Progressive Direct Iodination of Sterically Hindered Alkyl Substituted Benzenes

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Abstract: Benzene derivatives bearing at least one bulky alkyl group (*i*-Pr or *t*-Bu) were selectively and effectively iodinated using elemental iodine activated by 1-(chloromethyl)-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (Selectfluor™, F-TEDA-BF_4). Iodine atoms were progressively introduced at the most electron-rich and sterically less hindered position on the benzene ring. Not more than three iodine atoms could be progressively bonded to a target molecule bearing a *i*-Pr or *t*-Bu group.

Key words: iodination, sterically hindered benzenes, Selectfluor™ (F-TEDA-BF_4)

Aromatic iodides have for a long time been recognised as valuable synthetic tools of routine use, above all in carbon–carbon bond formation.[1] In addition, many iodoarenes are biologically active molecules used as drugs or diagnostic aids, as contractors and radioactive labelled markers in radioimmunoassay studies and in nuclear magnetic imaging.[2] Selective introduction of an iodine atom into organic molecules has thus attracted broad interest in the wider scientific community and the related chemistry has been reviewed.[3]

The direct iodination of aromatic molecules under mild reaction conditions needs an additive in order to increase the low reactivity of iodine. In the last decade intensive investigations in the field of iodoorganic chemistry revealed many new synthetic methods for the iodination of aromatics by using different iodonium donating systems, such as bis(pyridinium)iodonium(I) tetrafluoroborate (IPy_2BF_4),[3d] *N*-iodosaccharin,[4] iodine/mercury(II) salts[5] or iodine/mercury(II) oxide,[6] iodine/nitrogen dioxide,[7] iodine/chromium(VI) oxide,[8] iodine/tetrabutylamonium peroxydisulphate,[9] and potassium dichloroiodate.[10] Recently we introduced 1-(chloromethyl)-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (**1**), known under the commercial name of Selectfluor™ (F-TEDA-BF_4), as a mediator of selective direct iodination of aromatic ethers,[11] aryl alkyl ketones,[12] and alkyl substituted aromatics,[13] and recognised that F-TEDA-BF_4 is not only one of the most popular modern electrophilic fluorinating reagent,[14] but also a useful reagent for a variety of 'fluorine-free' functionalisations of organic compounds.[15] We now report further investigations of F-TEDA-BF_4 mediated direct iodination of benzene derivatives bearing bulky alkyl groups.

In a typical experiment, a mixture of *tert*-butylbenzene (**2**, 1 equiv), elemental iodine (0.6 equiv) and F-TEDA-BF_4 (0.6 equiv) in acetonitrile solution was stirred at 50 °C until the starting material was consumed, and after a workup procedure 1-(*tert*-butyl)-4-iodobenzene (**2a**) was isolated as the only product in almost quantitative yield. The *ortho* position in the target molecule **2** seemed sterically too restrained to be competitively iodinated, and this barrier was not overcome even by using an excess of the iodinating system (**2**/I_2/F-TEDA-BF_4 = 1:1.5:1.5). Only 4-(*tert*-butyl)-1,2-diiodobenzene (**2b**) was readily obtained in high yield whereas some traces of its 1,3-diiodo isomer was detected in the crude reaction mixture. Further iodination of the crude product **2b** resulted in a final product assigned as 5-(*tert*-butyl)-1,2,3-triiodobenzene (**2c**).

We started our investigation of the iodination of the dibulky-alkyl substituted benzene series with 4-methylethylbenzene (**3**) and we established that 3-iodo substituted derivative (**3a**) was primarily formed. With an excess of the reagent 2,5-diiodo-4-methylethylbenzene (**3b**) was found to be the sole product, while a mixture of both triiodo isomers, i.e. 2,3,5-triiodo-4-methylethylbenzene and 2,3,6-triiodo-4-methylethylbenzene was the final product of the iodination process. Similar results were obtained when 4-methyl-isopropylbenzene (**4**) was treated with different molar amounts of I_2/F-TEDA-BF_4 mixture. Thus 3-iodo- (**4a**), 2,5-diiodo- (**4b**), and 2,3,5-triiodo-4-methylisopropylbenzene (**4c**) could be selectively obtained as the result of this progressive iodination. In the case of 4-(*tert*-butyl)methylbenzene (**5**), 4-(*tert*-butyl)-2-iodomethylbenzene (**5a**) was primarily formed, treatment with a moderate excess of the reagent yielded selectively 5-(*tert*-butyl)-1,3-diiodo-2-methylbenzene (**5b**), while at this point the iodination process stopped and only traces of a derivative bearing three iodine atoms could be detected even after reaction with a ten fold excess of the reagent. Two isopropyl groups on the benzene ring did not prevent iodination and the expected aryl iodides **6a** or **7a** were readily obtained from 1,4-diisopropylbenzene (**6**) or 1,3-diisopropylbenzene (**7**), respectively, while further iodination resulted in 1,4-diiodo-2,5-diisopropylbenzene (**6b**) from **6** and 1,5-diiodo-2,4-diisopropylbenzene (**7b**) from **7**. Two *tert*-butyl groups bonded to the benzene nucleus caused some difficulties. Only a moderate yield of 1,4-di(*tert*-butyl)-2-iodobenzene could be obtained from the

