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Synthesis of Phenoxy Acetic Acid Esters of Phenols Using Phosphonitrilic Chloride as an Activator

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ABSTRACT

A simple procedure is described for the synthesis of phenoxy acetic acid esters by activation of carboxylic acid group of phenoxyacetic acid using Phosphonitrilic Chloride and N-methyl morpholine.

Keywords: Phenoxyacetic acid, Phenols, Phosphonitrilic chloride, N-methyl morpholine.

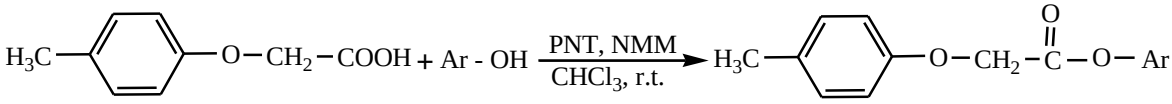
INTRODUCTION

Esterification is one of the most important and commonly used reactions in organic chemistry. In organic synthesis, the conversion of carboxylic acids to corresponding esters is an important and well known organic transformation [1-3]. Esterification reactions have great importance [4,5] in the synthesis of natural products containing two or more carboxylic groups.

In food chemistry, phenolic esters of organic acids, particularly those of cresols and phenols which are excellent flavor compounds as they possess a combination of sweet, floral and fruity odours were studied [6]. The corresponding esters having different functionalities have been used in the manufacture of insecticides, anti-oxidants and photosensitizers [7,8]. Several methods were developed for esterification using catalysts. The various catalysts/reagents used for the esterification are Me_2NSO_2Cl [9], Trifluoroacetic anhydride (TFAA) [10], Diisopropylazodicarboxylate (DIAD)/Ph_3P [11], CCl_4/PPh_3 [12], Anhydrous $ZnCl_2/AlCl_3$ [13], 2-Chloro-1-methylpyridinium iodide [14], N,N-Bis (2-oxo-3-oxazololidinyl) phosphordiamidic chloride [15], Paratoluene sulfonyl chloride (p-TSC) [16], Mn $(OAC)_3$ [17], TiO $(acac)_2$ [18], Montmorillonite-Ti^{4+} [19], Benzotriazol-1-yloxytris (dimethylaminophosphonium-hexafluorophosphate) [BOP] [20], Dicyclohexylcarbodiamide (DCC) [21], Diaryl ammonium arsen sulfonate [22-26].

Phosphonitrilic chloride (PNT) is a white crystalline compound which is thermally stable and soluble in variety of organic solvents. It is less moisture sensitive, non-irritating compound and easy to handle. PNT has been used as an activator in various organic transformations [27-33]. Therefore we report herein the PNT as an activator for the activation of phenoxy acetic acid.

In the present work, phenoxy acetic acid (I) was activated by using PNT and NMM in chloroform and coupled with variety of phenols (II) to get the corresponding phenoxy acetic acid esters (III) at room temperature (Scheme 1).



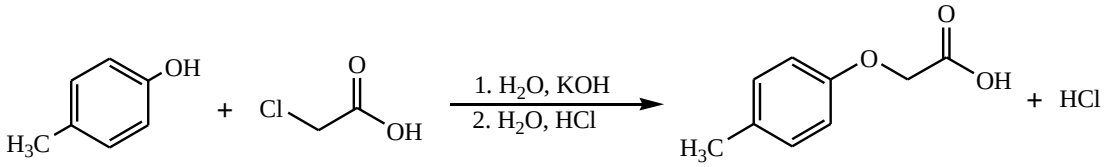
I **II** **III**

Scheme 1: Phenoxy acetic acid esters formation

EXPERIMENTAL PROCEDURE

Preparation of p-Methyl Phenoxy Acetic Acid

In a round bottom flask *p*-cresol (1 g) and NaOH (9 mol%) were taken. Chloro acetic acid (2.5 mL) was added drop-wise and little water was added in a round bottom flask. The contents of the flask were heated on water bath for 1 h, cooled and water (10 mL) was added. The contents were acidified with dilute HCl to congo-red and extracted with diethyl ether. The ethereal extract was then washed with water (10 mL). The aryloxy acetic acid obtained was then extracted by shaking with 5% Na_2CO_3 (25 mL) solution and acidified with dilute HCl. The *p*-methyl phenoxy acetic acid obtained was recrystallized from ethanol.

