



## Microwave-Induced Surface-Mediated Highly Efficient Regioselective Nitration of Aromatic Compounds: Effects of Penetration Depth

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Surface mediated highly regioselective nitration of aromatic compounds under diverse microwave-induced conditions was investigated in this work. The effects of the penetration depth of the surfaces were found to be more crucial than other dielectric parameters. Despite significant progress of microwave-induced reactions, no reports have examined the penetration depth of the surfaces used in these processes.

**Keywords:** Aromatic compounds, Microwave, Penetration depth, Nitration, Catalyst.

### INTRODUCTION

Syntheses of aromatic nitro compounds are important as the derivatives of these compounds can possess significant biological activities [1]. The nitro compounds needed for the synthesis of these derivatives were mainly made by the conventional nitric acid-sulfuric acid or nitronium tetrafluoroborate methods [2,3]. But these conventional methods produced a large amount of acid waste and the disposal of this acid-waste is one of the major concerns in this process. One way to avoid these complications associated with this method was to utilize the nitrating abilities of nitrate-salts under solid-phase conditions for the synthesis of the nitro compounds [4]. Nowadays extensive investigation is going on surface-mediated reactions as they are more ecologically friendly [5,6]. For instance, non-selective nitration of simple aromatic compounds was reported with sulfuric acid supported on silica gel [7]. Montmorillonite has shown considerable hope as solid support in carrying out different chemical reactions. Claycop (montmorillonite clay impregnated with anhydrous cupric nitrate) was used for aromatic nitration reaction [8]. However, a large amount of acetic anhydride was needed when claycop was used as the nitrating agent. Acetyl nitrate was the nitrating species in this case [8]. Likewise, clayfen (clay with ferric nitrate) was also used as the reagent for the nitration of estrone. However, the yields

were very poor [9] and extreme precautions were needed for the preparation of these types of reagents [10].

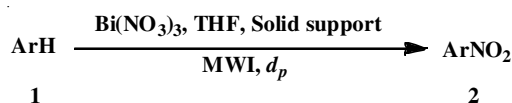
Among the several synthesis methods, methods assisted by microwave irradiation has several advantages compared to conventional methods [11-13]. However, not all the reactions work satisfactorily with microwave irradiation. The reacting materials must have certain dielectric properties to get efficient heating during microwave irradiation. Considering all these facts, in this study we have considered the nitration of aromatic compounds under microwave irradiation with diverse solid surfaces that have different penetration depth values.

### EXPERIMENTAL

**Chemicals:** All chemicals and solvents required to pursue this method were purchased from Aldrich Chemical Company.

**Instrumentation:** NMR data was recorded in Bruker and IR data was recorded in Perkin-Elmer Instruments. CEM automated microwave with frequency 2.45 GHz and power 300 W was used for irradiation.

**Synthesis:** The synthesis of nitro compounds by bismuth nitrate under various solid-phase conditions using microwave irradiation is shown in **Scheme-I**. The compound to be nitrated (1 mmol) and solid support were added to a suspension of bismuth nitrate (1 mmol) in THF (5 mL). The solvent was

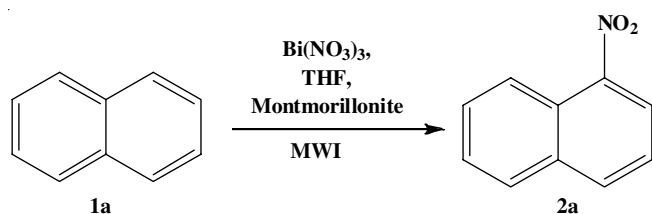


Scheme-I: Nitration of aromatic compounds

evaporated under reduced pressure and irradiated in a microwave oven for 1 to 2 min. The mixture was then washed with dichloromethane (10 mL) and it was concentrated to afford the crude product. The pure product was isolated after column chromatography. Several aromatic compounds (**1**), as well as solid supports, were considered in this study, and the corresponding products (**2**) were obtained in good yield.