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reaction of 1,4-di(*tert*-butyl)benzene with lower amounts of the reagent, while the attempt to obtain a selectively diiodo substituted product failed and a mixture of monoiodo derivatives and **2b**, as a result of the iodo-dealkylation process, was isolated after the corresponding reaction. It is obvious that in this case in order to decrease steric tensions in the molecule, a *tert*-butyl group, rather than a proton, left the benzene ring. Two *tert*-butyl groups bonded at the *meta* position, on the other hand, did not prevent the effective introduction of an iodine atom into the target molecule, and 1,3-di(*tert*-butyl)benzene (**8**) was readily converted to the 5-iodo substituted product **8a** in almost quantitative yield. In this case, the regioselectivity of the iodine introduction was exclusively regulated by steric factors, since the iodine atom was bonded to the electronically less favoured, but the sterically least hindered position 5 of the target molecule **8**.

In our preliminary publication[13] we showed that in the group of trimethylbenzenes monoiodo, diiodo and triiodo derivatives could be selectively obtained using the I_2/F-TEDA-BF_4 iodinating system, but as shown in the Table, on replacement of one methyl group by *tert*-butyl only one iodine atom could be introduced into the target molecule. 5-(*tert*-Butyl)-1,3-dimethylbenzene (**9**) was thus converted to 5-(*tert*-butyl)-2-iodo-1,3-dimethylbenzene (**9a**), while further iodination failed, and 1,3-di(*tert*-butyl)-5-methylbenzene (**10**) was in the first step iodinated to 1,5-di(*tert*-butyl)-2-iodo-3-methylbenzene (**10a**), while after further iodination iodo-dealkylation took place again and 5-(*tert*-butyl)-1,2-diiodo-3-methylbenzene (**10b**) was formed. Finally, 1,3,5-triisopropylbenzene (**11**) was readily iodinated to 2-iodo substituted derivative **11a** and use of an excess of the reagent did not result in further iodination of the molecule, nor could we iodinate 1,2,4,5-tetraisopropylbenzene under the mentioned reaction conditions.

Iodofunctionalisation of alkylbenzenes bearing bulky alkyl substituents seemed to be a difficult problem. According to our knowledge, until now few attemps to accomplish this task have been made.[16] According to the results collected in the Table we can conclude that an I_2/F-TEDA-BF_4 mixture is a useful iodinating system for the direct and selective iodofunctionalisation of sterically hindered alkyl benzenes, and that the method is also convenient for the progressive introduction of more than one iodine atom into target molecules. The method has many advantages, but when dealing with sterically very strained molecules, also has its limitations. The main advantage is that by following this method regioselective iodofunctionalisation of very high efficiency could be achieved under mild reaction conditions, using relatively low price chemicals. The iodination reaction has the characteristics of an electrophilic process since, as we already observed,[10–12] iodine was regiospecifically introduced at the most electron-rich position on the benzene ring. Both iodine atoms from elemental iodine were consumed in this iodofunctionalisation process, representing a considerable advantage in comparison to many other methods.[3d,5,6,10] The main disadvantage of the method is the fact that for the introduction of more than one iodine atom into the molecule an excess of the reagent is necessary and the degree of the excess increases considerably with the number of iodine atom introduced, but in this respect the I_2/F-TEDA-BF_4 iodinating sistem is not very different from other related reagents.[6,17]

Selectfluor™ (F-TEDA-BF_4) was purchased from Apollo and used as received. Alkyl substituted benzenes, I_2 (99.8%, ACS grade) and MeCN (ACS grade) were obtained from Sigma-Aldrich and used as received. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DPX 300 spectrometer at 300 MHz for ^{1}H and 75.5 MHz for ^{13}C resonance using TMS as internal standard. IR spectra were recorded on a Perkin-Elmer 1310 spectrometer using KBr as supporting material. Mass spectral measurements were carried out on an Autospec Q instrument using electron ionisation (EI) at 70 eV. Melting points were determined on a Büchi 535 apparatus and are uncorrected. Elemental analyses were carried out on a Perkin-Elmer 2400 CHN analyser.

