

Regioselective, facile and solvent free preparation of aryl iodides using quinolinium chlorochromate and iodine

Sonu

Chemistry Department, DAV College, Sector-10, Chandigarh-160010, India

ARTICLE DETAILS

Article History

Received: 30 May 2017

Accepted: 15 June 2017

Published Online: 15 July 2017

Keywords

Solvent free, selective, microwave irradiation, iodination, quinolinium chlorochromate.

ABSTRACT

A selective, efficient and simple protocol has been reported for the solvent-free preparation of iodoarenes from electron-rich aromatics using quinolinium chlorochromate (QCC) and elemental iodine under microwave irradiation (MWI) within 2-5 minutes. Studies dealing with effect of conventional thermal heating have also been carried out.

1. INTRODUCTION

Among aromatic halides, iodoarenes are the most reactive and form an important class of intermediates in organic synthesis, especially in radical and transition metal mediated coupling,¹ nucleophilic displacement reactions and pharmaceutical research. Research towards the selective and direct introduction of electrophilic iodine into the aromatic nucleus has been widely carried out.² As iodine shows moderate reactivity towards most aromatic substrates, compared to chlorine and bromine, its electrophilicity is enhanced with the help of oxidizing agents such as chromium trioxide, diiodine pentoxide, silvertrifluoro acetate, lead acetate, etc.³⁻⁶ More recent methods used for generating an activated iodonium specie⁷ from iodine are $\text{HIO}_3 / \text{AcOH} / \text{Ac}_2\text{O} / \text{conc. H}_2\text{SO}_4$,⁸ $\text{NaIO}_4 / \text{AcOH} / \text{Ac}_2\text{O} / \text{conc. H}_2\text{SO}_4$,⁹ ionic liquids such as [bmin][PF₆], [bpyr][BF₄], phenyltrimethylammonium dichloroiodate / [bmin][PF₆] and N-iodosuccinimide / CF₃COOH¹⁰⁻¹².

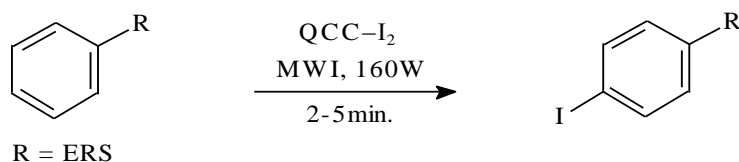
However, a majority of these methods employ toxic reagents with excess of solvents, catalysts or co-catalyst and tedious procedures with high reaction temperature and operational times. In certain cases a mixture of mono and polyiodinated products was obtained.

As a consequence of our studies involving organic transformations utilizing benign methodologies¹³⁻¹⁷ we wish to report that a combination of the mild oxidizing agent, quinolinium chlorochromate¹⁸ (QCC) and elemental iodine provides a good and efficient reagent for generating an activated iodonium ion. In the present communication the application of this reagent has been carried out on different aromatic precursors to yield the monoiodinated compound as the major product. We investigated other oxidizing agents and found that QCC was the most effective (Table 1).

Table 1: Iodination of arenes using various oxidants.

S.No.	Oxidant	MWI Time (min)	Thermal Heating (h)	Yield (%)
1.	None	5	24	0
2.	KmnO ₄	2	24	0
3.	K ₂ Cr ₂ O ₇	2	15	0
4.	HgCl ₂	--	12	45
5.	UHP	6	15	30

In a typical experiment (Scheme 1) a mixture of QCC (1equiv) freshly prepared as reported in literature,¹⁸ iodine (2.5equiv) and arene (1equiv)[carrying an electron releasing substituent 1a and 1c] was exposed to 160W of microwave energy in a domestic microwave oven (LGMS-194A, 800W) for 2-5min¹⁹.




