3194 J. Org. Chem. 1993, 58, 3194-3195

Iodination of Deactivated Aromatics with *N*-Iodosuccinimide in Trifluoromethanesulfonic Acid (NIS–CF_3SO_3H) via in Situ Generated Superelectrophilic Iodine(I) Trifluoromethanesulfonate[1]

George A. Olah,* Qi Wang, Graham Sandford, and
G. K. Surya Prakash

*Donald P. and Katherine B. Loker Hydrocarbon Research
Institute and Department of Chemistry, University of
Southern California, Los Angeles, California 90081-1661*

Received January 5, 1993

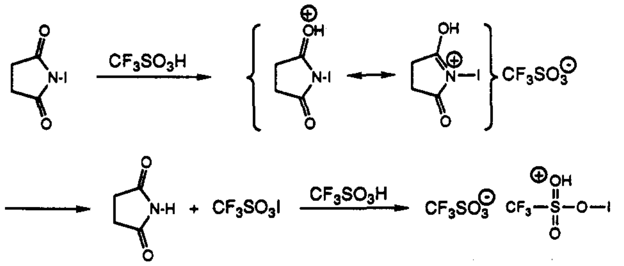
Iodoarenes are valuable, versatile synthetic intermediates and have found wide applications in medicine and biochemistry.[2,3] Although significant development has been achieved in the synthesis of iodoarenes, their preparation via direct iodination is generally limited to electron-rich aromatics.[2,4] Recent reports on the oxidative iodination of moderately deactivated arenes by using either electrochemical methods or elemental fluorine represents new progress in the field.[5] Special equipment required for these procedures, however, may restrict their general use.

Although *N*-iodosuccinimide (NIS) has been widely used for the iodination of ketones, aldehydes, and alkenes,[6] it has rarely been applied to the electrophilic iodination of aromatic compounds. Radhakrishnamurti and co-workers reported mechanistic studies of the iodination of aromatics such as phenols with NIS, but little information was given in their papers concerning the yields of the reactions.[7]

In recent years, we have been interested in exploring the effect of protic (electrophilic) solvation on the activation of electrophiles.[8] Under these conditions, the electrophilicity of an electrophile can be dramatically enhanced for reaction with weakly nucleophilic substrates. We considered that NIS could be activated in a similar fashion to allow iodination of deactivated arenes. Herein, we report our results.

Deactivated aromatics were found to react readily with *N*-iodosuccinimide in the presence of trifluoromethanesulfonic acid (triflic acid) to give iodoarenes in good yields (see Table I). Two molar equiv of triflic acid was used to achieve nearly quantitative iodination of moderately deactivated arenes, such as nitrobenzene or α,α,α-trifluorotoluene. A 5-fold excess of triflic acid was generally necessary to achieve satisfactory iodination of more severely deactivated arenes such as halo- or polyhalonitrobenzenes. In aprotic solvents such as dichloromethane the yields are either very low or no iodination takes place.

Scheme I



In the case of acetophenone phenacyl iodide was obtained instead of the ring substitution product. The formation of the α-iodo ketone can be explained by the enolization of acetophenone under strong acid conditions and then subsequent iodination of the intermediate enol by NIS. This second step is well documented in the literature.[6]

The electrophilic nature of the iodination is demonstrated by the nearly exclusive formation of the corresponding meta isomers in the iodination of nitrobenzene and α,α,α-trifluorotoluene. It is further supported by the iodination of toluene where only 53% *o*- and 47% *p*-iodotoluene were obtained.

Since no iodination of the studied deactivated aromatics occurs in the absence of triflic acid, the active species for the iodination is suggested to be either protonated NIS or more probably in situ formed iodine(I) trifluoromethanesulfonate in its protosolvated activated form (see Scheme I). The ^{13}C NMR spectrum of NIS in trifluoromethanesulfonic acid at -20 °C showed two carbonyl peaks at 189 and 192 ppm, deshielded by 11 ppm from the corresponding peak in NIS indicating the presence of both protonated NIS and protonated succinimide in accordance with Scheme I. The de facto iodinating species, i.e., in situ formed iodine(I) trifluoromethanesulfonate, in its monoprotonated form can act as a very reactive superelectrophile allowing iodination of severely deactivated aromatics. The formation and existence of iodine(I) trifluoromethanesulfonate was reported previously by Aubke.[9]

Iodine(I) trifluoromethanesulfonate, prepared in situ from iodine and silver trifluoromethanesulfonate, was reported previously to iodinate aromatics.[10] This reaction involving acid-free conditions, however, is only moderately efficient for electron-deficient arenes. For example, iodonitrobenzene was obtained in only 45% yield at 150 °C. The high yields of our procedure under mild conditions are in accord with the in situ formation of a superelectrophilic, protosolvated iodinating species.

