J. Braz. Chem. Soc., Vol. 21, No. 1, 3-6, 2010.
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0103 - 5053 $6.00+0.00

Article

A Mild and Simple Iodination of Phenols with Trichloroisocyanuric Acid/ I_2 /Wet SiO_2 System

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Iodo molecular na presença de ácido tricloroisocianúrico e solução aquosa de SiO_2 foi utilizado com eficiência na iodinação de fenóis em condições reacionais brandas.

Molecular iodine in the presence of trichloroisocyanuric acid and wet SiO_2 has been utilized efficiently for iodination of phenols under mild reaction conditions.

Keywords: iodination, trichloroisocyanuric acid, phenols, wet SiO_2

Introduction

Aromatic iodo compounds are important intermediates for the synthesis of various pharmaceutical and bioactive compounds.[1,2] They are also useful in metal-catalyzed cross coupling reactions, such as Heck, Stille and Negishi reactions which are utilized in C–C and C–N bond formation.[3,4] However, direct iodination of aromatic compounds is difficult due to the low electrophilicity of molecular iodine compared to that of molecular chlorine and bromine. Generally, arenes are iodinated by iodine in the presence of a Lewis acid or an oxidizing agent. Direct iodination methods have been reported using various iodonium donating systems, such as NIS–CF_3SO_3H,[5] iodine–Ag_2SO_4,[6] iodine–HgO,[7] NIS,[8] iodine–tetrabutylammonium peroxydisulfate,[9] *n*-BuLi–CF_3CH_2I,[10] ICl,[11] and triiodoisocyanuric acid.[12-14] However, most of these methods require toxic and costly reagents, high temperatures and long reaction times. Thus it is desirable to apply a simple, inexpensive and non-toxic reagent system for iodination of aromatic compounds.

Our goal, in undertaking this line of work, was to overcome the limitations and drawbacks of the reported methods which mentioned above and moreover to develop a high-yielding one-pot synthesis of iodo arenes using a novel combination of reagents.

In addition, any reduction in the amount of liquid acids needed and/or any simplification in handling procedures would be highly convenient in terms of risk reduction, economic advantage and environment protection.[15,16] On the other hand, there is intense current research and general interest in heterogeneous systems because of the perceived opportunities such systems present for basic research and because of the unquestioned importance they have in industry and in development technologies.[17] Recently, Zolfigol and co-workers[18,19] reported the mononitration and dinitration of phenols by using trichloroisocyanuric acid/$NaNO_2$/wet SiO_2. Trichloroisocyanuric acid,[20,21] which used primarily as a disinfectant has found little application in organic chemistry so far.[22,23] Therefore, in continuation of our study [24] we were interested in using this reagent for the iodination of aromatic compounds when used in conjunction with I_2 and wet SiO_2 in CH_2Cl_2.

Results and Discussion

We wish to report a simple method for the effective mono iodination of phenols by using trichloroisocyanuric acid as a cheap commercially available reagent, iodine and wet SiO_2 under mild and heterogeneous conditions.

Initially, the test reaction was carried out on 4-hydroxy benzaldehyde with trichloroisocyanuric acid/ I_2/ wet SiO_2 in CH_2Cl_2. 4-Hydroxy-3-iodo-benzaldehyde was obtained immediately in 98% yield**.**

Different substituted phenols were also subjected to iodination in the presence of trichloroisocyanuric acid, I_2, and wet SiO_2 (50% m/m) in dichloromethane (Scheme 1).

The iodo phenols were obtained immediately under mild and completely heterogeneous conditions at room temperature with 100% conversion (substrate consumption) which determined by GC (Table 1).

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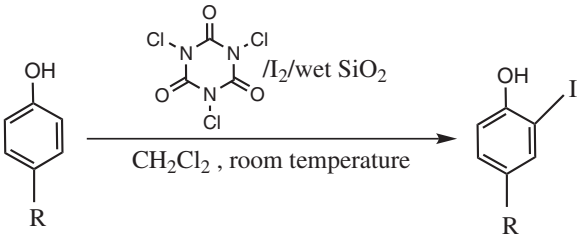
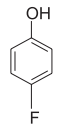
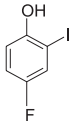
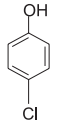
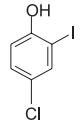
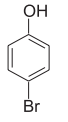
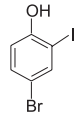
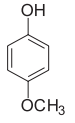
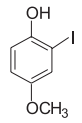
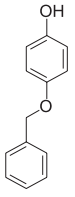
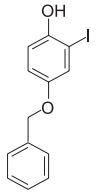
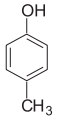
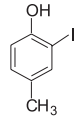
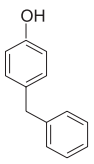
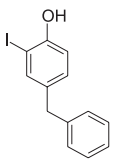
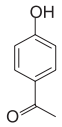
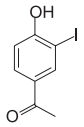
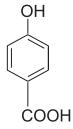
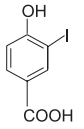
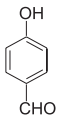
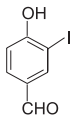
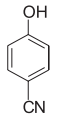
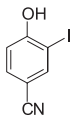


Scheme 1

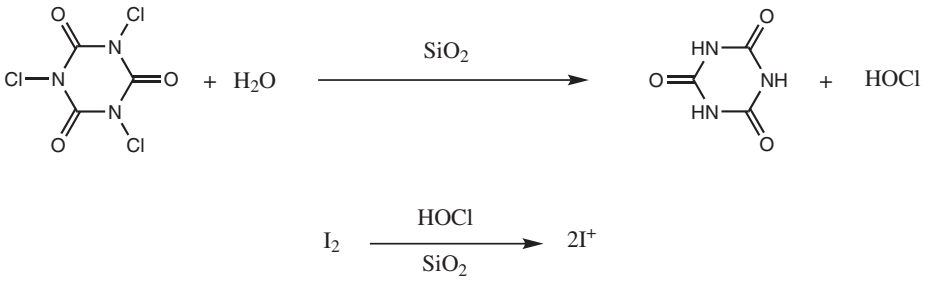
As expected, all the substrates undergo iodination reactions and delivered mono iodo product in good to excellent yields.