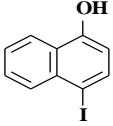
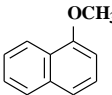
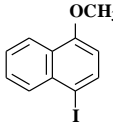

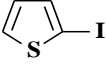
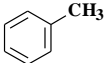
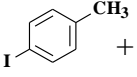
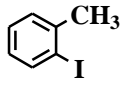

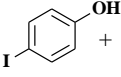
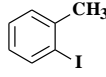
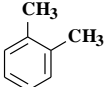
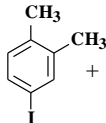
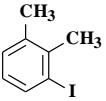
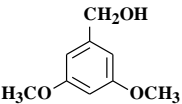
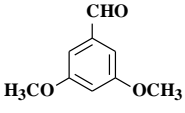
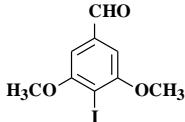
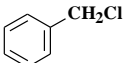
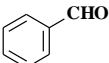
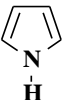
Scheme 1

After work-up and purification via column chromatography (hexane or 2% ethyl acetate in hexane) the *para*-iodinated arene was isolated as the only or major product in moderate to very good yields. Parallel studies were conducted employing conventional conditions, in which a mixture of QCC (1 equiv), iodine (2.5 equiv) and arene (1 equiv) was refluxed in anhyd CH_2Cl_2 , it was observed that refluxing in the absence of the solvent greatly increased the reaction time with reduced yields. The dichloromethane used in the work up was recovered on distillation and utilized for subsequent work ups.

The products were characterized by ^1H NMR spectral data and by comparison with authentic samples. Results of a number of commercially available arenes subjected to reaction with QCC / I_2 on MWI are given in Table 2..

Table 2: QCC- I_2 mediated solvent-free iodination of arenes 1 to iodoarenes 2

S.No.	Reactant	Product(s)	Microwave Irradiation at 160W		Conventional Thermal Heating	
			Time (min)	Yield (%)	TIME (h)	Yield (%)
1.			2	87	2	80
2.			2	88	5	71
3.			4	75	6	68
4.			2	79	6	70
5.			2	81	5	75
6.			2	80	5	73
7.			2	75	3	70

8.			2	70	4	72
	1h	2h				
9.			2	85	3	88
	1i	2i				
10.			2	88	1.5	75
	1j	2j				
11.		 + 	2	74 ^{a, b}	2	69
	1k	2k 2k'				
12.		 + 	3	68 ^{a, c}	6	54
	1l	2l 2l'				
13.		 + 	2	76 ^{c, d}	5	70
	1m	2m 2m'				
14.		 + 	5	79 ^{a, e}	10	68
	1n	2n 2n'				
15.			2	79	4.5	72
	1o	2o				
16.		Polymerized	2	-	2	-
	1p					

^a Overall yield of reaction. ^b Ratio of isomer yields of **2k** and **2k'** (3:2) was determined on the basis of ¹H NMR. ^c Ratio of isomer yields of **2l** and **2l'** (4:1) was determined on the basis of ¹H NMR. ^d Ratio of isomer yields of **2m** and **2m'** (3:1) was determined on the basis of ¹H NMR. ^e Ratio of yields of **2n** and **2n'** (2:1) was determined on the basis of ¹H NMR.

No reaction was observed on subjection of a mixture of anisole **1a** (1equiv) and elemental iodine (2.5equiv) without QCC to microwave irradiation (MWI) at 160W, even up to 5 minutes of irradiation time. Also increase in microwave irradiation time did not result in appreciable increase in the product yield. Iodination of arenes with electron releasing substituents (entries 1-8) proceeded with very good yields within 2-4min. Majority of the arenes gave a single product exclusively (**2a-j**) whereas both *o*-, *p*-products were obtained on iodination of compounds **1k-n** (entries 11-14). Benzyl chloride (entry 15) was oxidized²⁰ to benzaldehyde within 2min and pyrrole polymerized on subjection to the stipulated reaction conditions due to the highly acidic reaction medium. No reaction was observed in the case of benzene, benzaldehyde, acetophenone, 3,4-dihydroxybenzaldehyde, even up to 5min of microwave irradiation and cinnamaldehyde remained unchanged with neither nuclear nor alkene induction of iodine electrophile.

From a mechanistic point of view, we believe that the heterolysis of I-I bond of elemental iodine is assisted by the metal salt (QCC) through complexation, generating an active I^+ specie. The effect of which is further enhanced by the dielectric heating effect of microwaves resulting in extremely short reaction times.