Iodination of Bulky-Alkyl Substituted Benzene Derivatives with an I_2/F-TEDA-BF_4 Mixture; General Procedure

To a solution of alkyl substituted benzene derivative **2**–**11** (5 mmol) in MeCN (50 mL) were added the corresponding molar amounts (see Table) of I_2 and F-TEDA-BF_4 (**1**) and the reaction mixture was stirred at 55–65 °C for 1–24 h (see Table). The solvent was removed under reduced pressure and the crude mixture was dissolved in CH_2Cl_2 (100 mL). Insoluble material was filtered off, the solution was washed with aq 10 % $Na_2S_2O_3 \cdot 5H_2O$ (50 mL) and H_2O (50 mL), and dried (Na_2SO_4). The solvent was evaporated, and the crude mixtures were analysed by ^{1}H NMR, MS and TLC. The crude products were purified by flash chromatography over silica gel (elution by CH_2Cl_2), followed by crystallisation from MeOH in the case of solid products or distillation under reduced pressure in the case of liquid compounds. The physicochemical and spectroscopic characteristics of already known aryl iodides **2a**,[18] **5a**,[19] **6a**,[16a] **9a**[16b] and **11a**[20] were compared with the published data, while new compounds were validated as stated below.

4-(*tert*-Butyl)-1,2-diiodobenzene (2b)

Colourless oil; yield: 87%.

IR (neat): 2962, 1430, 1359, 1250, 1103, 983, 805 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.27 [s, 9 H, *t*-C_4H_9), 7.05 (dd, *J* = 8.3, 2.3 Hz, 1 H, H-Ar), 7.75 (d, *J* = 8.3 Hz, 1 H, H-Ar), 7.86 (d, *J* = 2.3 Hz, 1 H, H-Ar).

^{13}C NMR ($CDCl_3$): δ = 153.00 (ArC), 138.89 (ArC), 136.78 (ArC), 126.80 (ArC), 107.92 (C-I), 103.85 (C-I), 34.50 [*C*(CH_3)$_3$], 30.99 [C(*C*H_3)$_3$].

MS: *m*/*z* (%) = 386 ([M]$^+$, 60), 371 (100), 343 (18), 244 (20).

HRMS: *m*/*z* Calcd for $C_{10}H_{12}I_2$: 385.9029. Found: 385.9040.

Anal. Calcd for $C_{10}H_{12}I_2$: C, 31.12; H, 3.13. Found: C, 31.06; H 3.11.

4-Ethyl-2-iodo-1-methylbenzene (3a)

Colourless oil; yield: 84%.

IR (neat): 2950, 1480, 1430, 1370, 1320, 1270, 1020, 870, 810 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.20 (t, *J* = 7.5 Hz, 3 H, CH_3), 2.38 (s, 3 H, CH_3), 2.56 (q, *J* = 7.5 Hz, 2 H, CH_2), 7.05 (dd, *J* = 1.6, 7.5 Hz, 1 H, H-Ar), 7.13 (d, *J* = 7.5 Hz, 1 H, H-Ar), 7.65 (d, *J* = 1.6 Hz, 1 H, H-Ar).

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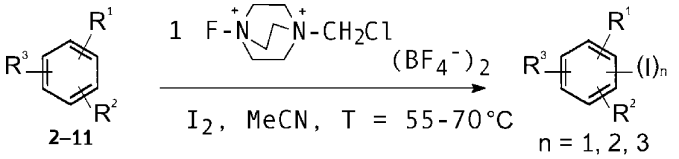
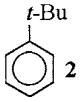
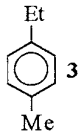
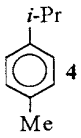
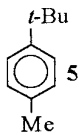
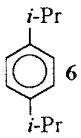
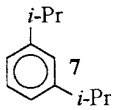
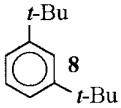
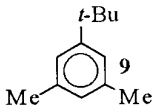
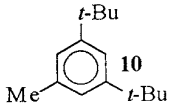
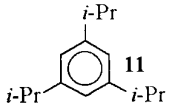
Table Direct Iodination of Alkyl Substituted Benzenes **2–11** Mediated by F-TEDA–BF_4 (**1**)