## RESULTS AND DISCUSSION

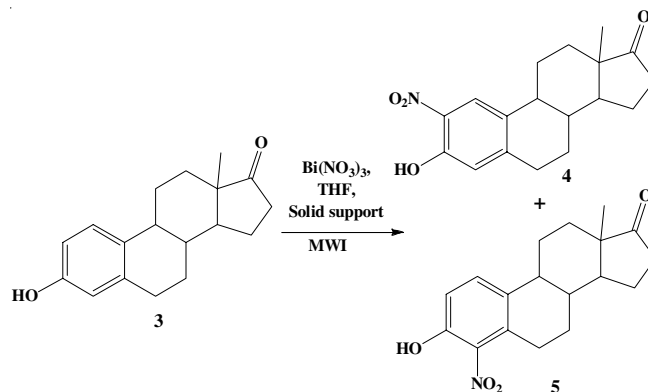
**Nitration of polycyclic aromatic hydrocarbons:** In order to establish the best reaction condition, an optimization study using naphthalene as a model substrate was performed (Scheme-II). Initially, a series of solid supports such as montmorillonite, silica gel, acidic alumina, and ground molecular sieves was examined. It was observed that with montmorillonite, the nitration took place very easily and the product obtained an excellent yield (>90%). For example, the reaction of naphthalene using silica gel as support under identical conditions as described with montmorillonite afforded nitronaphthalene in 70% yield. The same reaction failed to produce the nitro derivative without microwave irradiation. Molecular sieves and acidic alumina failed to produce any products. These results suggest that montmorillonite is the solid support of choice for aromatic nitration.



Scheme-II: Nitration of naphthalene

Mixing the substrates with bismuth nitrate and montmorillonite with tetrahydrofuran, evaporation of the solvent under rotavapor and irradiation of the crude mass in a microwave comprised the reaction conditions for successful, regiospecific nitration with several aromatic compounds (**2**) (Table-1). Chrysene (entry 1), fluorene (entry 2), dibenzofluorene (entry 3), anisole (entry 4), phenol (entry 5), and naphthol (entry 6) were regio-specifically converted into the corresponding nitro compounds by bismuth nitrate-montmorillonite under microwave in excellent yield [4]. The products from entries 1-5 were compared with respect to previous samples [4] and were found to be identical with respect to TLC, melting point and IR spectra. The site of the electrophilic attack by this reagent was observed to be identical with the conventional nitric acid or acetyl nitrate-mediated nitration reaction. The reaction failed to produce nitro derivatives in good yield if the reaction mass with THF was used in the microwave irradiation. Only approximately 10-20% of the nitro compound was obtained with naphthalene by this method.

**Nitration of estrone:** To examine the reactivity of phenolic substrates under the same reaction conditions, the nitration of estrone (**3**) with bismuth nitrate was carried out (Scheme-III). Among the various solid supports montmorillonite provided a good yield. The reaction produced a mixture of 2-nitro (**4**) and 4-nitro estrones (**5**) in a ratio of 1:1 in 95% yield [14]. These two products **4** and **5** were compared with respect to previous samples (TLC, melting point and IR spectra) reported earlier [14]. The formation of the mixtures of nitro derivatives and dinitro derivatives with phenolic substrates pointed out a lesser selectivity under this condition.



Scheme-III: Nitration of estrone

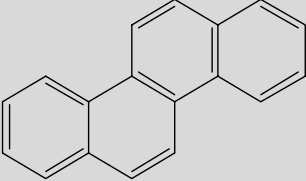
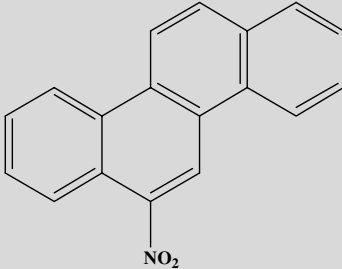
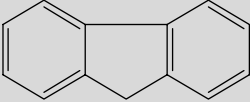
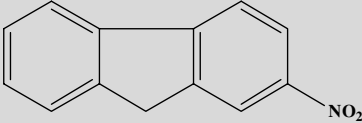
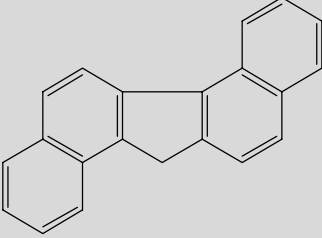
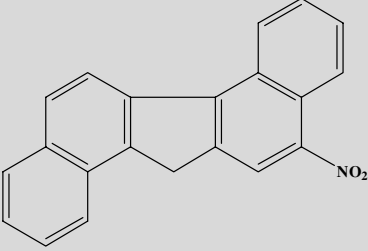
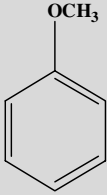
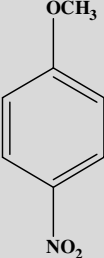
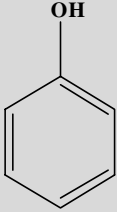
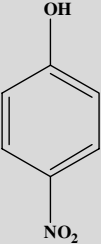
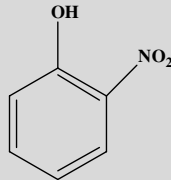
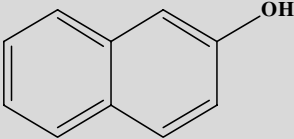
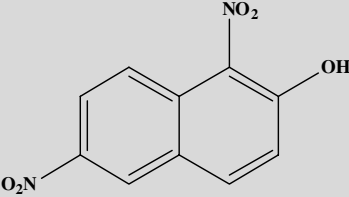
Present results showed that the nitration reaction depends strongly on the nature of the solid support. Besides, two solid adsorbents of similar structure with distinct surface area (particle size) provided different product distribution. Present on-going work in microwave-induced processes and several experiments have helped us to explain the superiority of montmorillonite in the nitration process. It is believed the penetration depth of the solid support in the microwave oven is an important factor, although this physical parameter is completely ignored by scientists.

