*The Direct Iodination of Polyalkylbenzenes by the Crossed Jacobsen Reaction*1)

By Hitomi SUZUKI,* Takashi SUGIYAMA and Ryozo GOTO

(Received June 19, 1964)

The direct iodination of aromatic compounds may be effected satisfactorily when these compounds contain such activating groups as hydroxyl or amino groups. If we wish to introduce an iodine atom directly into a nucleus not activated by such powerful activating groups, however, the reaction must be carried out in the presence of an effective oxidizing agent. The reagents commonly employed are iodic acid,2) common or fuming sulfuric acid,3) nitric acid,4) heavy metal oxides,5) sodium persulfate or perchlorate,6) silver salts,7) ferric chloride,8) and organic peroxides.9) In the literature, however, few of these reagents have been employed with the

---

1) Part V on the Jacobsen Reaction; Part IV: This Bulletin, **36**, 1642 (1963).

* Present address: Department of Chemistry, Faculty of Science, Kyoto University, Kyoto.

2) A. Kekulé, *Ann.*, **137**, 162 (1866); A. Klages and W. Storp, *J. prakt. Chem.*, (2), **65**, 568 (1902); F. Boedtker, *Bull. soc. chim. France*, (4), **45**, 649 (1929); H. O. Wirth, O. Königstein and W. Kern, *Ann.*, **634**, 84 (1960).

3) A. Neumann, *Ann.*, **241**, 84 (1887); E. Rupp, *Ber.*, **29**, 1625 (1896); J. F. Durand and M. Mancet, *Bull., soc. chim. France*, (5), **2**, 665 (1935); "Organic Syntheses," Vol. 27, 78 (1947); Vol. 30, 55 (1950).

4) R. L. Datta and N. R. Chatterjee, *J. Am. Chem. Soc.*, **39**, 435 (1917); ibid., **41**, 292 (1919); A. Edinger and P. Goldberg, *Ber.*, **33**, 2875 (1900); "Organic Syntheses," Coll., Vol. I, 323 (1956).

5) A. Töhl, *Ber.*, **25**, 1521 (1892); Th. Curtius and H. Thyssen, *J. prakt. Chem.*, (2), **65**, 1, (1902); "Organic Sytheses," Coll., Vol. II., 375 (1943).

6) K. Elbs and A. Jaroslawzew, *J. prakt. Chem.*, (2), **88**, 92 (1913).

7) L. Birckenbach and J. Goubeau *Ber.*, **65**, 395 (1932); D. H. Derbyshire and W. A. Waters, *J. Chem. Soc.*, **1950**, 3694; I. R. L. Barker and W. A. Waters, ibid., **1952**, 150; "Organic Syntheses," Vol. 36, 46 (1956).

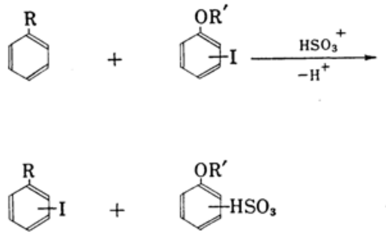
8) L. Meyer, *Ann.*, **231**, 195 (1885); *J. prakt. Chem.*, (2), **34**, 502 (1886).

9) H. Erlenmeyer, *Helv.*, **9**, 819 (1926); ibid., **10**, 620 (1927); Y. Ogata and H. Nakasima, *Tetrahedron*, **20**, 43 (1964).

highly alkylated benzenes. As the reaction proceeds through an electrophilic attack of an iodine atom on the nucleus, an increase in the number of alkyl groups attached to the ring enhances the reactivity of the compound. This increase, however, brings about an enhanced susceptibility of the compound to the undesired action of an oxidizing agent, and also to an increased steric repulsion to the entry of a bulky iodine atom into the nucleus. Both these effects reduce the yield of the product so markedly that most of the above reagents cannot be used successfully for the purpose of synthesizing iodo polyalkylbenzenes. Thus, from the synthetic point of view, the direct iodination of highly alkylated compounds is not necessarily a simple matter to effect. For example, if we use sulfuric acid or nitric acid as an oxidizing agent, the sulfonation or the nitration of the compound often proceeds in preference to iodination. Ferric chloride gives a complex mixture in which the desired iodinated product is a minor component, whereas iodic acid or organic peroxides afford the products, in most cases, in unsatisfactorily low yields.

