (C^4 aromatic); 50.3 ($C^{1'}$); 66.2 ($C^{2'}$); 66.5 ($C^{3'}$); 53.0 ($C^{4'}$).

(3,4-dihydroxyphenyl)(morpholin-4-yl)methanethione (f): The aldehyde reagent: 3,4-dihydroxybenzaldehyde (0.69 g; 5 mmol) has given the compound **f**, yellow powder with a final weigh 0.25 g (Yield=21%) and weigh 0.41 g (yield=34%) following methods A and B respectively.

mp: 251-252°C**. Rf (Hex/ AcOEt, v/v, 6/4):** 0.34. **HRMS** (ESI/TOF-MS ES+) m/z: $[M+H]^+$ Calcd for $C_{11}H_{14}NO_3S$ 240.0694; Found 240.0694. **NMR ^{1}H (**DMSO-d_6, δ ppm): 9.29 (OH, C^4); 9.17 (OH,C^3); 6.75 (1H,s, C^2aromatic); 6.70 (1H, d, C^5aromatic); 6.58 (1H, d, C^6aromatic); 4.25 (2H, t, $C^{1'}H_2$); 3.73 (2H, t, $C^{2'}H_2$); 3.59 (2H, t, $C^{3'}H_2$); 3.60 (2H, t, $C^{4'}H_2$). **NMR ^{13}C (**DMSO-d_6**,** δ ppm): 199.5 (C, thioamide); 133.4 (C^1 aromatic); 114.7 (C^2aromatic); 144.6 (C^3aromatic); 146.3 (C^4 aromatic); 114.7 (C^5 aromatic); 117.6 (C^6 aromatic); 49.7 ($C^{1'}$); 65.7 ($C^{2'}$); 66.1 ($C^{3'}$); 52.8 ($C^{4'}$).

[4-(dimethylamino)phenyl](morpholin-4-yl)methanethione (g): 4-dimethylaminobenzaldehyde (0.74 g; 5 mmol) is used to obtain the compound **g**, yellow orange powder with a final weigh 0.27 g (Yield=22%) and weigh 0.54 g (yield=43%) following methods A and B respectively.

mp: 149-150°C**. Rf (Hex/ AcOEt, v/v, 6/4):** 0.60. **HRMS** (ESI/TOF-MS ES+) m/z: $[M+H]^+$ Calcd for $C_{13}H_{19}N_2OS$ 251.1218; Found 251.1217. **NMR ^{1}H (**DMSO-d_6, δ ppm): 7.24 (1H, d, C^2,C,^{6}aromatic); 6.64 (1H, d, C^3, C^5aromatic); 3.39 (8H, t, morpholino); 2.9 (6H, s, CH_3). **NMR ^{13}C (**DMSO-d_6**,** δ ppm): 199.9 (C, thioamide); 129.3 (C^1 aromatic); 128.5 (C^2, C^6 aromatic); 110.7 (C^3, C^5 aromatic); 150.8 (C^4 aromatic); 65.9 ($C^{1'}$**,** $C^{4'}$); 65.9 ($C^{2'}$,$C^{3'}$); 40.0 (CH_3).

4-(morpholine-4-carbonothioyl)benzoic acid (h): novel thiobenzamide Acid 4-formylbenzoic (0.75 g; 5 mmol) is used to obtain the compound **h**, yellow solid with a final weigh 0.59 g (Yield=47%) and weigh 0.86 g (yield=68%) following methods A and B respectively.

mp: 227-228°C**. Rf (Hex/ AcOEt, v/v, 6/4):** 0.28. **HRMS** (ESI/TOF-MS ES+) m/z: $[M+H]^+$ Calcd for $C_{12}H_{14}NO_3S$ 252.0694; Found 252.0698. **RMN ^{1}H (**DMSO-d_6**,** δ ppm): 13.08 (OH, carboxylique); 7.38 (1H, d, C^4,C,^{6} aromatic); 7.94 (1H, d, C^3, C^7aromatic); 4.31 (2H, t, $C^{1'}H_2$);3,78 (2H, t, $C^{2'}H_2$); 3.58 (2H, t, $C^{3'}H_2$); 3.46 (2H, t, $C^{4'}H_2$). **RMN ^{13}C (**DMSO-d_6, δ ppm): 197.7 (C, thioamide); 146.6 (C^5 aromatic); 126.4 (C^4, C^6 aromatic); 129.9 (C^3, C^7 aromatic); 130.9 (C^2 aromatic); 167.2 (C^1); 49.5 ($C^{1'}$); 66.1 ($C^{2'}$); 66.4 ($C^{3'}$); 52.7 ($C^{4'}$).

