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Microwave-Accelerated Iodination of Some Aromatic Amines, Using Urea-Hydrogen Peroxide Addition Compound (UHP) as the Oxidant†

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Abstract: A fast and simple method for the oxidative iodination of some aromatic amines, *under microwave irradiation*, is reported, using diiodine and the the strongly H-bonded urea-hydrogen peroxide addition compound ($H_2NCONH_2 \cdots H_2O_2$, UHP) as the oxidant. The reactions were carried out in boiling $CHCl_3$ under a reflux condenser to afford, *within 10 minutes*, the purified monoiodinated products in 40-80% yields.

Keywords: Monoiodinated arylamines, urea-hydrogen peroxide as oxidant, microwave irradiation

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Introduction

The use of microwave irradiation to simplify and improve classic organic reactions has become a very popular technique because it often results in shorter reaction times, higher yields and cleaner reactions [1-3]. For example, Khalaj and co-workers recently reported *iodination* of *N*-succinyl-4-[3,3-(1,4-butanediyl)triazene]benzoate with trimethylsilyl iodide (generated *in situ* from trimethylsilyl chloride and regular $Na^{127}I$ in dry acetonitrile) at 75 ºC *for 45 minutes* [4]. *N*-Succinimidyl-4-I-benzoate was thus prepared in 90% yield, after isolation and purification. Activation of this reaction by exposure to *microwave irradiation* (in a domestic oven at 2450 MHz *for 8 minutes*) afforded the same pure monoiodinated product in 87% yield; in small scale preparations under the same *microwave assisted* conditions, but using radioactive $Na^{125}I$, the corresponding labelled aromatic iodide was obtained in 81% radiochemical yield. We propose, however, that this iodination method by no means belongs to the class of *microwave assisted* oxidative iodination reactions of aromatics that, as far as we know, are reported for the first time in this communication.

In our laboratory we have recently devised a novel (classical) method for the oxidative iodination of several aromatic amines using UHP as an effective oxidant, carrying out the reactions in neat *ethyl acetate* (at room temperature for 30 minutes, then at 45 ºC for 2-3 hours) [5]. So far, we have thus obtained the following yields of purified products: 4-$IC_6H_4NH_2$ (64%), 4-IC_6H_4NHMe (41%), 4-$IC_6H_4NMe_2$ (85%), 4-$IC_6H_4NEt_2$ (60%), 4-I-2-$MeC_6H_3NH_2$ (92%), 2-I-5-$MeC_6H_3NH_2$ (62%), 2,4-$I_2C_6H_3NH_2$ (58%), 2-Cl-4-$IC_6H_3NH_2$ (55%), and 3-Cl-4-$IC_6H_3NH_2$ (43%). All these reactions obeyed the following stoichiometry: $2ArH + I_2 + H_2O_2 \rightarrow 2ArI + 2H_2O$.

Results and Discussion

In this work, we have attempted to accelerate the aforementioned reactions *with microwave irradiation,* under an externally attached reflux condenser. We have established that the best results are attained by replacing ethyl acetate (b.p. 77 ºC) with *chloroform* (b.p. 61 ºC) as the solvent of choice. The reactions were complete after ca. 10 minutes. After pouring the reaction mixtures into vigorously stirred excess aqueous Na_2SO_3 solutions, the organic layers were separated, dried over Na_2SO_4, the solvent was distilled off, and the residues were recrystallized from an appropriate solvent. As expected for an oxidative aromatic iodination involving transient *iodine (I)* species, I^+, *para*-iodination of the *activated* monosubstituted benzene substrates was observed and no traces of the potential *ortho*-isomers were detected in the purified products, which were checked chromatographically (TLC) to establish their homogeneity, then they were microanalyzed (%I), and their ^{1}H-NMR spectra were scrutinized. Their melting points (uncorrected) were very close to those obtained with the classical method [5]. By comparing our novel results (Table 1) with those previously obtained (*vide supra*) it is seen that the *microwave assisted* iodination reactions afforded somewhat lower yields, but the previous reaction times were considerably shortened *to only 10 minutes*. In our opinion, these results suggest that further study of various aromatic iodination reactions under microwave irradiation is a worthwhile

pursuit. We speculate that results would probably be better with the use of focused monomode microwave irradiation, what is unfortunately not available in our laboratory.

Table 1. Final yields of the monoiodinated aromatic amines (after purification) and their melting points (uncorrected).

Iodinated product	Yield (%)	M. p. (ºC)	Lit.[6] m.p.(ºC)	Analyses [%I] Calcd/Found
4-$IC_6H_4NMe_2$	80	80-81	82	51.36/51.0
4-$IC_6H_4NH_2$	58	62-63	63-65	57.94/57.5
4-I-2-$MeC_6H_3NH_2$	60	87-88	88, 91-92	54.45/54.2
2,4-$I_2C_6H_3NH_2$ [a)]	50	95-96	95-96	73.58/73.2
2-Cl-4-$IC_6H_3NH_2$	50	71-72	68, 70-73	50.07/49.6
3-Cl-4-$IC_6H_3NH_2$	43	64-66	64-66	50.07/49.8
4-Br-2-$IC_6H_3NH_2$	40	69-70	70-71	42.59/42.2

a) synthesized from 4-$IC_6H_4NH_2$

Experimental

General

Our microwave experiments were performed using a microwave oven purchased from "Plazmatronika" (Wroclaw, Poland). The microwave reactor, working at 2450 MHz, consists of a multimode microwave power delivery system with an operator selectable power output between 0 and 750 W, and a tube allowing an external reflux condenser to be attached. The reactions were carried out in glass vessels (200 mL). All our experiments were performed using the stirring option, whereby the reaction mixtures are stirred by means of a rotating magnetic plate located below the floor of the microwave cavity and a teflon-coated magnetic stirring bar placed inside the vessel. The temperature of the vessel contents was monitored using a calibrated infrared temperature control mounted under the same. All chemicals were of reagent grade (Aldrich, Fluka), and were used without purification.

Microwave-Accelerated Iodination Reactions

UHP (1.53 g, 16.5 mmol, 10% excess) and finely powdered diiodine (3.81 g, 15 mmol) were suspended in $CHCl_3$ (50 mL). Then, 30 mmol of an appropriate *arylamine* was added, the mixture was placed inside the microwave cavity, a reflux condenser was attached, and the magnetic stirring was switched on. A suitable power output (500 to 750 W) was then chosen to ensure a slight, uninterrupted reflux of the solvent. After 10 minutes, the reaction mixtures were cooled to room temperature, then they were poured into vigorously stirred aqueous Na_2SO_3 solutions (5 g Na_2SO_3 in 50 mL of water).

The organic layers were separated, dried over anhydrous Na_2SO_4, filtered, and the solvent was distilled off. The residues were cooled, if they were oily, until they solidified, and then they were recrystallized from hexane, or, in the case of $4\text{-}IC_6H_4NMe_2$, from EtOH. The final results are shown in Table 1. The purities and homogeneities of the purified products were checked by TLC, ^{1}H-NMR spectroscopy and microanalyses (%I). The observed (uncorrected) m.ps. were very close to those reported in our earlier work [5].

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Sample Availability: Available from the authors.