Tetrahedron Letters, Vol.30, No.13, pp 1649-1650, 1989
Printed in Great Britain

0040-4039/89 $3.00 + .00
Pergamon Press plc

AROMATIC IODINATION BY POSITIVE IODINE ACTIVE SPECIES GENERATED BY ANODIC OXIDATION IN TRIMETHYL ORTHOFORMATE [1]

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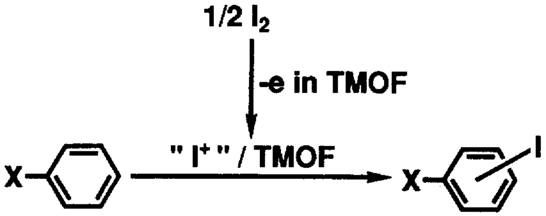
Summary: Anodic oxidation of iodine in trimethyl orthoformate afforded a solution of positive iodine active species which brought about more selective aromatic iodination than the hitherto known other methods.

Because of the importance of aromatic iodo compounds as drugs[2] and intermediates in organic synthesis,[3] simple and reliable methods of their preparation are worthwhile to be established. The anodic method is particularly interesting among the methods exploited so far[4] since it does not require any oxidizing agent to transform iodine to active species ("I^+"), though only following two types of anodic system have been investigated up to now.

Namely, (i) a solution of "I^+" prepared in acetonitrile ("I^+"/MeCN)[5] and (ii) a solution of "I^+" prepared in 1,2-dichloroethane containing 10% trifluoroacetic acid ("I^+"/TFA)[6] have been reported as the effective systems for aromatic iodination whereas their selectivity is not satisfactory as described below.

We report herein a new system of "I^+" which possesses remarkably higher selectivity than "I^+"/MeCN and "I^+"/TFA in the aromatic iodination.

A typical experimental procedure for this new system is as follows: A solution of trimethyl orthoformate (TMOF, 30 ml) containing iodine (I_2, 4 mmol) and hydrated lithium perchlorate ($LiClO_4 \cdot 3H_2O$, 2 g) was put into an anodic chamber of a divided electrolysis cell equipped with a ceramic diaphragm, two platinum electrodes (2 cm x 1 cm) and a magnetic bar, and a solution of $LiClO_4 \cdot 3H_2O$ (2 g) in TMOF (8 ml) was placed in a cathodic chamber. Anodic oxidation was carried out under the conditions of constant current (0.1 A/cm^2) at room temperature. After 3 F/mol of electricity was passed, the addition of anolyte solution (4 ml; equiv. to 0.53 mmol of I_2) into a solution of aromatic compound 1 (1 mmol) in TMOF (1 ml) gave iodinated product 2 (eq. 1). The yields of 2 are summarized in table 1.



(1)

1 2 TMOF ; $CH(OMe)_3$

Since the treatment of 1 with I_2 in TMOF has never resulted in the aromatic iodination,[7] the facts shown in the table 1 clearly indicate that a positive iodine active species was certainly generated in the anolyte solution.[8,9] One of the most important characters of "I$^+$"/TMOF is its high selectivity in comparison with "I$^+$"/MeCN and "I$^+$"/TFA. Namely, "I$^+$"/TMOF is able to iodinate selectively the aromatic compounds having an electron-donating substituent such as H, alkyl, or OMe, whereas "I$^+$"/MeCN or "I$^+$"/TFA iodinates aromatic compounds regardless the electronic nature of the substituents. These substituent effects are clearly shown in table 2. Furthermore, "I$^+$"/TMOF shows remarkably high para-selectivity in the aromatic iodination (table 1). These selectivities seem to be especially useful for the synthesis of speciality chemicals.

Table 1. Aromatic Iodination by "I$^+$"/TMOF

Aromatic Compound	Yield	Distribution (%)					
1	of 2[a]	by "I$^+$"/TMOF[b]			by "I$^+$"/MeCN[c]		
X	%	ortho	meta	para	ortho	meta	para
Cl	0	-	-	-	20	$\sim$0	80
H	60	-	-	-	-	-	-
Me	85	30	$\sim$0	70	47	$\sim$0	48
t-Bu	97	$\sim$0	$\sim$0	$\sim$100	25	$\sim$0	74
MeO	69	13	$\sim$0	87	33	10	57

[a] A solution of "I$^+$"/TMOF (equiv. to 0.53 mmol of I$_2$) was added to 1 mmol of 1.
[b] A solution of "I$^+$"/TMOF (equiv. to 0.13 mmol of I$_2$) was added to 2.7 mmol of 1.
[c] The reported data (see reference 5).

Table 2. Competitive Aromatic Iodination

	Relative Yield of Products[a,b]	
Substrates	"I$^+$"/TMOF System[c]	"I$^+$"/MeCN System[d]
benzene/chlorobenzene	∞	15.72 $\sim$ 24.8 / 1
toluene/benzene	600 / 1	7.33 $\sim$ 21.1 / 1
t-butylbenzene/benzene	73 / 1	7.07/ 1

[a] A mixture of regioisomers. [b] GLC analysis. [c] A solution of "I$^+$"/TMOF (equiv. to 0.13 mmol of I$_2$) was added to a mixture of equimolar amounts of substrates (total;5.0 mmol).
[d] The reported data (see reference 5).

References and Notes

1. Electroorganic Chemistry 117.
2. For example, T.Shono, Y.Ohmizu, T.Toda, N.Oshino, Drug Metab.Dispos., 10, 555 (1982).
3. For example, R.F.Heck, Org.React., 27, 345 (1982).
4. F.Radner, J.Org.Chem., 53, 3548 (1988), and references cited therein.
5. L.L.Miller, B.F.Watkins, J.Am.Chem.Soc., 98, 1515 (1976), and references cited therein.
6. R.Lines, V.D.Parker, Acta Chem.Scand., B34, 47 (1980).
7. Aromatic iodination also did not occur under conditions of I$_2$/H$_2$SO$_4$/TMOF.
8. An anodic solution was gradually faded from dark brown to clear yellow when 16 F/mol of electricity was passed through a solution of I$_2$ in TMOF.
9. "I$^+$" possibly existing in the anodic solution has not been identified by cyclic volutammetry because of the complicated waves.

(Received in Japan 11 January 1989)