

Microwave-Accelerated or Conventionally Heated Iodination Reactions of Some Aromatic Amines, Using *ortho*-Periodic Acid as the Oxidant[†]

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Abstract: A fast and simple method for the oxidative iodination of some aromatic amines, either under *microwave irradiation* or *conventional heating*, is reported, using diiodine and *ortho*-periodic acid as the oxidant. The reactions were carried out in boiling CH₂Cl₂ solutions under a reflux condenser. For the microwave assisted reactions, the reaction times were always notably shortened, but the yields were usually less influenced as compared with the conventional method.

Keywords: Monoiodinated arylamines; arylamines; *ortho*-periodic acid as oxidant; microwave irradiation.

Introduction

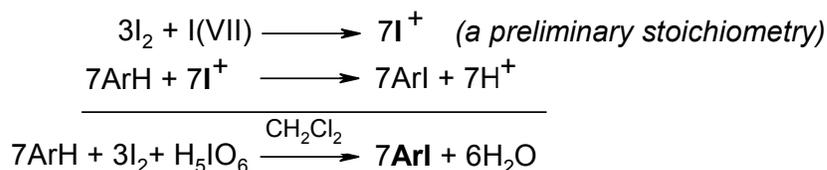
The development of the use of microwave technology in Organic Chemistry since the mid-1980s is mostly due to the increased availability of different commercial equipment and to an increased interest

in achieving shorter reaction times and expanded reaction ranges. A number of reflux systems have been developed in an effort to use *solvents* in microwave assisted organic synthesis without the risk of explosion, since they work at atmospheric pressure and flammable organic vapors cannot be released into the microwave cavity [1 - 4] – precisely with such a reflux system microwave enhanced reactions have been carried out in our laboratory during the last two years. We have always carried out the same, or nearly the same, conventionally heated reactions in order to compare the results afforded by the two different experimental techniques (*vide infra*).

Previously [5], we devised a novel (conventional) method for the oxidative iodination of several aromatic amines, carrying out the reactions in neat *ethyl acetate* (at room temperature within 30 minutes, next at 45 °C for 2-3 hours), with the use of a stable urea-hydrogen peroxide (**UHP**) complex as an effective, safe, and commercially available oxidant; we reported 41-92% yields for the purified monoiodinated products. Subsequently [6], we attempted to accelerate the aforementioned reactions using multimode microwave irradiation, under an externally attached reflux condenser. We established that in this case better results were attained by changing from ethyl acetate (b.p. 77 °C) to *chloroform* (b.p. 61 °C) as the solvent of choice. The reactions were complete after ca. 10 minutes. The isolated monoiodinated products were then recrystallized to afford 40-80 % yields of pure products. It should be emphasized that our former paper [6] did report *for the first time* on the use of *microwave irradiation* to enhance the oxidative iodination reactions of aromatics (exemplified there by reactive arylamines). At the end of our paper [6] we added the following remark: "The results would probably be better with the use of focused monomode microwave irradiation". Fortunately, in the present work we have already been able to use such focused monomode microwave irradiation to enhance our novel oxidative aromatic iodination reactions as reported below.

Results and Discussion

For the work we now report we have decided to carry out the oxidative iodination reactions of several highly activated arylamines (Table 1), but using *ortho*-periodic acid, **H₅IO₆**, as the oxidant. From preliminary experiments we had established that the most suitable solvent for the attempted reactions was neat *dichloromethane* (b.p. 42 °C), which was much better than acetonitrile or carbon tetrachloride. We also had established that the following reaction stoichiometry, which strongly favors the preponderant formation of transient *iodine(I)* species in the reaction mixtures, was the most effective, viz.



Thus, H_5IO_6 and powdered diiodine were suspended, with stirring, in a suitable volume of CH_2Cl_2 . Next, an appropriate *arylamine*, ArH , was added, and such composite reaction mixtures were further reacted *in two ways* as follows:

- by conventional heating*: the vigorously stirred reaction mixtures were gently boiled under a reflux condenser for 10-210 minutes (see Table 1);
- by focused monomode microwave irradiation*, under an externally attached reflux condenser and with stirring: the reaction mixtures were placed into the microwave cavity and were then irradiated for 2-20 minutes (Table 1); an appropriate power output was used to secure a mild, uninterrupted reflux of the solvent.

Table 1. Melting points (uncorrected) and final yields for the purified monoiodinated aromatic amines ^{a)}

Iodinated product	M.p. (°C)	Lit. [7] m.p. (°C)	Conventional method		MW method	
			time [min]	yield [%]	time [min]	yield [%]
4-I-C ₆ H ₄ NH ₂	62-63	62-63	30	62	5	68
4-I-C ₆ H ₄ NHMe	28-29	29-31	60	59	20	47.5
4-I-C ₆ H ₄ NMe ₂	79-80	81-82	30	79	2	77
4-I-C ₆ H ₄ NHEt	53.5-54.3	not found ^{b)}	60	66	10	61
4-I-C ₆ H ₄ NEt ₂	26-27	26-29	60	79	2	79
2-Cl-4-I-C ₆ H ₃ NH ₂	63-64	62-63	30	12	5	11
3-Cl-4-I-C ₆ H ₃ NH ₂ ^{c)}	67-69	64-68	210	46	10	19
4-I-2-Me-C ₆ H ₃ NH ₂	86-87	86-88	10	71	5	58
4-I-3-Me-C ₆ H ₃ NH ₂	43-44	40-42	30	57.5	2	71.5
2-Br-4-I-C ₆ H ₃ NH ₂	70-71	71-72	30	8	20	14
4-Br-2-I-C ₆ H ₃ NH ₂	76-77	77-78	60	11	10	11

a) Satisfactory microanalyses obtained for the purified products: I \pm 0.3%.

