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Nitric acid in the presence of P_2O_5 supported on silica gel—a useful reagent for nitration of aromatic compounds under solvent-free conditions

Abdol Reza Hajipour[a,b,*] and Arnold E. Ruoho[b]

[a]*Pharmaceutical Research Laboratory, Department of Chemistry, Isfahan University of Technology, Isfahan 84156, Iran*
[b]*Department of Pharmacology, University of Wisconsin Medical School, 1300 University Avenue, Madison, WI 53706-1532, USA*

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Abstract—A variety of aromatic compounds are nitrated to parent nitro aromatic compounds under solvent-free conditions using 65% nitric acid in the presence of P_2O_5 supported on silica gel is described. This methodology is useful for nitration of activated and deactivated aromatic rings.

1. Introduction

Nitroaromatic compounds are important chemicals that have application as solvents, dyes, pharmaceuticals, agrochemicals, explosives, and plastics in industry. They are also useful intermediates for the preparation of other compounds, particularly amines, by reduction of nitro groups.[1] Electrophilic aromatic nitration is one of the most important reactions in organic chemistry. However, the majority of the reported methods for nitration of aromatic compounds suffer from disadvantages such as low regioselectivity,[2] over nitration,[2b,d] strongly acidic media,[3] tedious work-up,[3] oxidation of the reagents,[2b,4] and safety problems (storage, handling, using toxic transition metal cations such as Hg^{+2}, Cu^{+2}, etc.).[5] These disadvantages have encouraged the researchers for extensive efforts to develop alternative procedures such as using solid acids[1b,2b,4b,5b,6], other sources of NO_2^+ (nitronium salts,[2a,7a] *N*-nitropyridinium salts,[7b] nitrogen oxide,[2b,c] and peroxynitrite[8]), organic nitrating agents (acetyl nitrate, benzoyl nitrate, and trimethylsilyl nitrate),[9] etc.[10]

Reaction under solvent-free conditions has recently attracted attention.[11–13] The advantage of these methods over conventional classical method is that they are cleaner reactions, decreased reaction time, and easier work-up.

2. Results and discussion

In continuation of our ongoing program to develop environmentally benign methods under solvent-free conditions,[14–16] we wish to report an extremely convenient method for nitration of aromatic compounds with 65% nitric acid in the presence of P_2O_5 supported on silica gel under solvent-free conditions. The P_2O_5/silica gel was prepared by mixing a mixture of P_2O_5 and silica gel (0.063–0.2 mm) in a mortar and grinding with a pestle for 1 min to obtain a homogeneous mixture. This reagent is stable and can be kept at room temperature for months without losing its activity.[17]

Aromatic compound **1** is mixed with one molar ratio of P_2O_5/silica gel in a mortar and then nitrated with one molar ratio of HNO_3 65% to the corresponding nitroaromatic compound **2** (Table 1). After extraction of the product with ether and evaporating the solvent, the product was purified by column chromatography to give the product in good to excellent yields and short reaction time. This method offers a simple, general, selective, and highly efficient route for converting aromatic compounds **1** to the corresponding nitro derivatives **2** in short reaction time.

Keywords: Nitration; Solvent free; Silica gel; P_2O_5; HNO_3.
* Corresponding author. Fax: +98 311 391 2350; e-mail: haji@cc.iut.ac.ir

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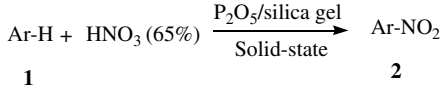
Table 1. Nitration of aromatic compounds **1** with 65% HNO_3 in the presence of P_2O_5/silica gel to nitroarens **2** under solvent-free conditions at room temperature

Entry	ArH (**1**)	$ArNO_2$ (**2**)[a] (*o:m:p* ratio)	Time (min)	Yield[b] (%)
1	Anisole	Nitroanisole (20:0:80)	2	97
2	Acetanilide	Nitroacetanilide (10:0:90)	2	89
3	3-Methylactanilide	4-Nitro-3-methylactanilide	4	95
4	3-Chloroacetanilide	4-Nitro-3-chloroacetanilide	7	80
5	1,2-Dimethoxybenzene	4-Nitro-1,2-dimethoxybenzene	5	96
6	Toluene	Nitrotoluene (40:0:60)	7	92
7	Phenol	Nitrophenol (10:0:90)	3	90
8	1,4-Dimethoxybenzene	2-Nitro-1,4-dimethoxybenzene	3	100
9	4-Hydroxybenzaldehyde	2-Nitro-4-hydroxybenzaldehyde	3	81
10	1,3,5-Trimethylbenzene	2-Nitro-1,3,5-trimethylbenzene	3	83
11	Naphthalene	1-Nitronaphthalene	3	92
12	$C_6H_5NO_2$	1,3-Dinitrobenzene	20	58
13	$4\text{-}MeC_6H_4NO_2$	4-Me 1,3-$(NO_2)2C_6H_3$	10	82
14	C_6H_5CHO	$3\text{-}NO_2C_6H_4CHO$	15	81
15	C_6H_5COOH	$3\text{-}NO_2C_6H_4COOH$	20	80
16	C_6H_5COPh	$3\text{-}NO_2C_6H_4COPh$	15	78
17	Benzylalcohol	Benzaldehyde	10	93
18	$C_6H_4(CH_2)_2COOH$	$NO_2C_6H_3(CH_2)_2COOH$ (10:0:90)	7	90
19	$C_6H_4(CH_2)_2COOMe$	$NO_2C_6H_3(CH_2)_2COOMe$ (12:0:88)	7	90
20	$C_6H_4CH_2COOH$	$NO_2C_6H_3CH_2COOH$ (15:0:85)	7	70
21	$C_6H_4CH_2COOMe$	$NitroC_6H_3CH_2COOMe$ (15:0:85)	3	95
22	Cocaine	3-Nitrocoaine	20	68

