



2,4,6,8-Tetraiodoglycoluril in sulfuric acid as a new powerful reagent for iodination of deactivated arenes

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Abstract

Deactivated arenes are iodinated readily at 0°C by the action of 2,4,6,8-tetraiodoglycoluril in sulfuric acid to give the iodoarenes in generally good yields. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: arenes; halogenation; *N*-imides; sulfuric acid.

Iodoarenes are valuable, versatile synthetic intermediates and have found wide applications in medicine and biochemistry.¹ However, the electrophilic nature of iodine is weaker than bromine and chlorine. For this and other reasons, there are only a limited number of methods for direct iodination of deactivated aromatics. Some arenes with electron-withdrawing substituents can be iodinated by I₂/HNO₃/H₂SO₄/AcOH,² I₂/Ag₂SO₄/H₂SO₄,³ I₂/oleum,⁴ I₂/F₂,⁵ or I₂/CrO₃.⁶ Nowadays, the most potent iodination agents appear to be *N*-iodosuccinimide in CF₃SO₃H⁷ and the superelectrophilic reagent obtained recently from ICl and Ag₂SO₄ in sulfuric acid (reagent 'I⁺').^{8,9} Thus, the former reagent converts nitrobenzene **1a** to 3-iodonitrobenzene **2a** (86%) within 2 h at room temperature.⁷ However, this method is limited on a large preparative scale by the expense of CF₃SO₃H. On the other hand, while reagent 'I⁺' is capable of iodinating nitrobenzene **1a** within 15 min at 20°C or 1.5 h at 0°C very effectively, along with the iodination, a chlorination process takes place to a small extent.^{8,9}

As an extension of our search for more potent and practical, non-oxidizing iodination reagents, we have found that 2,4,6,8-tetraiodoglycoluril (2,4,6,8-tetraiodo-2,4,6,8-tetraazabicyclo[3.3.0]octane-3,7-dione) (TIG)¹⁰ in sulfuric acid has an extremely strong ability for iodination of various deactivated aromatic compounds at 0°C.

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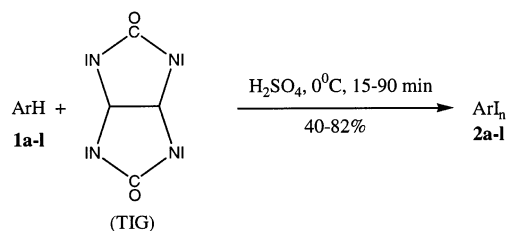


Table 1
Iodination of aromatics with 2,4,6,8-tetraiodoglycoluril (TIG) at 0°C

Substrate 1	Product 2	Time (min)	Yield ^a (%)	Mp (°C) (solvent)	Lit. mp (°C)
a	a	90	75	35–36 (EtOH)	36–37 ⁷
b	b	70	48	59–60 (EtOH)	60–61 ⁹
c	c	60	68	55–57 (EtOH)	58 ^{3a}
d	d	45	52	185–186 (50% <i>i</i> -PrOH)	185–187 ^{3b}
e	e	60	79	52–54 (EtOH)	54–55 ⁶
f	f	60	82	173–174 (<i>i</i> -PrOH)	174–176 ⁵
g	g	30	65	55–56 (EtOH)	57 ^{3a}
h	h	15	40	91–92 (EtOH)	92 ¹¹
i	i	15	45	128–129 (EtOH)	130–131 ¹²
j	j	90	58	249–250 (DMFA)	254 ¹³
k	k	60	60	205–206 (benzene)	205–206 ¹⁴
l	l	60	44	309–310 (toluene)	310 ¹⁵

^a Yields of pure, isolated products.

Deactivated arenes **1a–l** with electron-withdrawing substituents were shown to react readily with this reagent giving iodoarenes **2a–l** with generally good yields and with complete conversion of the starting materials (Table 1).

Products are obtained according to the rules for aromatic electrophilic substitution. Iodination of compounds **1b,h,i** resulted in addition to the iodarenes **2b,h,i**, alternative isomers in minor quantities. In Table 1 the yields of pure, isolated major products are shown.

For complete conversion of the substrates **1a–i** to the corresponding iodoarenes we use 0.5 equivalents of TIG (or double the amount of ‘active iodine’). In the case of the iodination of compounds **1j–l**, one equivalent of TIG per equivalent of the substrate was used.

A representative iodination procedure is as follows: 1.6 g (2.5 mmol) TIG was dissolved in 30 ml 90% concd sulfuric acid at room temperature with stirring. Substrates **1a–i** (5 mmol) or **1j–l** (2.5 mmol) were added in one portion to the well-stirred solution at 0°C. The mixture was then poured into ice-cold water. The products **2c,d,f,j–l** were removed by filtration and the products **2a,b,e,g–i** were extracted by CHCl₃. The solvent was removed in vacuo and the products were purified by recrystallization from a suitable solvent (Table 1) and identified by comparison of their melting points and spectroscopic data (IR, NMR) with authentic samples.

The yields, mild experimental conditions, and availability of the reagent are attractive features of this method. The reaction can be successfully applied to other arenes and heterocycles. Work is in progress to optimize results, to expand further the scope and applications of this iodination reagent.

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