b) Probably a new compound. Calcd. for C₈H₁₀IN: C, 39.02; H, 4.07; I, 50.96%;
Found: C, 39.0; H, 4.2; I, 50.9%.

c) Admixed with ca. 10% of its *ortho* isomer (as established from its ¹H- and ¹³C-NMR spectra).

After completion of the reactions carried out in these two different ways (which was monitored by TLC), the cooled reaction mixtures were poured into a vigorously stirred excess of aqueous Na₂SO₃

solution (*a reducing agent*, used to destroy any unreacted diiodine and all possible oxidized species). The organic layers were separated, dried over anhydrous Na_2SO_4 , the solvent was distilled off, and the solidified residues were recrystallized from appropriate organic solvents (see Experimental) to produce pure monoiodinated arylamines, **ArI**, in 8-79% yields (Table 1). The purities and homogeneities of the purified products were checked by TLC, ^1H and ^{13}C NMR spectra, and satisfactory microanalyses (% I). The (uncorrected) melting points were very close to those reported in the literature (Table 1), which confirmed the chemical structures.

From the Table it is seen that the microwave assisted iodination reactions afforded 11-79% yields for the purified products, whereas those heated conventionally gave 8-79% yields. But there is one evident advantage of the microwave-enhanced iodination reactions: they were always *notably accelerated* by microwave irradiation. Hence, the present results do confirm our former conclusions [6] that it is worthwhile to apply microwave irradiation for the enhancement of at least some oxidative aromatic iodination reactions. Further studies are in progress to extend the scope of the reaction to other substrates.

Experimental

General

The melting points for the freshly recrystallized and microanalyzed (% I) monoiodinated amines are uncorrected (Table). All the reagents and solvents were commercial (Fluka, Riedel de Haën), and were used without further purification. Elemental microanalyses were performed at the Analytical Laboratory, Institute of Organic Chemistry, Polish Academy of Sciences in Warsaw, Poland. The ^1H - and ^{13}C -NMR spectra (not given here) were recorded at r.t. with a Bruker AVANCE DMX 400 MHz spectrometer in CDCl_3 solutions, using TMS as an internal standard.

Our microwave experiments were performed using a microwave oven purchased from “Plazmatronika” (Wroclaw, Poland), described in detail in our former paper [6]. A few months ago the producer provided us with the additional attachment, which allows us to perform the experiments with focused monomode microwave irradiation at 2450 MHz, as well as with cylindrical glass vessels, each of a 50 mL volume.

Microwave-Accelerated Iodination Reactions

H_5IO_6 (0.63 g, 2.75 mmol; 10% excess) and finely powdered diiodine (1.9 g, 7.5 mmol; 0% excess) were suspended with stirring in CH_2Cl_2 (25 mL). Then, 19.25 mmol (10% excess) of an appropriate *arylamine*, **ArH**, was added, the reaction mixtures were put into the microwave cavity, and the magnetic stirrer was switched on. An appropriate power output was applied (50%, 500 W) to secure a slight, uninterrupted boil of the solvent. After a definite time (2-20 min; see the Table), the reaction mixtures were cooled to r.t. Next, they were poured into a vigorously stirred aq. Na_2SO_3 solution (2 g

Na₂SO₃ in 100 mL of water). The organic layers were separated, dried over anhyd. Na₂SO₄, filtered, and the solvent was distilled off. The residues were cooled to solidify (if they were still oily, they were cooled externally in an ice-water bath), and next they were mostly recrystallized from *hexane*; only 4-IC₆H₄NMe₂ and 4-IC₆H₄NEt₂ were recrystallized from EtOH, while 4-Br-2-IC₆H₃NH₂ was recrystallized from diethyl ether. The final yields are given in Table 1, where they are compared with those obtained with the conventional heating (*vide supra*); the yields were calculated on the basis of the quantity of diiodine used in a strictly stoichiometric amount (0% excess). The ¹H- and ¹³C-NMR spectra as well as TLC of the freshly recrystallized and analyzed products showed that the starting arylamines with free *para* positions were mostly monoiodinated in the *para* position with respect to their amino groups, with trace amounts (if any at all) of the corresponding *ortho* substituted products being produced. Only in the case of the purified 3-Cl-4-IC₆H₃NH₂ were two isomers clearly identified (in a 9:1 *para-ortho* ratio). Of course, 4-bromoaniline was monoiodinated *ortho* to its amino group.

References and Notes

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Sample Availability: Available from the authors.