Microwave radiation does not always heat the entire material. When electromagnetic radiation enters the surface of a material, a portion of the radiation reflects from the surface and the remaining portion penetrates the material. The radiation which penetrated the material interacts with the molecules and ions. The radiation penetrates the material at various depths depending on the material's properties. In microwave heating, the penetration depth is an important parameter. The penetration depth of a field can be defined as the distance from the material surface to a certain internal point where the magnitude of field strength reduces to  $1/e$  ( $=36.8\%$ ) of the original magnitude at the surface of the material [15]. The penetration depth can be expressed mathematically [16,17] as :

$$d_p = \frac{\lambda_0}{2\pi} \left( \frac{1}{2\pi\epsilon_0\epsilon'} \right)^{1/2} \left[ \left( 1 + (\tan \delta)^2 \right)^{1/2} - 1 \right]^{-1/2}$$

where  $d_p$  = penetration depth;  $\lambda_0$  = wavelength at vacuum conditions,  $\mu_0$  = magnetic permeability of free space,  $\mu'$  = magnetic relative permeability,  $\epsilon^0$  = permittivity in free space,  $\epsilon'$  = relative permeability,  $\tan \delta$  = the loss angle.

TABLE-1  
NITRATION OF VARIOUS POLYCYCLIC AROMATIC HYDROCARBONS

Entry	Substrate	Product	Time (min)	Yield (%)
1			2.0	95
2			2.0	90
3			2.0	90
4			1.5	93
5		 	1.5	90
6			2.0	80

Penetration depths of the 2.45 GHz microwaves for the selected solid supports are shown in Table-2. It was found that the lower penetration depth of solid support is helpful for the nitration experiment. On this basis, we see that the montmorillonite (3-19 cm) acts as better solid support for the nitration experiments. Because of the small penetration depth compared to other solid support, electromagnetic radiation penetrates only a very small distance. Thus, controlled and effective heating

occurs in the case of montmorillonite. Controlled and effective heating generates the products in a better way compared to bulk heating of the whole substances together. In the same manner silica (silicon dioxide or quartz), alumina (aluminum oxide), molecular sieves (zeolites) are not effective for this purpose, due to their high penetration depth [15,18-21]. Although the penetration depth of these materials is measured nearly at room temperature, we are aware that this value may increase

TABLE-2  
DIELECTRIC CONSTANT AND PENETRATION DEPTHS OF  
THE 2.45 GHz MICROWAVES FOR SELECTED MATERIALS

Material	Penetration depth (cm)	Dielectric constant
Montmorillonite	3-19	2-40
Silicon dioxide/quartz	1000-20000	3.5-5
Aluminium oxide	300-3000	8.5-9
Molecular sieves/zeolites	>100	1-3

at a higher temperature. It is also important to note down that all these four materials have comparable dielectric constant and are low. Thus, the dielectric constant has less importance in nitration reaction under the microwave. It was also reported that binding of bismuth nitrate to the free hydroxyl group of the multi-metallic montmorillonite is important for nitration reaction and that this complex makes the nitronium ion [22]. The lower penetration depth of the montmorillonite helps to produce nitronium ions in an effective way. Nevertheless, it is not clear if the high penetration depth factors will be equally applicable to other reactions.

### Conclusion

Regioselective nitration of aromatic compounds under diverse microwave-induced conditions was reported. The penetration depth of the solid support is more crucial in microwave induced nitration rather than widely accepted high dielectric constant values. Despite significant progress of microwave-induced reactions, no reports have examined the penetration depth of the solid supports. The lower penetration depth of solid support is helpful for the nitration experiment. Because of the small penetration depth, electromagnetic radiation penetrates only a very small distance and in that way, controlled and effective heating occurs in the case of montmorillonite.

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### CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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