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Microwave-Assisted Oxidation of α-Substituted Carbonyl Compounds to Carboxylic Acids in Aqueous Media

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MICROWAVE-ASSISTED OXIDATION OF α-SUBSTITUTED CARBONYL COMPOUNDS TO CARBOXYLIC ACIDS IN AQUEOUS MEDIA

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ABSTRACT:

Carbonyl compounds containing electron-withdrawing substituents are efficiently oxidized by aqueous sodium hypochlorite in the absence of added organic solvents using microwaves.

Sodium hypochlorite, the active ingredient in commercial bleaches, has been utilized to carry out a number of reactions, including epoxidations,[1,2] decarboxylations of amino acids,[3] haloform reactions,[4] and oxidations of alkylbenzenes,[5] sulfides,[6,7] alcohols[8,9,10] and ketones.[11] Since the organic reactants are generally insoluble in aqueous hypochlorite solutions, long reaction times are often required as well as the addition of cosolvents or phase-transfer media.[12,13,14] Microwaves have been utilized to enhance the rates of a number of organic reactions[15,16,17] including Diels-

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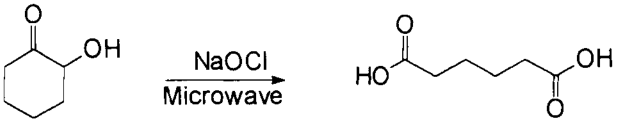
Alder cycloadditions,[18] the hydrolysis of phospho-anhydride bonds,[19] deacetylation sequences,[20] and the synthesis of α-aminolactams.[21]

We now wish to report that oxidations of α-substituted carbonyl compounds with sodium hypochlorite are accelerated by microwave irradiation. Reaction times are often reduced a hundredfold and the yields are comparable to those previously reported. Even more significant is the fact that the reactions are carried out in the absence of organic solvents which greatly simplifies waste disposal. As an example, the microwave assisted reaction of 2-hydroxycyclohexanone with aqueous sodium hypochlorite is complete in three minutes and affords adipic acid in 86% yield which compares favorably to a control experiment carried out at 100 °C in the absence of microwaves (81% yield in 6 hours) or with ultrasound assistance (87% in 30 minutes).[22]



Organic reagents which can be converted to α-substituted carbonyl reagents by hypochlorite are also oxidized to the expected carboxylic acids. Examples include α-haloacids and alcohols. The results of the current microwave study are presented in Table 1 along with the results (when available) of parallel thermal reactions which were carried out for comparison.

In each case, the yields are comparable to those reported in the literature and with much shorter reaction times. The oxidation of benzoin is representative of the microwave assisted procedure. Benzoin (1.0 mmol, 212 mg) and an excess of sodium hypochlorite (53 ml of a commercially available bleach solution, approximately 37 mmol equivalent) were mixed in a 125 round bottomed flask which was irradiated in a common household

TABLE 1: Microwave Assisted Hypochlorite Oxidations

Substrate	Product[a]	Time	Mp, °C (lit.)	Yield, %[b]
Acenaphthene-quinone	Naphthalic Acid	12 min	259-261(265)[23]	92 (80, 22 hr)
Benzil	Benzoic Acid	10 min	120-122 (122)[24]	82
Benzoin	Benzoic Acid	10 min	120-122 (122)[24]	90 (91, 20 hr)
α-Bromophenyl Acetic Acid	Benzoic Acid	5 min	120-122 (122)[24]	84 (85, 7 hr)
Ethyl Mandelate	Benzoic Acid	14 min	120-122 (122)[24]	70 (90, 2 hr)
Furil	2-Furoic Acid	11 min	129-131 (130-132)[25]	67 (72, 5 hr)
Furoin	2-Furoic Acid	5 min	129-131 (130-132)[25]	65 (72, 1 hr)
2-Hydroxy-cyclohexanone	Adipic Acid	3 min	148-150 (150-151)[26]	86 (81, 6hr)
2-Ketoglutaric Acid	Succinic Acid	10 min	184-186 (185-186)[27]	65 (85, 2 hr)

[a] All products exhibited physical and spectral characteristics in accord with literature values. [b] When available, the yield of the thermal (control) reactions, which were run at 100° C, are given in brackets along with the reaction times required.

microwave (900 watt) for one minute and then allowed to cool for five minutes. This cycle was repeated ten times. The reaction was monitored by thin layer chromatography and, after the starting material was consumed, aqueous sodium bisulfite was added to destroy the excess hypochlorite. The mixture was acidified by the dropwise addition of concentrated HCl. The crude product was isolated by filtration and recrystallized from hot water to give 220 mg (90%) of pure benzoic acid, m.p. 121-122° C.[23]

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