In conclusion a selective and efficient preparation of iodoarenes has been described via a process involving quinolinium chlorochromate enhanced electrophilicity of elemental iodine, towards various arenes under solvent-free microwave conditions. The advantage of this process is that it eliminates use of large excess of metal salts, organic solvents and toxic reagents, endorses operational ease and good yields of the products.

Acknowledgements

Support for this work was provided by CSIR, UGC and to JK (SR/WOS-A/CS-67/2003) by DST, New Delhi.

References

1. Chun, J. H.; Pike, V. W. *J. Org. Chem.*, 2012, 77, 1931-1938.
2. Seidl, T. L.; Sundalam, S.K.; McCullough, B.; Stuart, D. R. *J. Org. Chem.*, 2016, 81, 1998-2009.
3. Carreras, V.; Sandtorv, A. H.; Stuart, D. R. *J. Org. Chem.* 2017, 82, 1279-1284.
4. Möckel, R.; Hilt, G. *Org. Lett.* 2015, 17, 1644-1647.
5. Sudalai, A.; Khenkin, A.; Neumann, R. *Org. Biomol. Chem.*, 2015, 13, 4374-4394.
6. Haines, B. E.; Xu, H.; Verma, P.; Wang, X.-C.; Jin-Quan Yu, J.-Q.; Musaev, D. G. *J. Am. Chem. Soc.* 2015, 137, 9022-9031
7. Teskey, C. J.; Soheli, S.M.A.; Bunting, D.L.; Modha, S.G., Greaney, M. F. *Angew. Chem.* 2017, 56, 5263-5266.
8. Krassowska-Swiebocka, B.; Prokopienko, G.; Skulski, L. *Molecules* 2005, 10, 394.
9. Lulinski, P.; Sosnowski, M.; Skulski, L. *Molecules* 2005, 10, 516.
10. Chiappe, C.; Pieraccini, D. *Arkivoc.* 2002, 249.
11. Muthyala, M. K.; Choudhary, S.; Pandey, K.; Shelke, G. M.; Jha, M.; Kumar, A. *Eur. J. Org. Chem.* 2014, 11, 2365-2370.
12. Ninomiya, K.; Harada, Y.; Kanetou, T.; Suenaga, Y.; Murafuji, T.; Tsunashima, R. *New J. Chem.*, 2015, 39, 9079-9085
13. Singh, J.; Gupta, N.; Kad, G.L.; Kaur, J. *Synth. Commun.* 2006, 36, 2389.
14. Kad, G.L.; Bhandari, M.; Singh, J.; Kaur, J. *J. Org. Res. Dev.* 2003, 7, 339.
15. Singh, V.; Khurana, A.; Kaur, I.; Sapeliyia, V.; Kad, G.L.; Singh, J. *J. Chem. Soc., Perkin Trans. 1* 2002, 1766.
16. Kad, G.L.; Bhandari, M.; Kaur, J.; Rathee, R.; Singh, J. *Green Chem.* 2001, 3, 275.
17. Kad, G.L.; Singh, V.; Chaudhary, S.; Setia, S.; Bhandari, M.; Singh, J. *Ultrasonics Sonochemistry* 2001, 8, 123.
18. Singh, J.; Bhandari, M.; Kaur, J.; Kad, G.L. *Indian J. Chem.* 2003, 42B, 4
19. General procedure: A mixture of arene 1 (1mmol), QCC (1mmol) and iodine (2.5mmol) was irradiated at 160W in a domestic microwave oven for 2-5minutes. On cooling, the mixture was diluted with dichloromethane (2x5mL), filtered through a short silica pad. The filtrate was subsequently washed with aq. sodium thiosulphate solution (2x5mL) and dried over $CaCl_2$. Evaporation of solvent *in vacuo* followed by purification using silica gel column chromatography (hexane or 2% ethyl acetate in hexane) furnished the pure iodoarenes 2.
20. Ozgun, H.B.; Degirmenbasi, N. *J. Chem Res.(S)* 1997, 32.