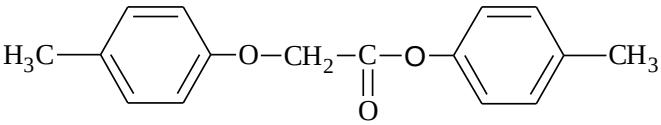


p-Cresol Chloroacetic acid *p*-Methylphenoxyacetic acid

Preparation of Phenoxy Esters of Phenols

Typical procedure: PNT (0.025 mmol), NMM (1.5 mmol) and chloroform were stirred at room temperature for about 5 minutes. *p*-Methyl phenoxy acetic acid (1.5 mmol) was added and stirred at room temperature for 30 minutes. Then *p*-cresol (1.5 mmol) was added to the reaction mixture and stirring was continued at room temperature. The progress of reaction was monitored by TLC and after completion of the reaction, the contents of the flask were transferred to separating funnel, washed 3-4 times by 10% NaOH, water, dried over Na_2SO_4 and filtered. The organic layer obtained was evaporated in vaccum and purified by flash column chromatography. A similar procedure was used for the synthesis of other esters.

Spectral analysis: The products were confirmed by their physical constants and characterized by spectral analysis IR, ^{1}HNMR and mass spectroscopy. The spectral analysis of the representative compound is given as:



P-(tolylphenoxy)-4-methylphenoxyacetate

IR (cm^{-1}): 1755 -C(=O)-O ester

1220 Ar-O-C

^{1}HNMR (δ ppm): 2.3, S, 3H, Ar-CH_3; 2.3, S, 3H, Ar-CH_3;

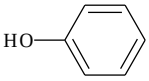
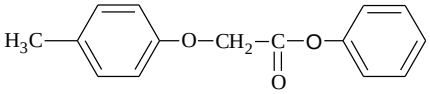
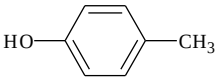
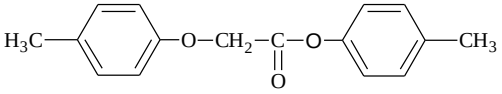
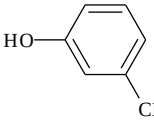
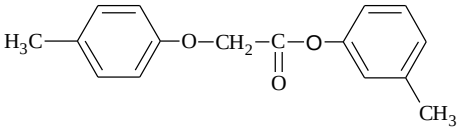
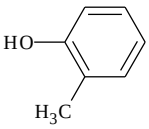
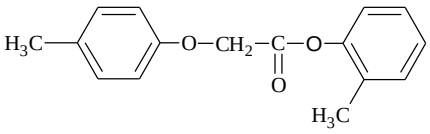
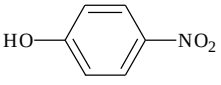
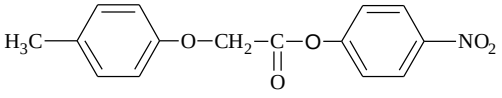
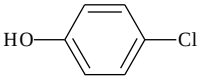
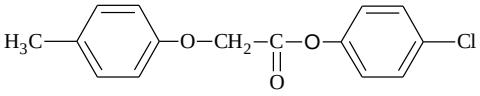
4.5, S, 2H, -CH_2-; 6.8-7.3, M, 8H, Ar-H

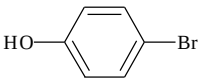
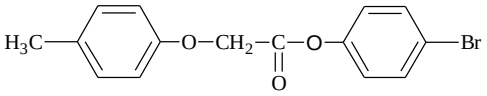
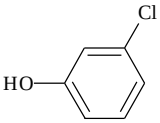
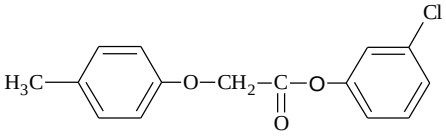
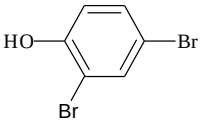
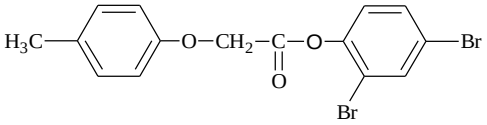
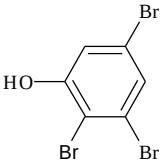
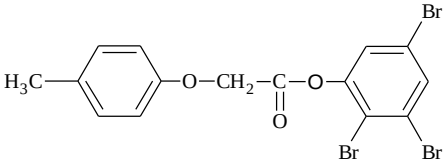
Mass: (M+) 256

RESULTS AND DISCUSSION

Condensation of *p*-methyl phenoxy acetic acid with a variety of phenols was carried out by using PNT together with NMM as activator in chloroform at room temperature. The results are summarized in Table 1. In this method, PNT was activated with NMM in chloroform at room temperature which then activates phenoxy acetic acid. The activated *p*-methyl phenoxy acetic acid then reacted with various phenols to afford the corresponding phenoxy esters in good yields.

Table 1. Synthesis of phenoxy acetic acid esters of phenols using PNT/NMM

Entry	Phenol	Phenoxy acetic acid ester	Yield (%)
1			92
2			91
3			89
4			92
5			93
6			92

7			91
8			89
9			92
10			91

CONCLUSION

PNT in combination with NMM was proven to be an effective activator of phenoxy acetic acid to couple with phenols for the preparation of biologically important phenoxy acetic acid esters under mild conditions in good yields.

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