Recycling of K-10: The solid mixture (sulfur, K-10) obtained after filtering, is put in a solution of cyclohexane. The choice of cyclohexane is justified by its low toxicity compared to hexane. The liquid-solid heterogeneous mixture obtained is is put under agitation for a few minutes. To this mixture was added a distilled water where the sulfur in cyclohexane floates aqueous phase, leaving the clay at the bottom of the recipient. The clay is colled after a decantation centrifuge. This is used after drying.

Results and Discussion

In this work, all thiobenzamides were synthesized by the Willgerodt-Kindler reaction under microwave activation at a power of 940W in DMF. In a first step, the synthesis of a series of phenyl (morpholino) methanethione derivatives is carried out without a catalyst (Method A). The yields obtained in products vary between 18% and 26%. Secondly, to improve the yields and to appreciate the effect of the catalyst K-10, the series of derivatives was again made in acid heterogeneous catalyze with catalyst K-10 (Method B). The yields of the synthesized thioamides vary between 34% and 68% (Scheme 1). The yields of the thiobenzamides derivatives, according to the synthesis method described are reported in Table 1. Spectrometric data of the molecules synthesized confirmed and characterized the structures proposed (Figure 1).

Indeed, chemical shifts in ^{1}H NMR (around $\delta \approx 7$ ppm) reveals the presence of an aromatic ring. The ^{13}C NMR analysis indicated the thioamide group to a chemical shift around δ=199 ppm. Morpholino group has this chemical shift in ^{1}H and ^{13}C NMR similar to those indicated in the literature [11]. Furthermore, the mass molar obtained by high-resolution mass spectrometry HRMS (ESI/TOF-MS ES$^+$) is quite close to the calculated mass. This confirms in part the structures of thioamides synthesized with their Rf different to that of their corresponding substrate. The Interpretation of different correlations by spectra COSY ^{1}H-^{1}H, the spectra HSQC and HMBC confirm the structure of the thioamides.

Thioamides (**a**-**g**) of our work were already reported in the literature [6,11,12] especially during the work of Poupaert et al. and Kapanda et al., where it was synthesized by the Willgerodt-Kindler reaction in homogeneous catalysis with as catalyst 4-methylmorpholine under microwave activation [6] et with p-toluenesulfonic acid in reflux [12], respectively.

However thiobenzamide: 4-(morpholine-4-carbonothioyl)benzoic acid (**h**) from the 4-formylbenzoic acid, to our knowledge, is a new molecule which has never been synthesized. We had synthesized it by method B (Figure 1). Its methyl ester was obtained during the work of Kapanda et al. by the Willgerodt-Kindler reaction in homogeneous catalysis in the presence of p-toluene sulfonic acid [11]. These authors during this reaction with several substrates substituted including benzaldehyde, 3 - nitrobenzadehyde, had given a yield of 60 to 70% [4,13].

The reaction of benzaldehyde and derivatives with morpholine in the presence of sulfur under microwave irradiation, without a catalyst (method A) giving yields between 18%-26% (Table 1) confirm the importance of the catalyst in this reaction as reported in the literature [14,15]. Our work has shown that the WK reaction in heterogeneous catalysis acid with the K-10 for benzaldehyde derivatives is not only possible, but also optimizes the reaction compared to that in the conditions without a catalyst.

