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PII: S0040-4039(17)30005-9
DOI: http://dx.doi.org/10.1016/j.tetlet.2017.01.003
Reference: TETL 48506

To appear in: *Tetrahedron Letters*

Received Date: 2 December 2016
Revised Date: 21 December 2016
Accepted Date: 2 January 2017

Please cite this article as: Iskra, J., Shaun Murphree, S., Rapid aerobic iodination of arenes mediated by hypervalent iodine in fluorinated solvents, *Tetrahedron Letters* (2017), doi: http://dx.doi.org/10.1016/j.tetlet.2017.01.003

Tetrahedron Letters
journal homepage: www.elsevier.com

Rapid aerobic iodination of arenes mediated by hypervalent iodine in fluorinated solvents

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ARTICLE INFO

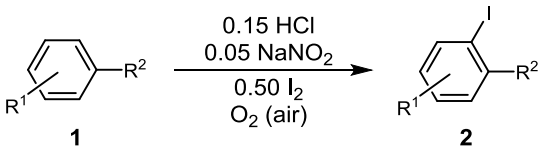
Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
aromatic substitution
hypervalent compounds
iodination
fluorinated solvents

ABSTRACT

Arenes are rapidly converted to the corresponding iodides by aerobic oxidative iodination at room temperature by treatment with iodine and catalytic quantities of nitrous acid in a fluorinated solvent. Dichloroiodic acid is proposed as the actual iodination reagent.

Iodoarenes[1,2] are valuable synthetic intermediates for the construction of complex organic targets, since they serve as convenient precursors for Grignard reagents[3,4] and as electrophilic substrates for various cross-coupling methodologies.[5,6] Consequently, the preparation of iodoarenes continues to command attention within the synthetic community.[7] Recently reported innovations include the use of *N*-iodosuccinimide activated by iron(III),[8] gold(I),[9] or rhodium(III)[10] catalysts; hydrogen iodide in DMSO,[11] and molecular iodine in the presence of a sulfated ceria-zirconia catalyst in ethylene glycol[12] or potassium 4-iodylbenzenesulfonate in acetonitrile.[13] With this backdrop, in connection with our ongoing program investigating the catalytic activation of iodine or iodide toward electrophilic aromatic substitution using environmentally benign terminal oxidants,[14–18] we wish to disclose our findings with respect to electrophilic aromatic iodination (Scheme 1) using elemental iodine in the presence of a substoichiometric amount of nitrous acid, which mediates the in situ generation of a hypervalent iodine reagent via aerobic oxidation.



Scheme 1. Electrophilic aromatic iodination catalyzed by nitrous acid generated in situ.

Prior work in our laboratory[16] had demonstrated the efficacy of nitrite catalysis in aromatic iodination, and there was evidence that fluorinated solvents could further facilitate the reaction.[17] Thus, we surveyed a variety of reaction media (Table 1) for the aerobic oxidative iodination of anisole using a sodium nitrite/hydrochloric acid system. After 90 min, the reaction did not show appreciable progress in seven solvents, including protic (ethanol), moderately polar (ether, ethyl acetate, dichloromethane, and acetone), and polar aprotic (DMF and DMSO) types. However, good to excellent results were observed in the fluorinated solvents hexafluoroisopropanol (HFIP), trifluoroacetic acid (TFA), and trifluoroethanol (TFE). Mixtures of fluorinated and non-fluorinated solvents were ineffective, as illustrated by the absence of reactivity in a 1:1 ethanol/TFE medium (entry 17).

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