Entry	Alkylbenzene **2–11**	Reaction Conditions Alkylbenzene:I_2:**1**	Time (h)	Alkyliodobenzene	Yield (%)
1	 **2**	1:0.75:0.75	3	1-(*tert*-butyl)-4-iodobenzene (**2a**)[18]	90
2		1:1.5:1.5	6.5	4-(*tert*-butyl)-4-iodobenzene (**2b**)	87
3		1:4:4	24	5-(*tert*-butyl)-1,2,3-triiodobenzene (**2c**)	73
4	 **3**	1:0.6:0.6	3	4-ethyl-2-iodo-1-methylbenzene (**3a**)	84
5		1:1.5:1.5	5	1-ethyl-2,5-diiodo-4-methylbenzene (**3b**)	73
6	 **4**	1:0.6:0.6	3	2-iodo-4-isopropyl-1-methylbenzene (**4a**)	72
7		1:1.5:1.5	5	1,4-diiodo-2-isopropyl-5-methylbenzene (**4b**)	77
8		1:5:5	24	1,3,4-triiodo-5-isopropyl-2-methylbenzene (**4c**)	70
9	 **5**	1:0.6:0.6	3	4-(*tert*-butyl)-2-iodo-1-methylbenzene (**5a**)[19]	88
10		1:2.5:2.5	5	5-(*tert*-butyl)-1,3-diiodo-2-methylbenzene (**5b**)	80
11	 **6**	1:0.75:0.75	4	2-iodo-1,4-diisopropylbenzene (**6a**)[16a]	77
12		1:2.5:2.5	6	1,4-diiodo-2,5-diisopropylbenzene (**6b**)	81
13	 **7**	1.0.6:0.6	3	1-iodo-2,4-diisopropylbenzene (**7a**)	89
14		1:2.2:2.2	6	1,5-diiodo-2,4-diisopropylbenzene (**7b**)	71
15	 **8**	1:0.6:0.6	4.5	1,3-di(*tert*-butyl)-5-iodobenzene (**8a**)	83
16	 **9**	1:0.6:0.6	1.5	5-(*tert*-butyl)-2-iodo-1,3-dimethylbenzene (**9a**)[16b]	88
17	 **10**	1:0.75:0.75	5	1,5-di(*tert*-butyl)-2-iodo-3-methylbenzene (**10a**)	58
18		1:5:5	24	5-(*tert*-butyl)-1,2-diiodo-3-methylbenzene (**10b**)	77
19	 **11**	1.0.75:075	2	2-iodo-1,3,5-triisopropylbenzene (**11a**)[20]	90

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^{13}C NMR ($CDCl_3$): δ = 143.65 (ArC), 139.75 (ArC), 138.25 (ArC), 129.49 (ArC), 127.78 (ArC), 101.16 (C-I), 27.79 (CH_2), 20.25 (CH_3), 15.49 (CH_3).

MS: *m*/*z* (%) = 246 ([M]$^+$, 100), 231 (76), 119 (35), 104 (26), 91 (23), 77 (12).

HRMS: *m*/*z* Calcd for $C_9H_{11}I$: 245.9906. Found: 245.9911.

Anal. Calcd for $C_9H_{11}I$: C, 43.92; H, 4.51. Found: C, 43.36; H 4.65.

1-Ethyl-2,5-diiodo-4-methylbenzene (3b)
White crystals; mp 36.5–38 °C; yield: 73%.

IR (KBr): 2940, 1450, 1430, 1030, 875 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.16 (t, *J* = 7.5 Hz, 3 H, CH_3), 2.33 (s, 3 H, CH_3), 2.63 (q, *J* = 7.5 Hz, 2 H, CH_2), 7.61 (s, 1 H, H-Ar), 7.65 (s, 1 H, H-Ar).

^{13}C NMR ($CDCl_3$): δ = 145.81 (ArC), 140.75 (ArC), 139.69 (ArC), 138.21 (ArC), 101.02 (C-I), 99.87 (C-I), 33.11 (CH_2), 26.87 (CH_3), 14.47 (CH_3).

MS: *m*/*z* (%) = 372 ([M]$^+$, 90), 357 (52), 245 (44), 230 (30), 118 (85), 117 (100), 103 (37), 91 (56), 77 (43).

HRMS: *m*/*z* Calcd for $C_9H_{10}I_2$: 371.8872. Found: 371.8887.

Anal. Calcd for $C_9H_{10}I_2$: C, 29.06; H, 2.71. Found: C, 28.75; H, 2.50.

2-Iodo-4-isopropyl-1-methylbenzene (4a)
Colourless oil; yield: 72%.

