Syntheses of Diiodo and Triiodo Derivatives of 1,2,3-Trimethylbenzene *(Hemimellitene)* and 1,2,4-Trimethylbenzene *(Pseudocumene)*. A Convenient Use of Polyiodo Derivatives for the Characterization of Polyalkylbenzenes and Their Derivatives⁽¹⁾

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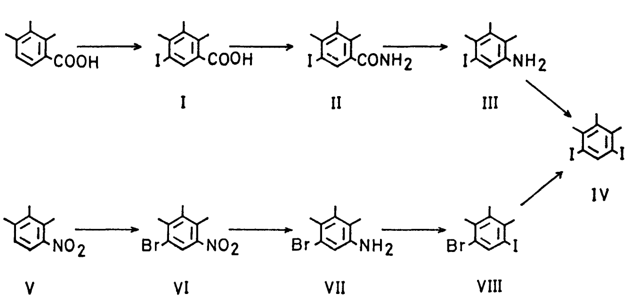
A complete set of diiodo and triiodo derivatives of 1,2,3-trimethylbenzene and 1,2,4-trimethylbenzene has been prepared and their physical properties are recorded. Use of polyiodo derivatives as a means for characterizing polyalkylbenzenes and their derivatives has been proposed.

In a reinvestigation of the Jacobsen reaction of 5-iodo-1,2,4-trimethylbenzene,[2] some diiodo and triiodotrimethylbenzenes were required as reference compounds. A survey of literature revealed that only one[3] of the six diiodotrimethylbenzenes and one triiodotrimethylbenzene[3] have so far been characterized. The present paper describes the synthesis of a complete set of diiodo and triiodo derivatives of the trimethylbenzenes given in the title.

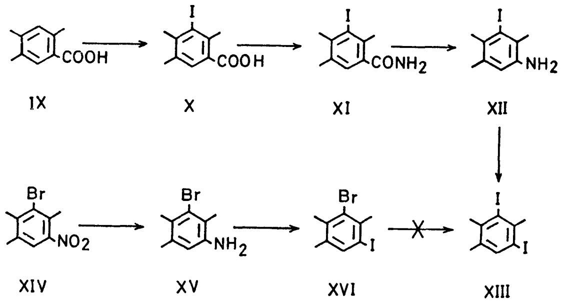
Diiodotrimethylbenzenes. In a previous paper,[5] the Jacobsen reaction of 5-iodo-1,2,3-trimethylbenzene was reported to give diiodo-1,2,3-trimethylbenzene melting at 114°C. Reinvestigation of the product revealed that it was in fact an intimate mixture of two diiodo-1,2,3-trimethylbenzenes. The major component was identified as 4,6-diiodo-1,2,3-trimethylbenzene (IV; mp 129—130°C) through the synthesis *via* two routes from 1,2,3-trimethylbenzene (Scheme 1). The minor component was identical with the authentic 4,5-diiodo-1,2,3-trimethylbenzene (mp 67—69°C) obtained from the iodination of 5-iodo-1,2,3-trimethylbenzene.

Direct iodination of 1,2,3-trimethylbenzene with two equivalent amounts of iodinating agent (iodine–periodic acid dihydrate)[6] gave a mixture of the 4,5- and 4,6-diiodo isomers in the ratio 1: 1.95. Less soluble IV was readily obtained as beautiful needles, but a small amount of isomeric impurity tenaciously clinging to the product was difficult to remove.



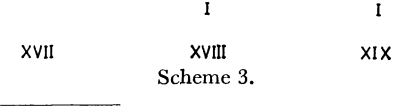
Scheme 1.

Two diiodo-1,2,4-trimethylbenzenes of unidentified structures were reported to be formed from the Jacobsen reaction of 5-iodo-1,2,4-trimethylbenzene.[7] Direct iodination of 1,2,4-trimethylbenzene with two equivalents of the iodinating agent was found to give 3,5-diiodo-1,2,4-trimethylbenzene (XIII) as the major product (*ca.* 80%).[8] However, separation of this product from the accompanying isomers was difficult due to a slight difference in boiling point. Pure XIII was obtained from 2,4,5-trimethylbenzoic acid (IX; durylic acid) according to the sequence shown in Scheme 2.



Scheme 2.

