

## A green and fast aromatic iodination procedure

**Kelvin Oliveira<sup>1</sup>(IC), Murilo B.M. de Mello<sup>1</sup> (PG), Rogério Gariani<sup>2</sup> (PQ), Alfredo R.M. de Oliveira<sup>1</sup> (PQ)\***

<sup>1</sup> Universidade Federal do Paraná – Departamento de Química – Centro Politécnico – Curitiba –PR

<sup>2</sup> Universidade do Estado de Santa Catarina – Dep. de Química – Centro de Ciência Tecnológica – Joinville –SC

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### Introduction

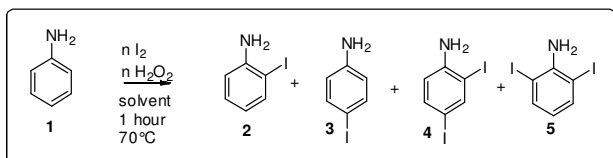
Aromatic compounds bearing a halogen atom are among the most useful building blocks in synthetic organic chemistry, pharmaceutical industry and agrochemical industries. Its versatility comes from the easy with they form new carbon-carbon bonds, allowing diverse functional transformations<sup>1</sup>. Chlorine and bromine are very reactive and their corresponding electrophilic aromatic substitution reaction is well known and useful. Iodine, however, is the least reactive of the halogens and is introduced essentially by two methods: a) by displacement of another group such as carbonyl or diazonium salt (Sandmeyer reaction) or b) by electrophilic iodine substitution reaction of a C-H bond.<sup>2</sup>

Here we report an efficient and green method to introduce iodine in several aromatic compounds bearing activation or deactivation groups utilizing glycerol as solvent.

### Results and Discussion

Iodine is sixteen times more soluble in glycerin than it is in water. The first essays were made in 1 mmol of iodine in 12,5 ml of glycerin to form a homogeneous solution. This is a high diluted solution and we found that using 1 mol/L at 70°C gave the same results with an easy workup procedure.

To investigate the reactivity of iodine towards aniline we mixed both in a proportion of 1:0,5 equivalents and use water or glycerin as solvent. After 24 hours at 70°C the *p*-iodoaniline was identified by GC-MS in 40% and 60% respectively. In both reaction was possible to identify the formation of *o*-iodoaniline and 2,4-diiodoaniline. Next was studied the influence of H<sub>2</sub>O<sub>2</sub> on the progress of reaction. Table 1 shows the results obtained using several stoichiometry ratios of aniline: I<sub>2</sub>: H<sub>2</sub>O<sub>2</sub>. (Scheme 1).



**Scheme 1.** Synthesis of iodo-aniline products.

**Table 1.** Preliminary results of aniline iodination.

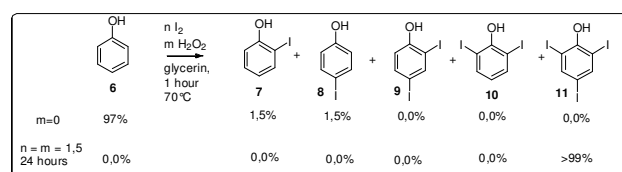
Entry	Solvent	2*	3*	4*	5*
1	Glycerin (n=0,5)**	11	59	0,9	0,0
2	Water (n=0,5)**	22	40	8,7	0,0
3	Glycerin (n = 0,5)	5,2	89	2,0	0,2
4	Glycerin (n= 1,0)	0,2	49	51	0,0
5	Glycerin (n = 1,5)	0,0	10	91	0,0

\*conversion determined by gas-chromatography (%)

\*\*reaction time = 24 hours without H<sub>2</sub>O<sub>2</sub>

Mono-iodination of aniline was obtained with 89% (entry 3) yield and with 97% conversion. The *o*-iodoaniline, 2,4-diiodoaniline and 2,6-diiodoaniline accounts for less than 10% yield.

We also investigated the iodination of phenol under similar conditions, as shown in Scheme 2. Using a reaction ratio of 1: 1,5: 1,5 of aniline:iodine:H<sub>2</sub>O<sub>2</sub> gives >99% yield of 2,4,6-triiodophenol after 24 hours, with great atom economy.



**Scheme 2.** Synthesis of iodo-phenol products and preliminary results.

### Conclusions

The results presented here shows a green procedure to obtain *p*-iodoaniline and 2,4,6-triiodophenol with great atom economy.

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<sup>1</sup> S. S. Kahandal, S. R. Kale, M. B. Gawande, R. Z. Rajender S. Varma and R. V. Jayaram, *RSC Adv.*, **2014**, *4*, 6267

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