IR (Neat): 2961, 1487, 1455, 1395, 1029, 819 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.19 (s, 3 H, CH_3), 1.21 (s, 3 H, CH_3), 2.38 (s, 3 H, CH_3), 2.79 (hept, *J* = 6.8 Hz, 1 H, CH), 7.07–7.15 (m, 2 H, H-Ar), 7.66 (s, 1 H, H-Ar).

^{13}C NMR ($CDCl_3$): δ = 148.33 (ArC), 138.53 (ArC), 136.93 (ArC), 129.35 (ArC), 126.33 (ArC), 101.26 (C-I), 33.23 (CH_3), 27.52 (CH), 23.90 (CH_3).

MS: *m*/*z* (%) = 260 ([M]$^+$, 75), 245 (100), 133 (18), 118 (76), 117 (28), 91 (22).

HRMS: *m*/*z* Calcd for $C_{10}H_{13}I$: 260.0062. Found: 260.0070.

Anal. Calcd for $C_{10}H_{13}I$: C, 46.17; H, 5.04. Found: C, 45.99; H, 5.26.

1,4-Diiodo-2-isopropyl-5-methylbenzene (4b)
Yellow oil; yield: 77%.

IR (Neat): 2962, 1454, 1375, 1315, 1060, 1020, 877 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.18 (s, 3 H, CH_3), 1.22 (s, 3 H, CH_3), 2.33 (s, 3 H, CH_3), 3.06 (hept, *J* = 6.8 Hz, 1 H, CH), 7.59 (s, 1 H, H-Ar), 7.66 (s, 1 H, H-Ar).

^{13}C NMR ($CDCl_3$): δ = 149.75 (ArC), 140.85 (ArC), 139.79 (ArC), 135.99 (ArC), 101.43 (C-I), 100.55 (C-I), 37.36 (CH), 26.90 (CH_3), 23.00 (CH_3).

MS: *m*/*z* (%) = 386 ([M]$^+$, 100), 371 (82), 244 (58), 119 (34), 117 (34), 91 (22).

HRMS: *m*/*z* Calcd for $C_{10}H_{12}I_2$: 385.9029. Found: 385.9041.

Anal. Calcd for $C_{10}H_{12}I_2$: C, 31.12; H, 3.13. Found: C, 31.17; H, 3.17.

1,3,4-Triiodo-5-isopropyl-2-methylbenzene (4c)
Yellow oil; yield: 70%.

IR (Neat): 2961, 2924, 1460, 1408, 1306, 1073, 1039, 996, 875 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.18 (s, 3 H, CH_3), 1.20 (s, 3 H, CH_3), 2.99 (s, 3 H, CH_3), 3.28 (hept, *J* = 6.8 Hz, 1 H, CH), 7.68 (s, 1 H, H-Ar).

^{13}C NMR ($CDCl_3$): δ = 153.43 (ArC), 144.09 (ArC), 136.89 (ArC), 117.81 (C-I), 116.67 (C-I), 100.30 (C-I), 43.00 (CH_3), 40.59 (CH), 23.73 (CH_3).

MS: *m*/*z* (%) = 512 ([M]$^+$, 100), 497 (53), 128 (65), 91 (86).

HRMS: *m*/*z* Calcd for $C_{10}H_{11}I_3$: 511.7995. Found: 511.8010.

Anal. Calcd for $C_{10}H_{11}I_3$: C, 23.46; H, 2.17. Found: C, 23.60; H, 2.17.

5-(*tert*-Butyl)-1,3-diiodo-2-methylbenzene (5b)
Yellow oil; yield: 80%.

IR (Neat): 2963, 2909, 1522, 1443, 1379, 1258, 1036, 872 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.26 (s, 9 H, *t*-C_4H_9), 2.70 (s, 3 H, CH_3), 7.80 (s, 2 H, H-Ar).

^{13}C NMR ($CDCl_3$): δ = 152.55 (ArC), 139.90 (ArC), 136.93 (ArC_4, ArC_6), 99.29 (C_1-I, C_3-I), 34.43 (2-CH_3), 34.03 [*C*(CH_3)$_3$], 31.07 [C(*C*H_3)$_3$].

MS: *m*/*z* (%) = 400 ([M]$^+$, 55), 385 (100), 258 (15), 128 (52), 127 (26), 91 (21), 57 (50).

HRMS: *m*/*z* Calcd for $C_{11}H_{14}I_2$: 399.9185. Found: 399.9199.

Anal. Calcd for $C_{11}H_{14}I_2$: C, 33.02; H, 3.53. Found: C, 32.73; H, 3.32.