In conclusion, we report an efficient new method for the electrophilic iodination of deactivated aromatic compounds using *N*-iodosuccinimide–trifluoromethanesulfonic acid. Protonated iodine(I) trifluoromethanesulfonate is considered to be the likely de facto iodinating species since up to 5-fold excess triflic acid is required for the reactions.

---

[1] Synthetic Methods and Reactions. 181. For Part 180, see: Olah, G. A.; Wang, Q.; Li, X. Y.; Prakash, G. K. S. *Synthesis* 1993, 32.

[2] Merkushev, E. B. *Synthesis* 1988, 923.

[3] Seevers, R. H.; Counsell, R. E. *Chem. Rev.* 1982, 82, 575.

[4] Galli, C. *J. Org. Chem.* 1991, 56, 3238.

[5] (a) Lines, R.; Parkev, V. D. *Acta Chem. Scand. Ser. B* 1980, 34, 47. (b) Rozen, S.; Zamir, D. *J. Org. Chem.* 1990, 55, 3552.

[6] (a) March, J. *Advanced Organic Chemistry*; John Wiley & Sons: New York, 1985; p 529. (b) Adionlfi, M.; Parrilli, M.; Barone, G.; Laonigro, G.; Mangoni, L. *Tetrahedron Lett.* 1976, 40, 3661.

[7] (a) Radhakrishnamurti, P. S.; Panda, B. K. *Ind. J. Chem.* 1983, *22A*, 770. (b) Radhakrishnamurti, P. S.; Janardhana, C. *Ind. J. Chem.* 1978, *16A*, 142.

[8] (a) Olah, G. A. *Angew. Chem.*, in press. (b) Olah, G. A.; Prakash, G. K. S.; Lammertsma, K. *Res. Chem. Intermed.* 1989, 12, 141.

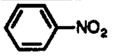
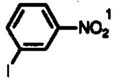
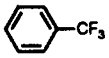
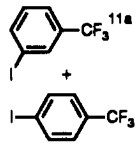
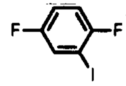
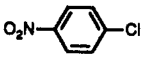
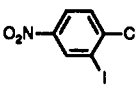
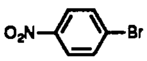
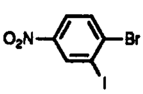
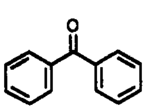
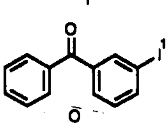
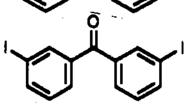
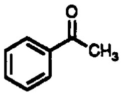
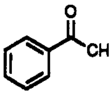
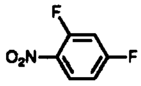
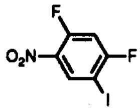
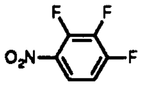
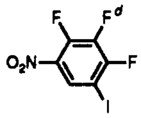
[9] Dalziel, J. R.; Aubke, F. *Inorg. Chem.* 1973, 12, 2707.

[10] Kobayashi, Y.; Kumadaki, I.; Yoshida, T. *J. Chem. Res., Synop.* 1977, 215.

[11] (a) *Aldrich Handbook of Fine Chemicals*; Aldrich Chemical Co. (b) Namkung, M. J.; Fletcher, T. L. *Can. J. Chem.*, 1967, 45, 2569. (c) Sugiura, M.; Hirano, K. *Biochem. Med.* 1977, 17, 222. (d) Moriconi, E. J.; O'Connor, W. F.; Forbes, W. F. *J. Am. Chem. Soc.* 1962, 84, 3928. (e) Rubottom, G. M.; Mott, R. C. *J. Org. Chem.* 1979, 44, 1731.

