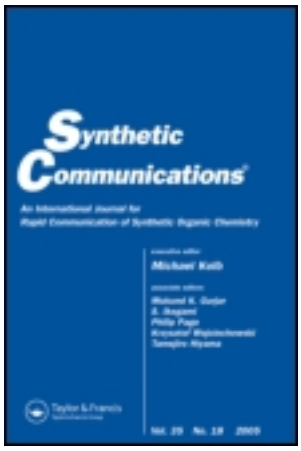

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Synthesis of Salicylic Acid Derivatives in Presence of Ultrasonic Irradiation Using Water as Solvent

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ABSTRACT

An improved synthesis of salicylic acid using ultrasonic irradiation and water as solvent can be achieved with copper and pyridine as catalysts. A number of salicylic acids were prepared in good yield and in a short reaction time.

The development of a new synthesis of salicylic acid derivatives is interesting, as these derivatives are widely used in organic synthesis, in laboratory works, and as antimicrobial cleaning compositions.[1]

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Acceleration of organic reactions by the use of ultrasound irradiation has been largely exemplified[2] and has gained popularity over usual homogenous and heterogeneous reactions.[3] It offers a reduction in reaction time and a saving in energy; often these are accompanied by increased yields and purity of products. There are few references in the literature related to the hydrolysis of 2-halogenobenzoic acids in order to obtain salicylic acid, the hydrolysis of 2-bromobenzoic acid is reported by Lisitsyn and Shestakov[4] in presence of copper acetate and aqueous piperidine.

Recently, we have studied the use of copper and pyridine as catalyst for the hydrolysis of 2-chlorobenzoic derivatives using water as solvent.[5] In the present communication we have studied the use of ultrasound irradiation in the synthesis of salicylic acid derivatives in order to reduce the reaction time.

RESULTS AND DISCUSSION

The best yield obtained in our previous investigation for the hydrolysis of 2-chlorobenzoic acid in presence of water as solvent was reported using 3 equivalents of potassium carbonate, 1 equivalent of pyridine, 3% (by weight) of copper per mole of 2-chlorobenzoic acid in 2 h reaction time. These conditions were used for the synthesis of several salicylic acid derivatives.

First, we studied the reaction time in presence of ultrasonic irradiation and we took as a model the hydrolysis of 2-chlorobenzoic acid in the conditions previously reported. As we can see in Table 1, in only 15 min reaction time the best yield was obtained. All experiments performed in this work were repeated five times. The yields reported represent a media of the obtained values for each reaction.

Table 2 shows the results from several experiments for the hydrolysis of 2-chlorobenzoic acid with different quantities of pyridine using copper powder (3% in weight) and 3 equivalents of potassium carbonate per mole of 2-chlorobenzoic acid, the reaction time in all cases was 15 min. In these reaction conditions the best results were obtained using 0.5 equivalents of pyridine.

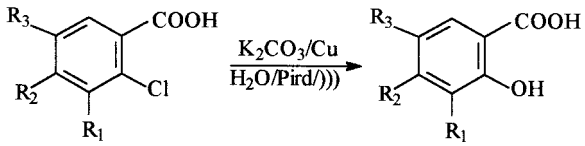


Table 1. Effect of the time on the reaction yield using ultrasonic irradiation in presence of water as solvent.

Ultrasonic irradiation time (min)	Yield of salicylic acid (%)	Standard deviation (%)
30	95	2.0
25	96	1.5
20	95	1.0
15	94	2.0
10	57	2.0

Table 2. Effect of pyridine on the reaction yieid using ultrasonic irradiation in presence of water as solvent.

Equivalents of pyridine	% yield of salicylic acid	Standard deviation (S)
1.00	94	1.5
0.75	95	1.0
0.50	95	1.0
0.25	61	1.5

Once the quantity of pyridine necessary for the reaction was established, a series of salicylic acid derivatives, employing the conditions above studied were obtained.

Table 3 shows the results of salicylic acid derivatives synthesized from the corresponding 2-chlorobenzoic acid derivatives, the melting points (uncorrected), the elemental analysis, and the yields obtained were compared with the method using reflux water during 2 h reaction time.

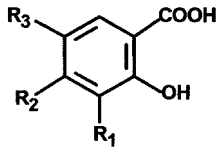
EXPERIMENTAL PART

General Procedure

Synthesis of Salicylic Acid Derivatives Using Water as Solvent

A mixture of 2-chlorobenzoic acid derivative, (6.26 g; 0.04 mol), anhydrous potassium carbonate (8.28 g; 0.06 mol), pyridine (1.58 g; 0.02 mol), copper powder (0.2 g) and water (25 mL) was irradiated for 15 min a sonic horn at 20 kHz. The reaction mixture was cooled, poured into water and

Table 3. Salicylic acid synthesised from the corresponding 2-chlorobenzoic acid derivatives.



No.	R_1	R_2	R_3	Yield using ultra-sound (%)	Yield in 2 h at reflux (%)	M.p. uncorrected (°C)	M.p Lit. (°C)
1	H	H	H	95	90	159	158–160[6]
2	H	Cl	H	95	88	212	210–212[7]
3	H	NO_2	H	96	90	225	226[8]
4	H	H	Cl	92	84	171	171–172[9]
5	H	H	NO_2	97	95	234	233–235[10]
6	NO_2	H	H	96	93	143–144	144[11]
7	H	H	CH_3O	92	87	141	141[12]

Calculated and experimental microanalysis

		Calculated (%)		Experimental (%)	
No.	Formula	C	H	C	H
1	$C_7H_6O_3$	60.87	4.35	61.05	4.04
2	$C_7H_5ClO_3$	48.70	2.90	48.96	2.68
3	$C_7H_5NO_5$	45.90	2.73	46.18	2.48
4	$C_7H_5ClO_3$	48.70	2.90	48.95	2.51
5	$C_7H_5NO_5$	45.90	2.73	45.71	2.61
6	$C_7H_5NO_5$	45.90	2.73	45.83	2.83
7	$C_8H_8O_4$	57.14	4.76	56.97	4.80
8	$C_7H_5ClO_3$	48.70	2.90	48.80	2.78

acidified with hydrochloric acid (1:1) to pH 3. The solid was filtered and crystallized from ethanol/water (1:2). The yield, melting point (uncorrected) for each salicylic acid obtained are reported in Table 3.

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