1,4-Diiodo-2,5-diisopropylbenzene (6b)
White crystals; mp 85.5–86.5 °C; yield: 81%

IR (KBr): 2923, 1460, 1340, 1300, 1225, 1180, 1000, 868 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.19 (s, 6 H, CH_3), 1.21 (s, 6 H, CH_3), 3.05 (hept, *J* = 6.8 Hz, 2 H, CH), 7.60 (s, 2 H, H-Ar).

^{13}C NMR ($CDCl_3$): δ = 149.91 (ArC_2, ArC_5), 136.60 (ArC_3, ArC_6), 101.42 (C_1-I, C_4-I), 37.48 (CH), 22.98 (CH_3).

MS: *m*/*z* (%) = 414 ([M]$^+$, 100), 399 (95), 272 (18), 257 (15), 145 (21), 128 (18), 115 (20).

HRMS: *m*/*z* Calcd for $C_{12}H_{16}I_2$: 413.9342. Found: 413.9357.

Anal. Calcd for $C_{12}H_{16}I_2$: C, 34.81; H, 3.89. Found: C, 34.51; H, 3.66.

1-Iodo-2,4-diisopropylbenzene (7a)
Yellow oil; yield: 89%.

IR (Neat): 2962, 1460, 1390, 1360, 1040, 995, 877, 805 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.22 (s, 6 H, CH_3), 1.24 (s, 6 H, CH_3), 2.85 (hept, *J* = 6.8 Hz, 1 H, CH), 3.17 (hept, *J* = 6.8 Hz, 1 H, CH), 6.76 (d, *J* = 8 Hz, 1 H, H-Ar), 7.08 (s, 1 H, H-Ar), 7.71 (d, *J* = 8 Hz, 1 H, H-Ar).

^{13}C NMR ($CDCl_3$): δ = 150.06 (ArC), 149.43 (ArC), 139.26 (ArC), 125.83 (ArC), 124.33 (ArC), 97.50 (C-I), 37.93 (CH), 33.91 (CH), 23.91 (CH_3), 23.12 (CH_3).

MS: *m*/*z* (%) = 288 ([M]$^+$, 63), 273 (100), 131 (30), 91 (18).

HRMS: *m*/*z* Calcd for $C_{12}H_{17}I$: 288.0375. Found: 288.0377.

Anal. Calcd for $C_{12}H_{16}I_2$: C, 50.01; H, 5.95. Found: C, 49.81; H, 6.25.

1,5-Diiodo-2,4-diisopropylbenzene (7b)
White crystals; mp 49–53 °C; yield: 71%.

IR (KBr): 2963, 1450, 1377, 1348, 1040, 1000, 874 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.20 (s, 6 H, CH_3), 1.22 (s, 6 H, CH_3), 3.11 (hept, *J* = 6.8 Hz, 2 H, CH), 7.09 (s, 1 H, H-Ar), 8.23 (s, 1 H, H-Ar).

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^{13}C NMR ($CDCl_3$): δ = 150.80 (ArC_2, ArC_4), 148.15 (ArC), 123.04 (ArC), 98.41 (C_1-I, C_5-I), 37.65 (CH), 23.00 (CH_3).

MS: *m/z* (%) = 414 ([M]$^+$, 100), 399 (95), 272 (28), 257 (20), 145 (34), 128 (32), 115 (36), 91 (26).

HRMS: *m/z* Calcd for $C_{12}H_{16}I_2$: 413.9342. Found: 413.9351.

Anal. Calcd for $C_{12}H_{16}I_2$: C, 34.81; H, 3.89. Found: C, 34.37; H, 4.07.

1,3-Di(*tert*-butyl)-5-iodobenzene (8a)
White crystals; mp 64–64.5 °C; yield: 83%.

IR (KBr): 2955, 1540, 1443, 1361, 1230, 981, 851, 824 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.29 (s, 9 H, *t*-C_4H_9), 1.33 (s, 9 H, *t*-C_4H_9), 7.36 (t, *J* = 1.6 Hz, 1 H, H-Ar), 7.52 (d, *J* = 1.6 Hz, 2 H, H-Ar).

^{13}C NMR ($CDCl_3$): δ = 153.09 (ArC_1, ArC_5), 131.79 (ArC_4, ArC_6), 121.80 (ArC), 94.77 (C-I), 34.86 [*C*(CH_3)$_3$], 31.28 [C(*C*H_3)$_3$].

MS: *m/z* (%) = 316 ([M]$^+$, 52), 301 (100), 159 (26), 57 (50).