Fractional distillation of the product from nitration of 1,2,4-trimethylbenzene gave the 3-nitro compound as an early distillate, which was reduced to 2,3,6-trimethylaniline (XVII) and treated with iodine under alkaline conditions to give 4-iodo-2,3,6-trimethylaniline (XVIII). Diazotization and the subsequent treatment with aqueous potassium iodide gave 3,6-diiodo-1,2,4-trimethylbenzene (XIX).



Scheme 3.

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[1] The Reaction of Polysubstituted Aromatics. XXXI. Part XXX: This Bulletin, **46**, 586 (1973).

[2] H. Suzuki and T. Sugiyama, *ibid.*, **46**, 586 (1973).

[3] 2,4-Diiodo-1,3,5-trimethylbenzene and 2,4,6-triiodo-1,3,5-trimethylbenzene; both were first obtained by the Jacobsen reaction of 2-iodo-1,3,5-trimethylbenzene.[4]

[4] A. Töhl and R. Eckel, *Ber.*, **26**, 1099 (1893).

[5] H. Suzuki and R. Goto, This Bulletin, **36**, 389 (1963).

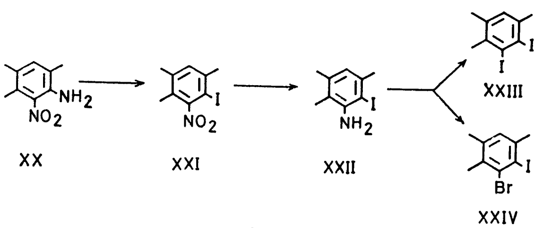
[6] H. Suzuki, K. Nakamura, and R. Goto, *ibid.*, **39**, 128 (1966); H. Suzuki, "Organic Syntheses," Vol. 51, p. 94 (1971).

[7] C. Kürzel, *Ber.*, **22**, 1586 (1889).

[8] The product was found to be a mixture of 3,5-diiodo-1,2,4-trimethylbenzene (79%), 5,6-diiodo-1,2,4-trimethylbenzene (17%), and 3,6-diiodo-1,2,4-trimethylbenzene (4%).

5,6-Diiodo-1,2,4-trimethylbenzene (XXIII) required a lengthy synthetic route. Attempts to introduce an iodine atom directly at the 6-position of 2,4,5-trimethylaniline failed due to the inevitable formation of tarry substance. *N*-Acetyl derivative could be iodinated at the 6-position but removal of the acetyl group was not possible under alkaline conditions. Under forced acidic conditions, elementary iodine was liberated instead.

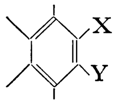
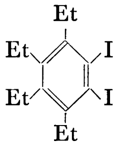
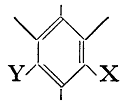
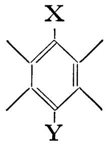
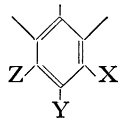
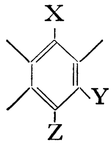
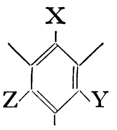
Triiodotrimethylbenzenes. Literature contains only 2,4,6-triiodo-1,3,5-trimethylbenzene (triiodomesitylene).[4] Iodine-periodic acid as iodinating agent readily converted 1,2,3- and 1,2,4-trimethylbenzenes into the corresponding triiodo derivatives, both of which were high-melting crystals poorly soluble in cold organic solvents. On storage under diffused light, 4,5,6-triiodo-1,2,3-trimethylbenzene gradually turned yellow.



Scheme 4.

Use of Polyiodo Derivatives for Characterization Purpose. Iodine–periodic acid as an iodinating agent provides a simple direct route to polyiodopolyalkylbenzenes. Ease