By far iodination of activated aromatic compounds was carried out by using molecular iodine or iodide ions together with an oxidizing agent. Oxidizing reagents can degrade sensitive groups present in the substrate. Other direct iodination methods have been recently developed using "I^+" donating systems. Most of these methods require hazardous or toxic reagents or high reaction temperature for long reaction time. The fresh finely powder obtained from mixing distilled water and SiO_2 (50% m/m) in the presence of trichloroisocyanuric acid as a commercially available reagent (slightly soluble in CH_2Cl_2) smoothly produces HOCl[28] as a mild oxidizing agent and isocyanuric acid as a highly polar compound which is completely insoluble in CH_2Cl_2 and was adsorbed by silica gel. Electrophilic iodine "I^+" is generated in situ by the reaction of HOCl with molecular iodine. Wet SiO_2 acts as a heterogeneous effective surface area for iodenium ion which making efficiently work-up easy (Scheme 2). However, highly iodo compounds were obtained by simple filtration and subsequent evaporation of the solvent.

Table 1. Iodination of different substituted phenols using trichloroisocyanuric acid/I_2/ wet SiO_2 in CH_2Cl_2 at room temperature

Entry	Substrate	Product[a]	Isolated Yield / %
1			97
2			98
3			97
4			98
5			95
6			98
7			97
8			94
9			98
10			98
11			95

[a]The product was identified by the comparison of its physical constants and IR and NMR spectral data with those of an authentic sample (4-fluoro-2-iodophenol, mp120-123 °C, Lit.[25] mp 123-124 °C, 4-chloro-2-iodo phenol, mp75-77 °C, Lit.[26] mp 78 °C, 1-(4-hydroxy-3-iodophenyl) ethanone, mp 151-154 °C, Lit.[27] mp 153-155 °C, 4-hydroxy-3-iodo-benzoic acid, mp171-174 °C, Lit.[26] mp 173.5-174.5 °C, 4-hydroxy-3-iodo-benzaldehyde, mp 111-114 °C, Lit.[15] mp 113-115 °C, 4-hydroxy-3-iodobenzonitrile ^{1}HNMR ($CDCl_3$) δ 7.96 (d,1H), 7.54 (dd, 1H), 7.04 (d, 1H), 5.92 (s, 1H), 2-iodo-4-methyl phenol, ^{1}HNMR ($CDCl_3$) δ 2.24 (s, 3H), 5.20 (br s, 1H, exchanges with D_2O), 6.86 (d, 1H), 7.02 (dd, 1H), 7.46 (d, 1H).



Scheme 2

Conclusions

Recently, iodination of benzene, naphthalene and other aromatic compounds using molecular iodine in the presence of trichloroisocyanuric acid and wet SiO_2 system was investigated by us.[24] This motivated us to use this mixed reagent in iodination of electron rich aromatic compounds. In this research iodination of different *para*-substituted phenols were studied. All iodo phenols were obtained rapidly and very efficiently in high yield. In conclusion we have provided a simple method for the direct, regioselective iodination of phenols. Cheapness and availability of reagents, easy and clean work-up and high yields make this method attractive for organic chemists.

Experimental

The products were purified by column chromatography and the purity determinations of the products were accomplished by GLC on a Shimadzu model GC-10A instrument or by TLC on silica- gel polygram STL G/UV 254 plates. FT-IR spectra were recorded on a Perkin Elmer RXI spectrometer. NMR Spectra were recorded on a Bruker Avance DPX 250 MHz instrument. All products were identified by their comparison with authentic samples.

Iodination of 4-hydroxyl benzaldehyde with trichloroisocyanuric acid/I_2/wet SiO_2

A mixture of substituted 4-hydroxyl benzaldehyde (0.122 g, 1 mmol), trichloroisocyanuric acid (0.196 g, 1 mmol), wet SiO_2 (50% m/m, 1 g) and iodine (0.254 g, 1 mmol) was stirred at room temperature in CH_2Cl_2.The progress of the reaction was monitored by TLC. 4-Hydroxy-3-iodo-benzaldehyde was obtained immediately. The reaction mixture was filtered and washed with 5% aqueous sodium thiosulfate solution (2 × 10 mL).The resulting mixture was dried over anhydrous $MgSO_4$ and then applied on a silica-gel column (using n-hexane as eluent) to afford 4-hydroxy-3-iodo-benzaldehyde in 98% yield. mp111-114°C, (Lit.[15] mp 113-115 °C).

Acknowledgments

We gratefully acknowledge the partial support of this study by Damghan University Research Council.

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Received: January 8, 2009
Web Release Date: September 11, 2009