[a] Confirmed by comparison with authentic samples (IR, TLC, and NMR).[18–22]
[b] Yield of isolated pure product after purification.

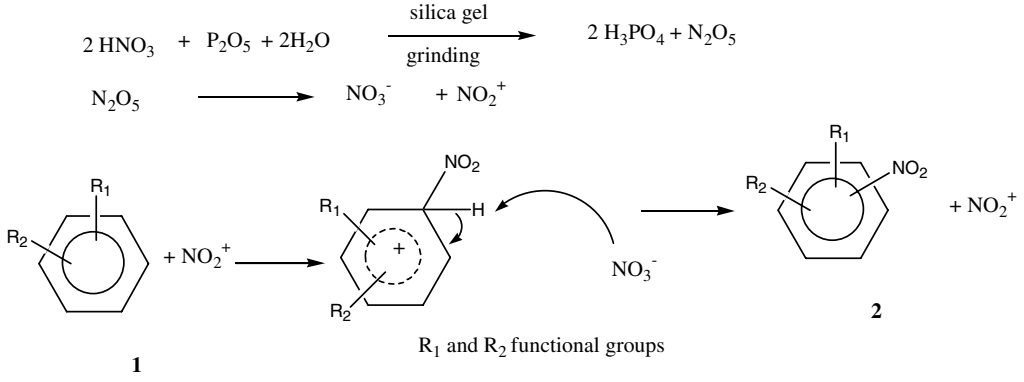
Activated aromatic compounds were converted to the corresponding nitro-aromatic compounds under solvent-free conditions at room temperature in excellent yields in 2–7 min; deactivated aromatic compounds converted to nitrobenzene derivatives with HNO_3 65% in the presence of P_2O_5/silica gel in moderate to good yields in 15–20 min under solvent-free conditions at room temperature (Scheme 1 and Table 1). The reagent is not suitable for nitration of aromatic compounds with oxidizable functional groups, such as hydroxyl and amino groups (Table 1). The site of the electrophilic attack by this reagent was found to be identical to the conventional methods (Table 1).



Scheme 1.

The possible mechanism for nitration of aromatic compounds **1** to the corresponding nitroaromatic compounds **2** using nitric acid in the presence of P_2O_5 supported on silica gel under solvent-free conditions is outlined in Scheme 2.

In summary, we report here a novel method for nitration of aromatic compounds under solvent-free conditions. This procedure is an efficient and novel method for nitration of activated and deactivated aromatic compounds to the corresponding nitro derivatives under solvent-free conditions. This method is not suitable for nitration aromatic compounds with oxidizable functional groups.



Scheme 2.

3. Experimental section

3.1. General

Yields refer to isolated pure products after column chromatography. The products were characterized by comparison of their spectral (IR and ^{1}H NMR) and physical data with those of authentic samples.[18–22] All ^{1}H NMR spectra were recorded at 300 and 500 MHz in $CDCl_3$ relative to TMS (0.00 ppm) and IR spectra were recorded on Shimadzu 435 IR spectrometer. All reactions were carried out under solvent-free conditions at room temperature in a hood with strong ventilation.

3.2. Preparation of reagent [P_2O_5/silica gel (64%w/w)]

In a mortar, 4.5 g of P_2O_5 (31.69 mmol) and 2.5 g of silica gel (0.063–0.2 mm) was ground for 1 min to a homogeneous mixture.

3.3. Typical experimental procedure: nitration of 1,4-dimethoxybenzene with 65% nitric acid in the presence of P_2O_5 supported on silica gel to 2-nitro-1,4-dimethoxybenzene

Two grams of P_2O_5/silica gel (64% w/w) (1 mmol) and 1,4-dimethoxybenzene (1 mmol, 0.14 g) were ground for 30 s, and then 0.5 mL of HNO_3 65% was added and the mixture was ground with a pestle at rt for the time specified in Table 1 until a deep-yellow color appeared. When TLC (*n*-hexane/EtOAc 80:20) showed complete disappearance of 1,4-dimethoxybenzene, to the reaction mixture was added ether (10 mL) and the solid was separated through a short pad of silica gel and washed with ether (15 mL). The filtrate was washed with $NaHCO_3$ 10% (20 mL) and dried ($MgSO_4$). The solvent was evaporated under reduced pressure and the residue was purified by short column chromatography (*n*-Hexane/EtOAc, 3:1), 1,4-dimethoxybenzene was obtained (1 mmol, 0.18 g 100%) as a yellow solid.

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