The use of the solid catalyst such as K-10 is to meet the principles of Green Chemistry [16]. The idea of its use in this reaction is not new because it has been used for the ketone compounds by Gbaguidi et al. [7]. Its extension, in our work, to benzaldehyde and derivatives applies to the generalization of acid catalysis in the reaction of WK to carbonyl compounds. The chemoselectivity observed on derivatives of benzaldehyde and those acetophenones during work of Aghapoor et al. [17] is not observed in acid catalysis conditions, with the K-10 in DMF solvent.

The optimization of this reaction with the K-10 acid catalyst could be justified by the possibility of the formation of an imine in acid condition before an addition with sulfur to give the sulfide evoked by hypotheses of mechanism's reaction to explain migration of the carbonyl group along a chain of methylene units in the case of arylketones [18,19]. Furthermore, analysis of yields (Table 1) shows an influence of the substrate structure on the yield as reported in the literature whose the work of Lundstedt et al. on a series of acetophenones substituted about the study of optimization of WK reaction no catalysed [20]. Our work has shown that substrate-yield relationship also exists with the benzaldehyde derivatives, where in addition to congestion factor related to the position of the substituent on the phenyl group, it should

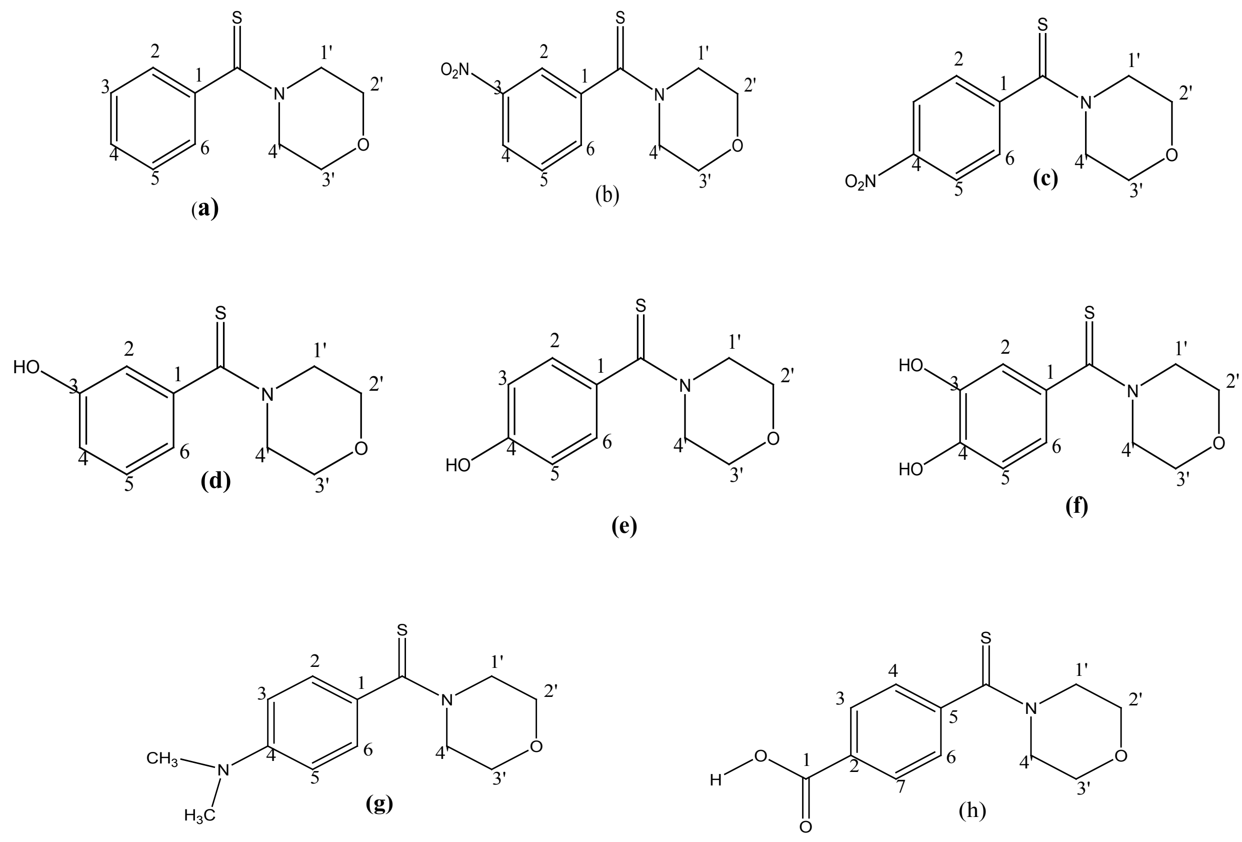
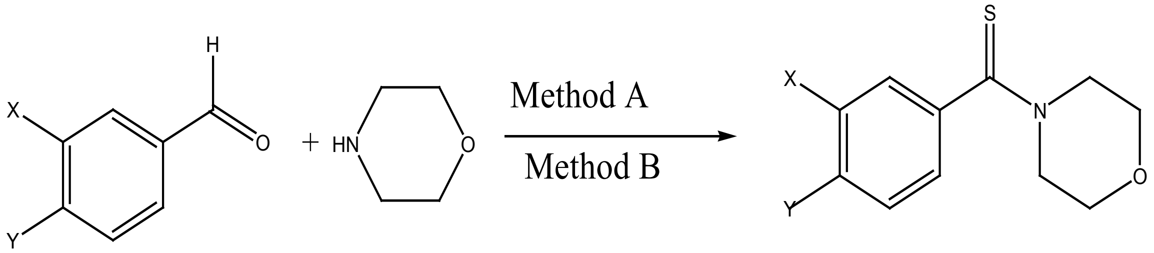