0022-3263/93/1958-3194$04.00/0

Table I. Iodination of Aromatics

substrate	arene:NIS:acid ratio	product[ref]	yield[a]/%	bp/mmHg (mp, °C)	^{13}C NMR (ppm)	MS (70 eV), *m/e*
	1.05:1:2	 [11a]	86	(36–37)	93.4, 130.6, 132.3, 143.4, 148.4	249 (M^+, 100), 203 (70), 127 (15), 76 (71)
	2:1:2	 [11a] 94:6	91	82/25	93.8, 122.9 ($^{1}J_{C-F}$ = 272.3 Hz), 124.5 ($^{3}J_{C-F}$ = 3.7 Hz), 130.4, 132.4 ($^{2}J_{C-F}$ = 32.4 Hz), 134.2 ($^{3}J_{C-F}$ = 3.8 Hz), 140.9	272 (M^+, 100), 253 (10), 145 (84)
	1:1:5	 [11b]	79	81/16	80.7 ($^{2}J_{C-F}$ = 28.8 Hz, $^{3}J_{C-F}$ = 8.9 Hz), 115.9 ($^{2}J_{C-F}$ = 26.8 Hz, $^{3}J_{C-F}$ = 8.6 Hz), 116.5 ($^{2}J_{C-F}$ = 23.7 Hz, $^{3}J_{C-F}$ = 7.6 Hz), 125.8 ($^{2}J_{C-F}$ = 26.7 Hz, $^{3}J_{C-F}$ = 2.4 Hz), 158.3 ($^{1}J_{C-F}$ = 241.9 Hz, $^{4}J_{C-F}$ = 4.7 Hz), 158.4 ($^{1}J_{C-F}$ = 246.4 Hz, $^{4}J_{C-F}$ = 2.4 Hz)	240 (M^+, 100), 127 (19), 113 (33), 63 (21)
	1:1:5	 [5a]	79	(74–75)	97.9, 124.1, 129.5, 135.0, 145.8, 146.1	285 (M^+, 29), 283 (M^+, 100), 253 (9), 239 (11), 237 (36), 225 (19), 127 (10), 110 (36)
	1:1:5	 [11c]	74	(98–99)	101.2, 123.9, 133.0, 134.9, 137.6, 146.6	329 (M^+, 29), 327 (M^+, 100), 299 (10), 97 (10), 271 (21), 269 (21), 156 (32), 154 (33), 127 (15), 75 (42)
	1:1:5	 [11d]	53[b]	(41–42)	94.1, 128.5, 129.1, 129.9, 130.0, 132.9, 138.5, 138.6, 141.2, 141.6, 195.1	308 (M^+, 100), 231 (29), 203 (12), 105 (95), 77 (44), 76 (27)
			17	(148–150)	94.3, 129.1, 130.1, 138.6, 138.8, 141.6, 193.5	434 (M^+, 100), 231 (69), 203 (27), 76 (22)
	1:1:1	 [11e]	72	(35–36)	1.8, 128.8, 129.0, 133.8, 192.8	246 (M^+, 27), 105 (100), 91 (26), 77 (36), 51 (24)
	1:1:5	 [c]	66	65–67/0.1	74.7, 106.4 ($^{2}J_{C-F}$ = 29.2 and 25.4 Hz), 134.3, 136.6 ($^{3}J_{C-F}$ = 4.9 and 2.5 Hz), 156.4 ($^{1}J_{C-F}$ = 269.6 Hz, $^{3}J_{C-F}$ = 12.2 Hz), 164.7 ($^{1}J_{C-F}$= 257.7 Hz, $^{3}J_{C-F}$ = 11.0 Hz)	285 (M^+, 100), 239 (26), 227 (19), 112 (52)
	1:1:5	 [d]	64	55–57/0.1	74.6 (dd, $^{2}J_{C-F}$ = 24.4 Hz, $^{3}J_{C-F}$ = 4.8 Hz), 129.2 (m, $^{3}J_{C-F}$ = 3.4 Hz), 134.8 (m), 140.0 (ddd, $^{1}J_{C-F}$ = 260.1 Hz, $^{2}J_{C-F}$ = 18.0 and 14.8 Hz), 146.4 (ddd, $^{1}J_{C-F}$ = 270.2 Hz, $^{2}J_{C-F}$ = 13.1 Hz, $^{3}J_{C-F}$ = 3.5 Hz), 154.7 (ddd, $^{1}J_{C-F}$ = 257.8 Hz, $^{2}J_{C-F}$ = 11.0 Hz, $^{3}J_{C-F}$ = 3.1 Hz)	303 (M^+, 100), 273 (12), 257 (24), 130 (76)

[a] Isolated yield. [b] Separated by column chromatography on silica gel with hexane/dichloromethane as eluant (4:1). [c] $C_6H_2NO_2F_2I$ requires 284.9098. Found: 284.9102 amu. [d] $C_6HNO_2F_3I$ requires 302.9004. Found: 302.9006 amu.

Further work regarding the use of *N*-chloro- and *N*-bromosuccinimide in similar chemistry will be subsequently reported.

Experimental Section

NMR spectra were recorded in $CDCl_3$ solution on a Varian VXR-200 spectrometer with TMS as internal standard. Mass spectra were recorded on a Hewlett-Packard 5971 mass spectrometer. High-resolution mass spectra were determined by the mass spectroscopy service at U.C. Riverside, Los Angeles, CA.

Typical Procedure for the Iodination of Aromatics. NIS (10 mmol) was added in small portions to a well-stirred solution of the desired arene (excess) in CF_3SO_3H which was cooled by an ice bath. The reaction mixture was then stirred for 2 h at room temperature. The reaction mixture was quenched with ice–water and extracted with CH_2Cl_2 (3 × 25 mL). The combined organic extracts were washed with aqueous 10% sodium bisulfite solution and water, dried over $CaCl_2$, and evaporated under reduced pressure. The product was further purified either by distillation, recrystallization, or column chromatography. Experimental details and data are collated in Table I.

Acknowledgment. Support of our work by the National Science Foundation is gratefully acknowledged.