HRMS: *m/z* Calcd for $C_{14}H_{21}I$: 316.0688. Found: 316.0695.

Anal. Calcd for $C_{14}H_{21}I$: C, 53.17; H, 6.69. Found: C, 53.04; H, 6.61.

1,5-Di(*tert*-butyl)-2-iodo-3-methylbenzene (10a)
Yellow oil; yield: 58%.

IR (Neat): 2963, 1442, 1375, 1343, 1217, 982, 853 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.31 (s, 9 H, *t*-C_4H_9), 1.60 (s, 9 H, *t*-C_4H_9), 2.52 (s, 3 H, CH_3), 7.15 (d, *J* = 2.3 Hz, 1 H, H-Ar), 7.56 (d, *J* = 2.3 Hz, 1 H, H-Ar).

^{13}C NMR ($CDCl_3$): δ = 150.29 (ArC), 150.15 (ArC), 142.96 (ArC), 124.93 (ArC), 122.55 (ArC), 100.02 (C-I), 37.80 [*C*(CH_3)$_3$], 34.55 [(*C*(CH_3)$_3$], 32.66 [C(*C*H_3)$_3$], 31.26 [C(*C*H_3)$_3$], 30.46 (CH_3).

MS: *m/z* (%) = 330 ([M]$^+$, 45), 315 (100), 287 (35), 207 (20), 173 (25), 128 (45), 127 (20).

HRMS: *m/z* Calcd for $C_{15}H_{23}I$: 330.0845. Found: 330.0856.

Anal. Calcd for $C_{15}H_{23}I$: C, 54.55; H, 7.02. Found: C, 54.28; H, 7.13.

5-(*tert*-Butyl)-1,2-diiodo-3-methylbenzene (10b)
Yellow oil; yield: 77%.

IR (Neat): 2967, 1450, 1380, 1260, 1130, 1000, 860, 750 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.27 (s, 9 H, *t*-C_4H_9), 2.59 (s, 3 H, CH_3), 7.18 (d, *J* = 2.3 Hz, 1 H, H-Ar), 7.71 (d, *J* = 2.3 Hz, 1 H, H-Ar).

^{13}C NMR ($CDCl_3$): δ = 152.80 (ArC), 143.75 (ArC), 134.43 (ArC), 126.08 (ArC), 110.38 (C-I), 109.90 (C-I), 34.36 [*C*(CH_3)$_3$], 32.80 [C(*C*H_3)$_3$], 31.00 (CH_3).

MS: *m/z* (%) = 400 ([M]$^+$, 54), 385 (100), 357 (15), 258 (25), 131 (30), 91 (90), 57 (37).

HRMS: *m/z* Calcd for $C_{11}H_{14}I_2$: 399.9185. Found: 399.9191.

Anal. Calcd for $C_{11}H_{14}I_2$: C, 33.02; H, 3.53. Found: C, 33.15; H, 3.61.

5-(*tert*-Butyl)-1,2,3-triiodobenzene (2c); Optimized Typical Procedure
The optimal selectivity and effectivity of the progressive iodination of **2** to **2c** was achieved following a slightly changed general procedure as follows:

To a solution of *tert*-butylbenzene (**2**; 670 mg, 5 mmol)) in MeCN (50 mL) were added I_2 (2.54 g, 10 mml) and F-TEDA-BF_4 (3.54 g, 10 mmol) and the reaction mixture was stirred at 65 °C for 6 h. The solvent was removed under reduced pressure and the crude mixture was dissolved in CH_2Cl_2 (100 mL). The insoluble materials were filtered off, the solution washed with aq 10% $Na_2S_2O_3$•$5H_2O$ (50 mL) and H_2O (50 mL), and dried (Na_2SO_4). The solvent was evaporated to give 1.98 g of a crude reaction mixture. To a solution of the so obtained crude material in MeCN (50 mL) were added I_2 (2.54 g, 10 mmol) and F-TEDA-BF_4 (3.54 g, 10 mmol) and the reaction mixture was stirred at 65 °C for 16 h. After the already mentioned workup procedure, 2.05 g (80%) of crude 5-(*tert*-butyl)-1,2,3-triiodobenzene was isolated. Flash chromatography over silica gel (elution by CH_2Cl_2), followed by distillation under reduced pressure gave 1.86 g (73%) of the pure product **2c**; yellow oil; yield: 73%.

IR (Neat): 2970, 1500, 1465, 1388, 1369, 1248, 1127, 983, 860 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.25 (s, 9 H, *t*-C_4H_9), 7.83 (s, 2 H, H-Ar).