Figure 1: Structure and characterization of thiobenzamides synthetised.



Scheme 1: Formation of thioamides by the WK's reaction. Method A (whithout catalyst); Méthode B (catalyst K-10).

Compounds	X	Y	Yields (%)	
			Method A	Method B
a	H	H	26	67
b	NO_2	H	23	64
c	H	NO_2	23	65
d	OH	H	18	37
e	H	OH	20	39
f	OH	OH	21	34
g	H	$N(CH_3)_2$	22	43
h	H	COOH		68

Table 1: Comparative study of catalytic potential of Montmorillonite K-10. Method A: synthesis without catalyst; Method B: synthesis with catalyst K-10.

be noted that the substituents having a mesomeric attractor effect, give good yield. These substituents do not establish a mesomerie with the carbonyl group which is more available in the nucleophilic attack of the amine during addition.

Thus, the substrates 3-nitrobenzadehyde, 4-nitrobenzadehyde whose products are respectively the compounds (**b**) and (**c**) give a better yield (64 to 67%) comparable to that of benzaldehyde (Compound **a**) in DMF under microwave irradiation in acid catalysis with K-10. However, the electron-donating substituents led to products with lower yields. Thioamides from hydroxybenzadehydes have a yield between 34 and 39%.

Conclusion

The catalytic synthesis methods are a quest in the research of bioactive molecules. These methods should reflect the new requirements of environmental legislation. The reaction of Willgerodt-Kindler under microwave irradiation with a solid acid catalyst, montmorillonite K-10 for the synthesis of thiobenzamides from benzaldehyde derivatives is our contribution to this perspective to generalise this reaction to carbonyl compounds in heterogeneous catalysis while meeting this requirement of Green Chemistry. The solid catalyst K-10 has not only optimized this reaction, but may be recyclable at least two (02) without losing its reactivity.

Acknowledgments

We wish to thank and to encourage the cooperation South-North, particularly between our Laboratory and laboratory partners for the spectrometric analysis.

