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A NOVEL OXIDATIVE AZIDATION OF AROMATIC COMPOUNDS WITH HYPERVALENT IODINE REAGENT, PHENYLIODINE(III) BIS(TRIFLUOROACETATE) (PIFA) AND TRIMETHYLSILYL AZIDE

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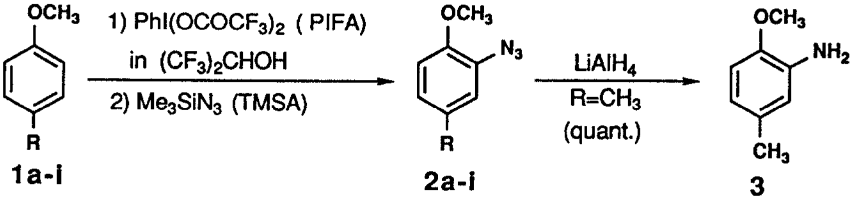
Summary: A novel and useful method for the azidation of aromatic compounds by the reaction of hypervalent iodine reagent, phenyliodine(III) bis(trifluoroacetate) (PIFA) in 1,1,1,3,3,3-hexafluoro-2-propanol followed by treatment of trimethylsilyl azide (TMSA) was developed. The possible mechanism is also discussed.

Combination of hypervalent iodine reagent and trimethylsilyl azide (TMSA) has been known to generate hypervalent azidoiodine(III) species[1,2] and used for the oxidative azidation of olefins into α-azidoketones[1] and vicinal diazides,[2,3] β-dicarbonyl compounds into α-azido-β-dicarbonyl compounds,[4] and 2-(trimethylsilyloxy)furan into 5-azido-2(5H)-furanone.[5] These hypervalent azidoiodine(III) species, however, may not be active enough for the oxidative azidation of aromatic carbons and there is no report on these types of reactions. As a part of our continuous studies on the hypervalent iodine chemistry,[6] we describe here a novel and useful oxidative azidation of aromatic compounds using hypervalent iodine reagent, phenyliodine(III) bis(trifluoroacetate) (PIFA) and TMSA.

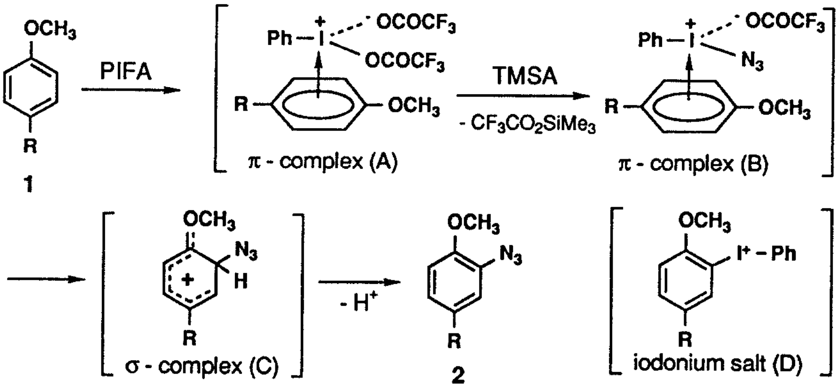
As expected, treatment of the aromatic compound (**1**) with the hypervalent azidoiodine(III) reagent generated from PIFA and TMSA in methylene chloride did not give any aromatic azido compound. On the other hand, reaction of **1** with PIFA at first and the subsequent treatment with TMSA gave the mono azido compound (**2**). A typical experimental procedure for the reaction of 1,4-dimethoxybenzene (**1a**) is as follows. To a solution of **1a** in anhydrous 1,1,1,3,3,3-hexafluoro-2-propanol [$(CF_3)_2CHOH$] was added 1.0 equiv of PIFA at room temperature under nitrogen. After a few minutes, 5.0 equiv of TMSA was added to the mixture. The mixture was stirred for 15 min under the same conditions to give 2-azido-1,4-dimethoxybenzene (**2a**) in 68% yield. Similarly, other aromatic compounds (**1b-i**) bearing high electron donating groups reacted smoothly with PIFA to give the corresponding mono azido compounds (**2b-i**) in considerable yields. However, aromatic hydrocarbons bearing an electron-deficient group such as an ester or a nitro group could not give the azido compounds under the same conditions. The *ortho*-orientation of the products was ascertained by the reduction of **2b** to *p*-cresidine (**3**) with lithium aluminum hydride (Scheme 1).