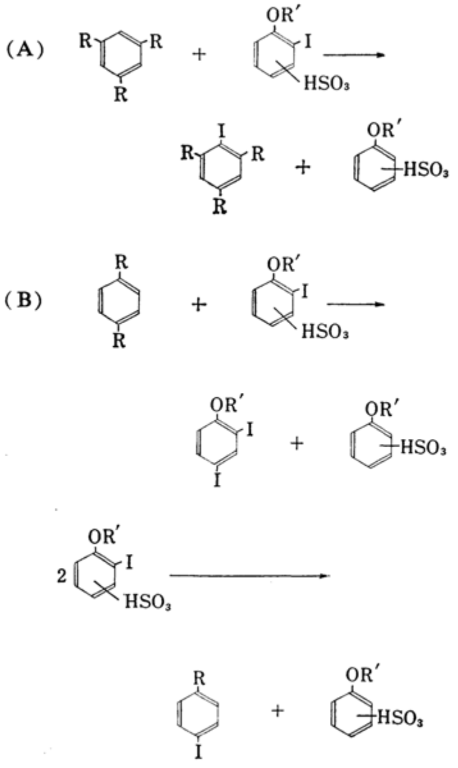
In earlier papers of this series,[10] we have shown that iodophenols and iodoanisoles, in the presence of sulfuric acid, readily undergo the disproportionation at room temperatures and afford polyiodo compounds in fairly high yields. This fact suggested to us that iodophenols or iodoanisoles might be used in conjunction with sulfuric acid as iodinating agents. The present work will present the results of an attempt to use these compounds as iodinating agents for polyalkylbenzenes.

This reaction may be represented by the following general equation:



In the present work, we used *o*-iodoanisole as an iodinating agent. In this reaction (the crossed Jacobsen reaction), the iodination of polyalkylbenzene competes with the disproportionation of *o*-iodoanisole. Since the iodine cation reacts more readily with iodoanisole to form polyiodo anisoles, care must be taken to select conditions which do not favor their formation. This was done by carrying out the reaction in an excess of hydrocarbon, thus avoiding the presence of excess iodoanisole in the system. Under these conditions, iodoanisole cannot successfully compete with the hydrocarbon, and the iodine cation, once formed, goes on to react with the excess hydrocarbon to give the iodinated product. On the other hand, the presence of a large excess of sulfuric acid causes such undesirable side reactions as sulfonation, the migration of the alkyl group, and the further decomposition of the iodinated products (iodo polyalkylbenzenes are generally unstable towards sulfuric acid and are readily decomposed to the resinous materials and free iodine). In order to prevent these side reactions, the hydrocarbon was brought to the simultaneous action of *o*-iodoanisole and sulfuric acid; that is, to the polyalkylbenzene to be iodinated, sulfuric acid and *o*-iodoanisole were simultaneously added drop by drop, while their proportion was maintained slightly in excess of the sulfuric acid.

Nine polyalkylbenzenes were subjected to the crossed Jacobsen reaction: pseudocumene, durene, pentamethylbenzene, *sym*-triethylbenzene, *sym*-tetraethylbenzene, *p*-diisopropylbenzene, *sym*-triisopropylbenzene, *sym*-tetraisopropylbenzene, and *p*-di-*t*-butylbenzene. Only polymethyl- and polyethylbenzenes underwent



---

[10] H. Suzuki and R. Goto, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **84**, 167 (1963); ibid., **84**, 284 (1963); This Bulletin, **36**, 389 (1963).

this reaction smoothly at room temperature and gave acceptable yields of the products. Polyisopropyl- and poly-*t*-butylbenzenes, as would be expected from our previous works,[10] gave the iodinated products in poor yields. With some compounds, one of the isopropyl or *t*-butyl groups which occupied a position favorable, with respect to the directing effect of other groups present, to the entry of the iodine cation, is in part replaced. Thus, depending upon the structure of the polyalkylbenzenes, the reaction may occur by two different routes, A and B.

With polymethyl- and polyethylbenzenes which are activated by alkyl groups but not so overcrowded with them, the reaction proceeds through the route A. With polyisopropyl and poly-*t*-butylbenzenes, the aversion to the entry of a bulky iodine atom into the nucleus suppresses the formation of normal products so markedly that the reaction proceeds chiefly through the route B and results in either the replacement of an alkyl group or the disproportionation of *o*-iodoanisole.

The direct iodination of polyalkylbenzenes by the crossed Jacobsen reaction is characterized by the absence of a powerful oxidizing reagent, mild reaction conditions, and the easy separation of the products. This reaction, the use of which as a practical means of synthesis seems to be somewhat limited, affords a simple one-step preparation of iodinated polyalkylbenzenes from readily-available starting materials.