References

1. Padwa A, Scott Beall L, Heidelbaugh TM, Liu B, Sheehan SM (2000) A One-Pot Bicycloannulation Method for the Synthesis of Tetrahydroisoquinoline Systems. J Org Chem 65: 2684-2695.
2. Aghapoor K, Darabi HR, Heydar KT (2002) The different, but interesting behaviors of benzyl systems in the Willgerodt-Kindler reaction under solvent-free conditions. Phosphurous, Sulfur, Silicon 177: 1183-1187.
3. Metzger JV (1985) Comprehensive Heterocyclic Chemistry. Katritzky AR, Rees CW (eds.), Oxford: Pergamon, pp: 235-294.
4. Jensen OE, Lawesson SO, Bardi R, Piazzesi AM, Toniolo C (1985) Studies on Amino Acids and Peptides VIII. Synthesis and Crystal Structure of Two Monothiated Analogues of Boc-GlyS-Ala-Aib-OMe. Tetrahedron 41: 5595-5606.
5. Amupitan J (1983) Oxidation and reduction. Org Synth, p: 730.
6. Poupaert JH, Duarte S, Colacino E, Depreux P, McCurdy CR, et al. (2004) Willgerodt-Kindler's microwave-enhanced synthesis of thioamide derivatives. Phosphorus, Sulfurs and Silicom 179: 1959-1973.
7. Gbaguidi AF, Kapanda CN, Ahoussi AL, Lambert DM, Accrombessi CG, et al. (2010) General Acid-base catalysis in the Willgerodt-Kindler Reaction. J Soc Ouest-Afr Chim 29: 89-94.
8. Agnimonhan FH, Ahoussi L, Kpoviessi DSS, Gbaguidi AF, Kapanda CN, et al. (2014) Comparative study of acid and basic catalysis in microwave assistance of Willgerodt-Kindler reaction for thiobenzamides and derivatives synthesis. Int J Biol Chem Sci 8: 386-393.
9. Alas M, Gubelmann M, Popa JM (1994) Process for preparing acid anhydrides by passing a solution of this acid over an acidified clay. European Patent. EP 0317394.
10. Do-Rego T, Kpoviessi DSS, Gbaguidi F, Sagbo E, Yalo EN, et al. (2010) Transestérification de la tributyrine catalysée par la montmorillonite K10 en présence de l'éthanol. Int J Biol Chem Sci 4: 1501-1508.
11. Draoui N (2009) Synthèse, analyses et évaluations pharmacologiques de dévivés thioamides, thiourée et oxothioamides: inhibiteurs potentiels des enzymes de dégradation du système endocannabinoïde. Master en Sciences pharmaceutiques, Université Catholique de Louvain (UCL), Louvain.
12. Kapanda CN, Muccioli GG, Labar G, Draoui N, Lambert DM, et al. (2008) Search for monoglyceride lipase inhibitors: synthesis and screening of arylthioamides derivatives. Med Chem Res 18: 253.
13. Rolfs A, Liebscher J (1998) 3-morpholino-2-phenylthioacrylic acid morpholide and 5-(4-bromobenzoyl-2-(4-morpholino)-3phenylthiophene. Org Synth Coll 9: 99.
14. Poupaert JH, Kouinidane K, Renard DM, Lambert M, Isa M (2001) Base Catalysis in the Willgerodt-Kindler Reaction. Org Prep Proc Int 33: 335-340.
15. Okamoto K, Yamamoto T, Kanbara T (2007) Efficient Synthesis of Thiobenzanilides by Willgerodt-Kindler Reaction with Base Catalysts. Synlett and Synthesis 2667-2690.
16. Sheldon RA (1996) Catalysis and zeolites: fundamentals and applications. Journal of Molecular Catalysis 107: 275-258.
17. Aghapour K, Mohsenzadeh F, Khanalizadeh G, Darabi RH (2007) The willgerodt-kindler reaction in water: high chemoselectivity of benzaldehydes over acetophenone. Monatshefte für chemie 138: 61-65.
18. Carmack M, Spielman MA (1946) Organic Reactions. Adams R (ed.), John Wiley and Sons, New York, USA, pp: 83-107.
19. Bradford PM, Michael GE, Frank G, Favaloro Jr (2005) Name Reactions and Reagents in Organic Synthesis. 2nd edn. Wiley-Interscience, p: 690.
20. Lundstedt T, Carlson R, Shabana R (1986) Optimum condition for the Willgerodt-Kindler reaction 1: reaction of substituted acetophenones. Prediction of optimum conditions for new substrates by multivariate correlation. Acta Chem Scand 40: 534-544.