Oxidative azidation of **1** with PIFA and TMSA in other solvents such as 2,2,2-trifluoroethanol, acetonitrile, and methylene chloride gave the corresponding **2**, but in unsatisfactory yields. The present method is useful not only for the case of *p*-haloanisoles (**1d,e**), which are possible to bring about substitution on the *p*-position, but for that of the α-tetralone derivative (**1i**), which is possible to cause nucleophilic attack on the carbonyl carbon. Although typical aromatic compounds (**1j-l**) could not give the azido compounds under the conditions described above, activation of PIFA by the addition of 1eq of $BF_3 \cdot Et_2O$ in methylene chloride led to the corresponding azido compounds (**2j-l**). The reaction solvents, products and yields are listed in Table 1.



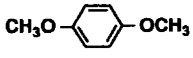
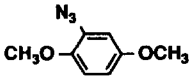
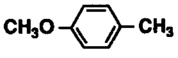
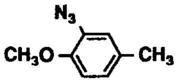
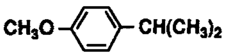
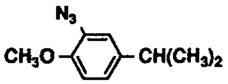
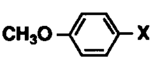
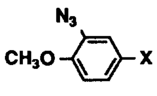
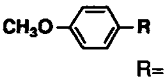
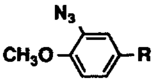
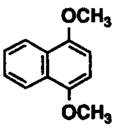
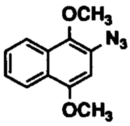
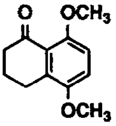
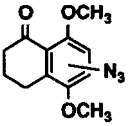
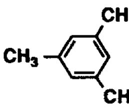
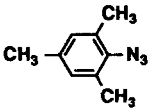
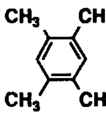
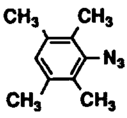
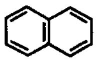
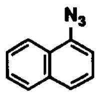
Scheme 1

The nucleophilic attack of the azido group to the electron-rich aromatic compounds (**1**) can be explained by assuming that π-complex of the hypervalent iodine reagent with **1** is formed at the first step as proposed in the reaction of **1** with the active hypervalent iodine reagent, perfluoroalkylated iodonium trifluoromethanesulfonate.[7] The initially formed π-complex (**A**) reacts with TMSA to yield another π-complex (**B**), which collapses to a σ–complex (Meisenheimer-type complex) (**C**) with the reductive elimination of iodobenzene. Aromatization occurs with the loss of proton to give a stable aromatic azido compound (**2**). Another possible route involving the phenyl-iodonium salt (**D**) is excluded because the more electron-deficient aromatic carbon of the iodonium salt is known to react with a nucleophile selectively[8] and this reaction should give azidobenzene instead of **2** (Scheme 2).



Scheme 2

Table 1. Oxidative Azidation of Aromatic Compounds (**1a - l**)

Runs	Aromatic Compounds **1**	Solvents	Azido Compounds **2**	Yields (%)
1	 **1a**	$(CF_3)_2CHOH$	 **2a**	68
2		CF_3CH_2OH		60
3		CH_3CN		27
4		CH_2Cl_2		5
5	 **1b**	$(CF_3)_2CHOH$	 **2b**	45
6		CF_3CH_2OH		28
7	 **1c**	$(CF_3)_2CHOH$	 **2c**	53
8		CF_3CH_2OH		17
9	 X=Cl **1d**	$(CF_3)_2CHOH$	 **2d**	43
10	X=Br **1e**	//	**2e**	58
11	 R=*t*-Bu **1f**	//	 **2f**	52
12	R=$CH_2CO_2CH_3$ **1g**	//	**2g**	50
13	 **1h**	//	 **2h**	85
14	 **1i**	//	 **2i** a)	70
15	 **1j**	CH_2Cl_2 b)	 **2j**	56
16	 **1k**	// b)	 **2k**	60
17	 **1l**	// b)	 **2l**	49

a) The position of the azido group has not been determined yet.

b) The reaction was carried out in the presence of 1.0 eq. $BF_3 \cdot Et_2O$.

The present azidation reaction of **1** is quite useful since the azido group is readily converted to a variety of other functional groups through the amino group and the diazonium salt. This may be considered as a novel type of nucleophilic substitution to electron-rich aromatic compounds without use of the metal-arene complexes[9] or metal-aryl salts[10].

References and Notes

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