TABLE 1. PHYSICAL PROPERTIES OF SOME POLYIODO AND HALOIODO DERIVATIVES OF POLYALKYLBENZENES

Compound		Mp (°C)	^{1}H NMR$^{a)}$ (τ)	IR (cm^{-1})
1,2,3,4-Tetramethylbenzene series				
	X=Cl, Y=I	168—169	7.84(1), 7.78(1) 7.61(1), 7.50(1)	776, 891, 956, 1195
	X=Br, Y=I	190—191	7.82(1), 7.79(1) 7.54(1), 7.47(1)	758, 880, 945, 1189
	X=I, Y=I	190—191	7.80(2), 7.40(2)	745, 876, 940, 1184
		84—85	8.86(2), 8.84(2) 7.31 (2 CH_2) 6.92 (2 CH_2)	786, 983, 1005, 1053, 1062, 1071, 1172, 1314
1,2,3,5-Tetramethylbenzene series				
	X=Cl, Y=I	166—168	7.76(1), 7.72(1) 7.56(1), 7.38(1)	919, 982, 1159
	X=Br, Y=I	177—178	7.71(1), 7.64(1) 7.54(1), 7.27(1)	915, 968, 1152
	X=I, Y=I	150—151	7.68(1), 7.54(2) 7.11(1)	911, 957, 1145
1,2,4,5-Tetramethylbenzene series				
	X=Cl, Y=I	171—172	7.62(2), 7.52(2)	692, 989, 1076
	X=Br, Y=I	175—176	7.53(2), 7.47(2)	681, 981, 1068
	X=I, Y=I	140—141	7.46(4)	675, 976, 1063
1,2,3-Trimethylbenzene series				
	X=I, Y=Et Z=I	98—99	8.87(1), 7.64(1) 7.49(2), 6.66 (CH_2)	777, 916, 981, 1058, 1144
	X=Br, Y=I Z=I	232—234	7.68(1), 7.47(1) 7.32(1)	920, 1001, 1207, 1335
1,2,4-Trimethylbenzene series				
	X=I, Y=Et Z=I	51—53	8.89(1), 7.42(2) 7.41(1), 6.95 (CH_2)	984, 1162
	X=Cl, Y=I Z=I	194—196	7.55(1), 7.31(1) 7.10(1)	846, 953, 1006, 1142, 1342
1,3,5-Trimethylbenzene series				
	X=Et, Y=I Z=I	63—64	8.92(1), 7.51(2) 7.19 (CH_2), 7.08 (1)	791, 927, 946, 971
	X=Cl, Y=I Z=I	174—175	7.31(2), 7.04(1)	944, 1347

a) Numerals in parentheses refer to the number of methyl groups.

of access makes polyiodo derivatives useful for the characterization of polyalkylbenzenes and their derivatives. They are especially so when the given sample is a liquid available only in a small amount, since the introduction of iodine atoms multiplies molecular weight and converts a liquid hydrocarbon into a well-crystallized solid with moderate melting range. Polyiodo derivatives are preferred to polynitro and polybromo derivatives, because the latters are often accompanied by side-chain substituted products and their mixture melting test is sometimes deceptive due to a slight depression of melting point. Physical properties of some polyiodo and mixed haloiodo derivatives of polyalkylbenzenes, most of which are new, are summarized in Table 1.

Experimental

All melting and boiling points are uncorrected. Infrared spectra were recorded in Nujol on a Jasco DS-402G spectrophotometer. ^{1}H NMR spectra were measured in carbon tetrachloride solutions on a JEOL PS-100 spectrometer against internal TMS.

5-Iodo-2,3,4-trimethylbenzamide (II). A mixture of 5-iodo-2,3,4-trimethylbenzoic acid (I, 14.0 g)[9] and thionyl chloride (10 g) was warmed until there was no more evolution of gaseous product. After removal of excess thionyl chloride under reduced pressure, the residual solid was dissolved in benzene, and dry ammonia gas was bubbled through the solution. The precipitate was filtered off and recrystallized from hot dioxane to give amide as white needles (13.1 g, 94%), mp 275—276°C. IR: 687, 716, 765, 884, 1041, 1113, 1187, 1542, 1624, 1649, 3160, and 3330 cm^{-1}.

Found: C, 41.60; H, 4.21%. Calcd for $C_{10}H_{12}NIO$: C, 41.54; H, 4.19%.

3-Iodo-2,4,5-trimethylbenzamide (*XI*; mp 236—237°C) was prepared in a similar manner from 3-iodo-2,4,5-trimethylbenzoic acid (X).[9] IR: 702, 827, 889, 990, 1125, 1405, 1624, 1649, 3150, and 3320 cm^{-1}.

Found: C, 41.52; H, 4.07%. Calcd for $C_{10}H_{12}NIO$: C, 41.54; H, 4.19%.

5-Iodo-2,3,4-trimethylaniline (III). A solution of potassium hydroxide (11.2 g) and bromine (12 g) in water (100 ml) was poured on II (9.6 g) suspended in ethanol (100 ml). The mixture was stirred at room temperature for 5 hr and then a solution of potassium hydroxide (15 g) in water (50 ml) was added. The temperature was maintained at 50—60°C for 3 hr and then at 60—70°C for 3 hr. Finally the reaction mixture was steam-distilled to give amine as white solid, which was recrystallized from light petroleum to yield pure product (1.6 g, 18%), mp 79—80°C. IR: 754, 844, 866, 947, 1115, 1206, 1273, 1288, 1573, 1618, 3320, and 3410 cm^{-1}; NMR; 8.03 (Me), 7.81 (Me), 7.70 (Me), 6.75 (NH_2), and 3.04 τ (aromatic H).

