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Regioselective *ortho*-Acylation of Phenol and Naphthol Derivatives Catalyzed by $FeCl_3$ under Microwave Conditions*

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Abstract—Phenol and naphthol derivatives were subjected to regioselective solvent-free *ortho*-acylation with organic acids in the presence of $FeCl_3$ under microwave irradiation. The reactions were complete in a short time, and the products were obtained in high yields.

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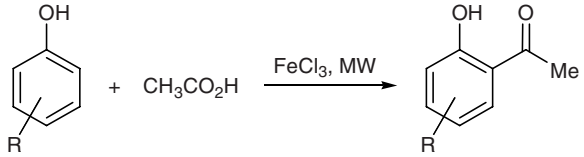
Development of regioselective reactions of aromatic compounds is a fundamental but still important theme in organic synthesis. For example, *ortho*-acylation of phenol and naphthol derivatives provides useful synthetic methods for the preparation of 2-hydroxyphenyl or 2-hydroxynaphthyl ketone derivatives [1], which are key intermediates in the synthesis of biologically active naphthoquinone derivatives [2], naphthalene-containing liquid crystalline polymers, and low molecular weight mesogens [3]. Hydroxyaryl ketones are widely used in perfumery, metallurgy, and pharmaceutics. Moreover, compounds of this class are also important synthetic intermediates [4].

Although some hydroxyaryl ketones exist in the nature, unnatural hydroxyaryl ketones have been synthesized by several methods from phenols and naphthols. Among these, Friedel–Crafts acylation of phenol and naphthol derivatives in the presence of Lewis acids is one of the common routes to these compounds [5]. The acylation can also be achieved by treating the free acid with a variety of condensing agents such as hydrogen fluoride [6], concentrated sulfuric acid [7], phosphorus(V) oxide [8], polyphosphoric acid [9], fluorosulfonic acid [10], and methanesulfonic acid on alumina [11].

Aromatic acylation with carboxylic acids instead of acid anhydrides and acyl chlorides has attracted attention because it is an environmentally benign reaction leading to formation of water as the only by-product [12]. On the other hand, microwave-assisted solvent-free organic syntheses [13] have aroused growing interest as efficient, economic, and clean procedures.

We previously reported [14] on the acylation of phenols and naphthols into the *ortho* position with carboxylic acids in the presence of some Lewis acids under microwave irradiation. The present communication describes the results of using microwave irradiation in the acylation of phenol and naphthol derivatives in the presence of $FeCl_3$. Initially we examined acylation of hydroxyaryl compounds with acetic acid in the presence of $FeCl_3$ under microwave irradiation (Scheme 1). The reactions were carried out without a solvent, and the corresponding *ortho*-acylated phenols and naphthols were obtained with high yields in a very short time (1–3 min; Table 1). The data in Table 1 show that the use of $FeCl_3$ ensures very high yields and regioselectivity: in most cases no *para*-acylated products were formed. For example, 2,6-dimethylphenol failed to produce the corresponding *para*-acyl derivative under the given conditions (run no. 10). It should also be noted that *ortho*-acylated products were not obtained from substrates having electron-withdrawing substituents, such as *m*- and *p*-nitrophenols and 1,4-dihydroxy-9,10-anthraquinone (run nos. 4, 7, 12). The yields of 2-acetyl-1-hydroxynaphthalene and 1-acetyl-2-hydroxy naphthalene from the corresponding naph-

Scheme 1.



R = 2,3-benzo, 3,4-benzo, *m*-Me, *p*-Me, *m*-OH, *p*-OH, *m*-O_2N, *p*-O_2N, *o*,*p*-Me_2 (see Table 1).

* The text was submitted by the authors in English.

Table 1. Acylation naphthol and phenol derivatives with 1.2 mmol of acetic acid in the presence of $FeCl_3$ under microwave irradiation

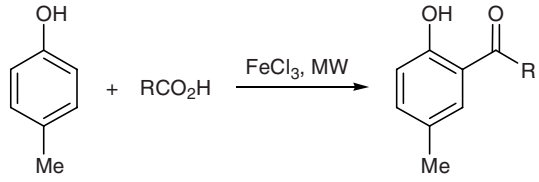
Run no.	Substrate	Substrate, mmol	$FeCl_3$, mmol	Power, W	Time, min	Yield,[a] %
1	Naphthalen-1-ol	0.69	0.31	500	>2	60
2	Naphthalen-2-ol	0.69	0.31	600	>2	35
3	*p*-Cresol	0.95	0.31	400	2	95
4	*m*-Nitrophenol	0.76	0.62	700	3	0
5	*m*-Cresol	0.95	0.31	400	2	98
6	Phenol	1.06	0.31	600	3	70
7	*p*-Nitrophenol	0.76	0.31	700	2	0
8	Resorcinol	0.9	0.31	300	1.33	98
9	Hydroquinone	0.9	0.31	300	1	98
10	2,6-Dimethylphenol	0.82	0.62	700	3	0
11	2,4-Dimethylphenol	0.83	0.31	300	>1	60
12	1,4-Dihydroxy-9,10-anthraquinone	0.84	0.62	800	3	0

[a] Yield of the pure product isolated by chromatography on silica gel.

thols (run nos. 1, 2) were lower as compared to phenol derivatives due to lower reactivity of the former.

We also examined acylation of *p*-cresol with other organic acids, such as propanoic, butanoic, and pentanoic (Scheme 2). The results are given in Table 2; it is seen that the yields of the corresponding *ortho*-acyl derivatives are very high.

Scheme 2.



R = CH_3, C_2H_5, C_3H_7, C_4H_9.

To check for possible intervention of any non-purely thermal specific microwave effect, we tried to perform analogous reactions under conventional thermal conditions at the same temperature as under microwaves. However, no acylated products were formed after a long time.

Table 2. Acylation of 0.95 mmol of *p*-cresol with various organic acids in the presence of $FeCl_3$ under microwave irradiation

Acid (mmol)	$FeCl_3$, mmol	Time, min	Power, W	Yield, %
CH_3CO_2H (1.2)	0.31	2	400	98
$C_2H_5CO_2H$ (1.3)	0.31	1	600	98
$C_3H_7CO_2H$ (1.08)	0.32	1	600	90
$C_4H_9CO_2H$ (0.95)	0.32	1	600	85

The structure of the products as *ortho*-acyl derivatives is confirmed by the presence in their IR spectra of a broadened absorption band from O–H stretching vibrations in the region 3100–3500 cm^{-1} and of a strong carbonyl absorption band at 1620–1670 cm^{-1}. Their ^1H NMR spectra contained a broadened singlet at δ 11.8–13.8 ppm from the hydroxy proton.

We can conclude that the described procedure for *ortho*-acylation of phenols and naphthols is advantageous due to its simplicity, high regioselectivity and yield, short reaction time, and easy work-up.

EXPERIMENTAL

General procedure for *ortho*-acylation of phenol and naphthol derivatives in the presence of $FeCl_3$ under microwave irradiation. A mixture of the corresponding phenol or naphthol, iron(III) chloride, and organic acid (for amounts of the reactants, see Tables 1 and 2) was irradiated in a microwave oven for a time indicated in Table 1 or 2. The progress of the reaction was monitored by TLC. After cooling to room temperature, the mixture was dissolved in 10 ml of methylene chloride, and the solution was washed with water (~20 ml) and aqueous $NaHCO_3$ (20 ml) to remove excess organic acid, filtered, and evaporated. The residue was purified by chromatography on silica gel

using petroleum ether as eluent. The products were identified by comparing their spectral parameters and physical constants with those reported in [4, 15–17].

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