Tetrahedron Letters,Vol.30,No.29,pp 3769-3772,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Maxwell Pergamon Macmillan plc

IODINATION OF ALKYLBENZENES WITH IODINE AND SILVER NITRITE

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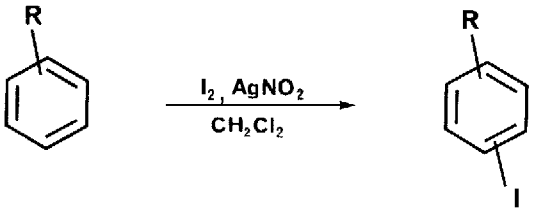
Abstract: Iodination of alkylbenzenes with iodine and silver nitrite at room temperature gives iodoalkylbenzenes in good yield.

Direct bromination and chlorination of aromatic compounds are well known reactions. In contrast, iodination of aromatic compounds with molecular iodine is difficult because this is the least reactive halogen in electrophilic aromatic substitutions.[1] Direct iodination usually requires the use of reagents such as nitric acid, iodic acid, sulphur trioxide or hydrogen peroxide to oxidize the iodine molecule to a better electrophile.[2-6] Aryl iodides may also be prepared by the Tronov-Novikov iodination method, i.e. with iodine in the presence of sulphuric acid or nitric acid in acetic acid.[7] However, all these reactions are with strong oxidizing reagents or under strongly acidic conditions. Clearly, for compounds sensitive to such conditions, a milder reagent is desirable.

In connection with the search for a more efficient nitration reagent for use in the synthesis of trimethoxyamphetamines,[8] we found nitryl iodide to be a mild and effective nitrating agent for substituted styrenes. Nitryl iodide is generated _in situ_ by reaction of silver nitrite with iodine.[9] Continuing our studies with this reagent, it has been found that the silver nitrite-iodine mixture is a mild iodinating reagent for alkylbenzenes (Scheme 1). A recent paper on the iodination of aromatic compounds, using lower nitrogen oxide species as catalysts, has prompted us to report our results.[10]



Scheme 1

The iodination of alkylbenzenes using silver nitrite and iodine was performed at room temperature in dichloromethane. Mono- and dialkylbenzenes gave monoiodo-compounds in good yield; even benzene itself could be iodinated, although requiring a longer reaction time. Monoiodoalkylbenzenes and diiodoalkylbenzenes, with traces of nitroalkylbenzenes and iodonitroalkylbenzenes, were obtained from tri- and tetra-alkylbenzenes under these conditions (Table 1).[11] Under similar conditions, methoxybenzenes gave a mixture of methoxynitrobenzenes and iodomethoxybenzenes (results in this series will be published separately in due course).

Results are summarized in Table 1.[12]

A representative experiment was performed as follows:

o-Xylene (212 mg, 2mM) was added to a mixture of I_2 (580 mg, 2 mM) and $AgNO_2$ (380 mg, 2mM) in CH_2Cl_2 (20ml) at room temperature. The mixture was stirred for 72h. After this time, the yellow precipitate was removed by filtration. The filtrate was washed with 10% aqueous $NaHSO_3$, saturated aqueous $NaHCO_3$ and water. After drying over anhydrous Na_2SO_4, the solvent was removed under reduced pressure to give a liquid (325 mg, 70%)

Acknowledgements: We wish to thank Messrs. H. Avdovich, H. Beckstead, R. Duhaime and J-C. Ethier of our laboratories for technical assistance.

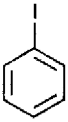
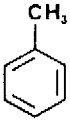
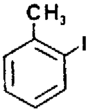
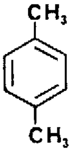
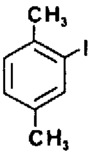
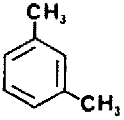
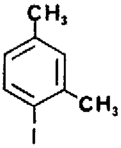
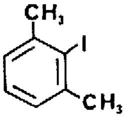
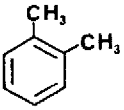
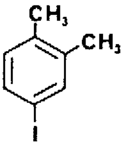
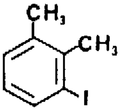
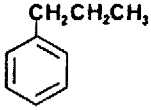
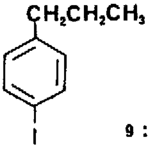
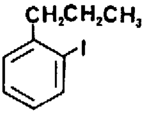
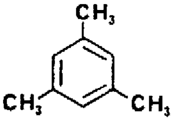
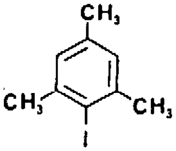
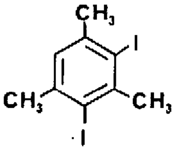
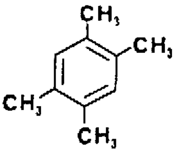
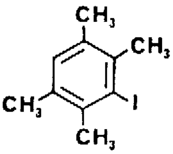
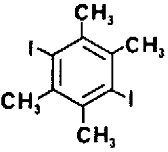
Entry	Starting material	Time	Yield	Products and ratio
1		72 h	13 %	
2		66 h	44 %	 5 : 2 
3		70 h	43 %	
4		22 h	69 %	  trace
5		72 h	70 %	 4 : 1 
6		72 h	77 %	 9 : 2 
7		24 h	90 %	 2 : 1 
8		24 h	95 %	 3 : 2 

Table 1. Iodination of alkylbenzenes with iodine and silver nitrite.

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  c. W.C. Baird and J.H. Surridge, **J. Org. Chem.**, 35, 3436 (1970)
  See also references 5, 6 and 7, and references cited therein.

12. All products were identified by GC/MS and ^{1}H NMR; product ratios were determined by GC or NMR.

^{1}H-NMR ($CDCl_3$):

Iodomesitylene: δ6.85 (s, 2H), 2.40 (s, 6H), 2.21 (s, 3H)
Diiodomesitylene: δ7.00 (s, 1H), 2.93 (s, 3H), 2.42 (s, 6H)
Iododurene: δ6.89 (s, 1H), 2.44 (s, 6H), 2.31 (s, 6H)
Diiododurene: δ2.63 (s)

GC conditions:

Column J&W Scientific 15DB-5, 0.25mm ID
Injector temperature 250°
Oven temperature 100° to 250° @ 15°/min.

(Received in USA 17 April 1989)