^{13}C NMR ($CDCl_3$): δ = 154.71 (ArC), 136.39 (ArC_4, ArC_6), 116.90 (C-I), 106.94 (C_1-I, C_3-I), 34.41 [*C*(CH_3)$_3$], 30.84 [C(*C*H_3)$_3$].

MS: *m/z* (%) = 512 ([M]$^+$, 94), 497 (100), 469 (20), 115 (35), 57 (28).

HRMS: *m/z* Calcd for $C_{10}H_{12}I_2$: 511.7995. Found: 511.8007.

Anal. Calcd for $C_{10}H_{11}I_3$: C, 23.46; H, 2.17; Found: C, 23.30; H 2.25.

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References

(1) (a) Heck, R. F. *Org. React.* **1982**, *27*, 345. (b) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508. (c) Negishi, E.; Coperet, C.; Ma, S.; Liou, S.; Liu, F. *Chem. Rev.* **1996**, *96*, 365.
(2) Seevers, R. H.; Counsell, R. E. *Chem. Rev.* **1982**, *82*, 575.
(3) (a) Merkushev, E. B. *Synthesis* **1988**, 923. (b) Sasson, Y. *Formation of Carbon–Halogen Bonds (Cl, Br, I),* In *The Chemistry of Halides, Pseudo Halides and Azides*, Supplement D2, Part 2; Patai, S.; Rappoport, Z., Eds.; Wiley: Chichester, **1995**, 535–620. (c) Steel, P. G. *Halobenzenes* In *Rodd's Chemistry of Carbon Compdounds*, 2nd Ed., Vol. 3 (Part 1); Sainsburry, M., Ed.; Elsevier: Amsterdam, **1996**, 178–224. (d) Barluenga, J. *Pure Appl. Chem.* **1999**, *71*, 431.
(4) Dolenc, D. *Synlett* **2000**, 544.
(5) Bachki, A.; Foubelo, F.; Yus, M. *Tetrahedron* **1994**, *50*, 5139.
(6) Orito, K.; Hatakeyama, T.; Takeo, M.; Suginome, H. *Synthesis* **1995**, 1273.
(7) Noda, Y.; Kashima, M. *Tetrahedron Lett.* **1997**, *38*, 6225.
(8) Luliski, P.; Skulski, L. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 1665.
(9) Yang, S. G.; Kim, Y. H. *Tetrahedron Lett.* **1999**, *40*, 6051.
(10) Garden, S. J.; Torres, J. C.; de Souza Melo, S. C.; Lima, A. S.; Pinto, A. C.; Lima, L. S. *Tetrahedron Lett.* **2001**, *42*, 2089.
(11) Zupan, M.; Iskra, J.; Stavber, S. *Tetrahedron Lett.* **1997**, *38*, 6305.
(12) Stavber, S.; Jereb, M.; Zupan, M. *Chem. Commun.* **2002**, 488.
(13) Stavber, S.; Kralj, P.; Zupan, M. *Synlett* **2002**, 598.

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(14) (a) Lal, G. S.; Pez, G. P.; Syvret, R. G. *Chem. Rev.* **1996**, *96*, 1737. (b) Banks, R. E. *J. Fluorine Chem.* **1998**, *87*, 1. (c) Taylor, S. D.; Kotoris, C. C.; Hum, G. *Tetrahedron* **1999**, *55*, 12431. (d) Furin, G. G.; Fainzilberg, A. A. *Russ. Chem. Rev.* **1999**, *68*, 653.
(15) (a) Banks, R. E.; Lawrence, N. J.; Popplewell, A. L. *Synlett* **1994**, 831. (b) Stavber, S.; Kralj, P.; Zupan, M. *Synlett* **2001**, 1152.
(16) (a) Suzuki, H.; Sugiyama, T.; Goto, R. *Bull. Chem. Soc. Jpn.* **1964**, *37*, 1858. (b) Suzuki, H.; Nakamura, K.; Goto, R. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 128.
(17) Barluenga, J.; Gonzáles, J. M.; García-Martín, M. A.; Campos, P. J. *Tetrahedron Lett.* **1993**, *34*, 3893.
(18) Ranganathan, S.; Ranganathan, D.; Singh, S. K. *Tetrahedron Lett.* **1985**, *26*, 4955.
(19) Tashiro, M.; Yamato, T. *J. Org. Chem.* **1979**, *44*, 3037.
(20) Myhre, P. C.; Edmonds, J. W.; Kruger, J. D. *J. Am. Chem. Soc.* **1966**, *88*, 2459.

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