Found: C, 41.53; H, 4.74%. Calcd for $C_9H_{12}NI$: C, 41.40; H, 4.63%.

3-Iodo-2,4,5-trimethylaniline (*XII*; mp 57—58°C) was obtained in a similar manner from XI. IR: 784, 855, 979, 1231, 1275, 1285, 1548, 1598, 1630, 3190, 3290, and 3380 cm^{-1}; NMR: 7.80 (Me), 7.73 (Me), 7.70 (Me), 6.65 (NH_2), and 3.70 τ (aromatic H).

Found: C, 41.67; H, 4.72%. Calcd for $C_9H_{12}NI$: C, 41.40; H, 4.63%.

4-Iodo-2,3,6-trimethylaniline (XVIII). To a suspension of sodium hydrogen carbonate (17 g) in water (150 ml), 2,3,6-trimethylaniline (XVII; bp 125—127°C/18 mmHg; 9.0 g) dissolved in ether (80 ml) was added. Stirring was continued for an hour, after which the solvent was removed and a black residual solid was steam-distilled. The amine separated as white needles in the distillate was collected by filtration and recrystallized from light petroleum, mp 100—101°C. Yield, 8.2 g (47%). IR: 754, 839, 854, 869, 972, 1080, 1167, 1311, 1560, 1621, 3270, and 3360 cm^{-1}; NMR: 7.96 (Me), 7.86 (Me), 7.71 (Me), 6.08 (NH_2), and 3.58 τ (aromatic H).

Found: C, 41.58; H, 4.56%. Calcd for $C_9H_{12}NI$: C, 41.40; H, 4.63%.

6-Bromo-4-nitro-1,2,3-trimethylbenzene (VI). A mixture of 4-nitro-1,2,3-trimethylbenzene (V; bp 147—149°C/18 mmHg; 7.0 g) and bromine (10 g) was allowed to stand overnight at room temperature. Hydrogen bromide evolved gently and a solid product was obtained, which was crystallized from hot ethanol to give pale yellow needles (9.1 g, 88%), mp 82—83°C. IR: 664, 711, 755, 819, 868, 943, 1038, 1188, 1353, and 1520 cm^{-1}; NMR: 7.69 (Me), 7.67 (Me), 7.55 (Me), and 2.22 τ (aromatic H).

Found: C, 44.46; H, 4.37%. Calcd for $C_9H_{10}NBrO_2$: C, 44.28; H, 4.13%.

5-Nitro-1,2,4-trimethylbenzene (mp 70—71°C; bp 127—129°C/22 mmHg) treated with bromine in a similar manner to that above gave *3-bromo-5-nitro-1,2,4-trimethylbenzene* (*XIV*; mp 89—90°C). NMR: 7.61 (Me), 7.56 (Me), 7.48 (Me), and 2.52 τ (aromatic H).

Found: C, 44.37; H, 2.48%. Calcd for $C_9H_{10}NBrO_2$: C, 44.28; H, 4.13%.

5-Iodo-6-nitro-1,2,4-trimethylbenzene (XXI). To a solution of 6-nitro-2,4,5-trimethylaniline (XX, 9 g)[10] in sulfuric acid (20 ml) was added finely powdered sodium nitrite (3.6 g) with stirring. The mixture was stirred for 30 min and then poured onto crushed ice. The resulting solution of diazonium salt was filtered and the filtrate was added to a solution of potassium iodide (10 g) in a small amount of water. After the mixture was left to stand overnight, the precipitated tan solid was filtered off and passed over a short alumina column with a mixture of benzene and ligroin. From the eluate the iodo compound was obtained as prisms (11.2 g, 77%), mp 130—131°C. IR: 759, 871, 905, 969, 1152, 1255, and 1523 cm^{-1}; NMR: 7.84 (Me), 7.73 (Me), 7.55 (Me), and 2.88τ (aromatic H).

Found: C, 37.29; H, 3.44%. Calcd for $C_9H_{10}NIO_2$: C, 37.13; H, 3.46%.

4-Bromo-6-iodo-1,2,3-trimethylbenzene (VIII), 3-bromo-5-iodo-1,2,4-trimethylbenzene (XVI), and 6-bromo-5-iodo-1,2,4-trimethylbenzene (XXIV) were prepared from the corresponding bromoanilines by a similar procedure. The products were purified through distillation followed by recrystallization from light petroleum.

VIII: mp 97—99°C. IR: 844, 856, 906, 1007, and 1155 cm^{-1}; NMR: 7.69 (Me), 7.68 (Me), 7.62 (Me), and 2.13 τ (aromatic H).

Found: C, 33.22; H, 3.05%. Calcd for $C_9H_{10}BrI$: C, 33.26; H, 3.10%.

XVI: bp 174—177°C/16 mmHg. IR: 734, 805, 866, 948, 993, 1151, and 1350 cm^{-1}; NMR: 7.80 (Me), 7.74 (Me), 7.40 (Me), and 2.48 τ (aromatic H).

Found: C, 33.80; H, 3.11%. Calcd for $C_9H_{10}BrI$: C, 33.26; H, 3.10%.

XXIV: mp 45—46°C; bp 173—176°C/14 mmHg. IR: 758, 804, 864, 961, 993, 1013, 1032, 1138, and 1355 cm^{-1};

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9) H. Suzuki, This Bulletin, **44**, 2871 (1971).

10) M. H. Huender, *Rec. Trav. Chim. Pays-Bas*, **34**, 1 (1913).

NMR: 7.79 (Me), 7.59 (Me), and 3.09 τ (aromatic H).

Found: C, 33.26; H, 3.16%. Calcd for $C_9H_{10}BrI$: C, 33.26; H, 3.10%.

6-Iodo-2,3,5-trimethylaniline (XXII). Stannous chloride dihydrate (30 g) was dissolved in a mixture of hydrochloric acid (d=1.18, 35 ml) and ethanol (35 ml). To this solution was added XXI (9.7 g) with stirring. After the end of reaction, sodium hydroxide solution was added until the precipitated stannic hydroxide redissolved, and the solution was steam-distilled. Amine was separated from the distillate by ether-extraction and recrystallized from light petroleum. Colorless needles (6.5 g, 75%), mp 81—82°C. IR: 838, 973, 1017, 1106, 1282, 1318, 1552, 1622, 3290, and 3370 cm^{-1}; NMR: 7.95 (Me), 7.85 (Me), 7.71 (Me), 6.03 (NH_2), and 3.57 τ (aromatic H).

Found: C, 41.40; H, 4.58%. Calcd for $C_9H_{12}NI$: C, 41.40; H, 4.63%.

5-Bromo-2,3,4-trimethylaniline (*VII*; mp 86—87°C) and *3-bromo-2,4,5-trimethylaniline* (*XV*; mp 57—59°C) were prepared in a similar manner from VI and XIV, respectively.

VII: IR: 766, 845, 874, 954, 1116, 1206, 1217, 1279, 1295, 1586, 1619, 3340, and 3430 cm^{-1}; NMR: 8.05 (Me), 7.85 (Me), 7.77 (Me), 6.73 (NH_2), and 3.36 τ (aromatic H).

Found: C, 50.59; H, 5.72%. Calcd for $C_9H_{12}NBr$: C, 50.48; H, 5.65%.

XV: IR: 800, 857, 986, 1232, 1278, 1290, 1554, 1607, 1635, 3190, 3290, and 3390 cm^{-1}; NMR: 7.83 (Me), 7.81 (Me), 7.76 (Me), 6.66 (NH_2), and 3.72 τ (aromatic H).

Found: C, 50.42; H, 5.91%. Calcd for $C_9H_{12}NBr$: C, 50.48; H, 5.65%.

4,6-Diiodo-1,2,3-trimethylbenzene (IV). *Method 1*: Sodium nitrite (0.5 g) was added below 10°C to a solution of III (1.4 g) in sulfuric acid (8 ml). After stirring for 30 min, the mixture was poured onto crushed ice, and the resulting solution was filtered and added to a solution of potassium iodide (1.5 g) in a small amount of water. The mixture was allowed to stand overnight, and the black precipitate was collected by filtration and passed over a short alumina column with light petroleum. From the eluate IV was obtained as colorless plates (0.8 g, 40%), mp 129—130°C. IR: 834, 856, 899, 999, and 1148 cm^{-1}; NMR: 7.68 (Me), 7.62 (2 Me), and 1.88 τ (aromatic H).

Found: C, 29.20; H, 2.78%. Calcd for $C_9H_{10}I_2$: C, 29.06; H, 2.71%.

Other diiodotrimethylbenzenes were prepared in a similar manner from the corresponding iodotrimethylanilines.

3,6-Diiodo-1,2,4-trimethylbenzene (XIX): mp 75—76°C. IR: 739, 852, 992, 1129, and 1248 cm^{-1}; NMR: 7.67 (Me), 7.53 (Me), 7.47 (Me), and 2.47 τ (aromatic H).

Found: C, 29.13; H, 2.66%. Calcd for $C_9H_{10}I_2$: C, 29.06; H, 2.71%.

3,5-Diiodo-1,2,4-trimethylbenzene (XIII): Mp 8—9°C; bp 202—204°C/21 mmHg. IR: 732, 791, 866, 942, 983, 1142, and 1342 cm^{-1}; NMR: 7.76 (Me), 7.66 (Me), 7.27 (Me), and 2.46 τ (aromatic H).

Found: C, 29.21; H, 2.62%. Calcd for $C_9H_{10}I_2$: C, 29.06; H, 2.71%.

5,6-Diiodo-1,2,4-trimethylbenzene (XXIII): Mp 51—52°C; bp 197—199°C/18 mmHg. IR: 746, 788, 865, 955, 990, 1013, 1031, 1131, and 1351 cm^{-1}; NMR: 7.76 (Me), 7.52 (Me), 7.47 (Me), and 3.07 τ (aromatic H).

Found: C, 29.19; H, 2.68%. Calcd for $C_9H_{10}I_2$: C, 29.06; H, 2.71%.

Method 2: The Grignard reagent was prepared in the usual manner from VIII (5.2 g), magnesium (0.4 g), and tetrahydrofuran (40 ml). To the reagent was added at one time dried magnesium iodide (4.5 g) and an additional amount of magnesium (0.6 g), and the mixture was stirred overnight under reflux. After being cooled the mixture was rapidly stirred and iodine (*ca.* 11—12 g) was added in small portions until the brown color began to persist. Excess dilute hydrochloric acid was added, and the organic layer was separated, dried, and evaporated to leave a light brown solid. It was fractionally distilled under reduced pressure and the fraction boiling at 190—200°C/17 mmHg was collected and crystallized from light petroleum. Colorless plates (0.8 g, 14%), mp 124—128°C, were spectroscopically identical with the compound obtained by method 1.

The above procedure applied to 3-bromo-5-iodo-1,2,4-trimethylbenzene (XVI) gave unsatisfactory results, since the bromine atom at the 3-position was found to be slow to react.

4,5-Diiodo-1,2,3-trimethylbenzene and triiodo derivatives of 1,2,3- and 1,2,4-trimethylbenzenes were prepared by the direct iodination of 5-iodo-1,2,3-trimethylbenzene and two corresponding hydrocarbons, respectively, with iodine–periodic acid dihydrare.[6]

4,5-Diiodo-1,2,3-trimethylbenzene: Mp 67—69°C. IR: 835, 858, 902, 997, and 1193 cm^{-1}; NMR: 7.86 (Me), 7.82 (Me), 7.42 (Me), and 2.47 τ (aromatic H).

4,5,6-Triiodo-1,2,3-trimethylbenzene: Mp 232—235°C. IR: 916, 999, 1198, and 1328 cm^{-1}; NMR: 7.65 (Me), and 7.31 τ (2 Me).

Found: C, 21.62; H, 1.70%. Calcd for $C_9H_9I_3$: C, 21.71; H, 1.82%.

3,5,6-Triiodo-1,2,4-trimethylbenzene: Mp 193—195°C. IR: 751, 814, 946, 984, 1128, 1225, and 1325 cm^{-1}; NMR: 7.46 (Me), 7.27 (Me), and 6.93 τ (Me).

Found: C, 21.58; H, 1.76%. Calcd for $C_9H_9I_3$: C, 21.71; H, 1.82%.

General Procedure for the Preparation of Polyiodo Derivatives from Polyalkylbenzenes. A polyalkylbenzene (*ca.* 0.1—0.3 g) dissolved in 80% acetic acid (5 ml) containing a catalytic amount of sulfuric acid was rapidly stirred and heated with iodine (1.0 g) and periodic acid dihydrate (0.45 g) at 70—80°C for 30 min—1 hr. The mixture was then poured into aqueous sodium hydrogen sulfite to remove excess reagent. The white precipitate was collected by filtration and crystallized from ethanol.