Experimental

1) **General Procedure.**—*a) Liquid Hydrocarbon.* —In a 100 ml. four-necked flask, fitted with a thermometer, a reflux condenser, and two dropping funnels, each a containing sulfuric acid and *o*-iodoanisole, the hydrocarbon was placed and magnetically stirred. The flask was then immersed in a water-bath and heated to the desired temperature. Sulfuric acid and *o*-iodoanisole were added drop by drop at such a rate that a slight excess of sulfuric acid was maintained in the system. Under these conditions, no alkyl migration occured. After completion of dropping, the mixture was stirred for some additional hours and then poured into water. The resulting organic layer was extracted with a small amount of ether, and the extract was washed with a diluted sodium bisulfite solution to remove free iodine and then dried over anhydrous calcium chloride. After this drying, the ether was removed by distillation. The fractionation of the residual oil gave some amounts of unchanged hydrocarbon, followed by the expected iodinated polyalkylbenzene.

b) Solid Hydrocarbon.—Solid hydrocarbon was dissolved in a small amount of cyclohexane and then subjected to iodination in the manner described above. After the completion of the reaction, the mixture was poured into water; the organic layer was separated, washed with a diluted solution of sodium bisulfite, and freed from the solvent. The crystalline residue was chromatographed on an alumina column. The elution of the column with petroleum ether gave unchanged hydrocarbon, followed by the desired iodinated product, which was then recrystallized from an appropriate solvent to yield the pure product. 2, 4-Diiodoanisole, a disproportionation product, was held on a column and readily removed from the iodinated polyalkylbenzene.

2) **Dialkylbenzenes.** — *p-Diisopropylbenzene.* — *p*-Diisopropylbenzene (24.3 g., 0.15 mol.) was stirred and warmed to 35∼40°C. *o*-Iodoanisole (23.4 g., 0.10 mol.) and sulfuric acid (15 g., 0.15 mol.) were added over a 1.5-hr. period. The reddish-violet mixture was, after 4 hours' agitation, poured into water and worked up as described in 1a). The distillation of the oil gave unchanged *p*-diisopropylbenzene (13.8 g., b. p. 91∼93°C/19 mmHg), a mixture of *o*-iodoanisole and a lower-boiling iodo compound (7.1 g., b. p. 105∼120°C/19 mmHg), a higher-boiling iodo compound (6.4 g., b. p. 140∼160°C/19 mmHg), and a residue (ca. 2.0 g.). The mixture fraction, on oxidation, gave a small amount of *p*-iodobenzoic acid, m. p. 262∼265°C. Thus, the iodination of *p*-diisopropylbenzene was accompanied by the partial replacement of one of the isopropyl groups. The redistillation of the higher-boiling fraction gave 6.0 g. of monoiodo-*p*-diisopropylbenzene, b. p. 143∼146°C/22 mmHg.

Found: C, 49.71; H, 5.81. Calcd. for $C_{12}H_{17}I$: C, 50.00; H, 5.95%.

p-Di-t-butylbenzene.—To the stirred solution of *p*-di-*t*-butylbenzene (3.7 g., 0.02 mol.) in cyclohexane (25 ml.) *o*-iodoanisole (5.9 g., 0.025 mol.) and sulfuric acid (3.0 g., 0.03 mol.) were added at 30∼33°C. The reaction mixture turned immediately dark-violet, and a remarkable liberation of free iodine was observed. After 3 hours' agitation, the mixture was worked up as described in 1b). The crystalline residue (6.4 g.), chromatographed on an alumina column, gave unchanged *p*-di-*t*-butylbenzene (3.1 g., m. p. 75∼76°C), a pink-colored oil (ca. 0.5 g.), and 2, 4-diiodoanisole (2.5 g., m. p. 65∼67°C). After the mixture had stood in the refrigerator, some feather-like crystals were separated out from the oil fraction, which, on recrystallization several times from petroleum ether, gave white soft needles, m. p. 49∼50°C. The elemental analysis of this material indicated that it was diiodinated di-*t*-butylbenzene, whose structure, inferred by analogy, might be 2, 5-diiodo-1, 4-di-*t*-butylbenzene.[11]

Found: C, 37.65; H, 4.27. Calcd. for $C_{14}H_{20}I_2$: C, 38.04; H, 4.56%.

The oily part was supposed to be a mixture of *p*-iodo-*t*-butylbenzene, a monoiodinated product, and unchanged *o*-iodoanisole, but none of them could be identified because of its small quantity.

3) **Trialkylbenzenes.**—*Pseudocumene (1, 2, 4-Trimethylbenzene).*—Pseudocumene (12.0 g., 0.1 mol.)

---

[11] The Jacobsen reaction of halogenobenzenes usually proceeds like the progressive halogenation of the parent compound. Cf. H. Suzuki, This Bulletin, 36, 1642 (1963).

was iodinated by using *o*-iodoanisole (15.6 g., 0.15 mol.) and sulfuric acid (10 g., 0.1 mol.), and 14.5 g. of a monoiodinated product, b. p. 121～125°C/17～18 mmHg, was obtained. This might be a mixture of several isomers, because it could not be completely solidified on standing in ice bath. The comparatively low yield (69% based on the unrecovered hydrocarbon) is attributed in part to the easy sulfonation of pseudocumene, and in part to the instability of the product towards the action of sulfuric acid. 5-Iodopseudocumene, m. p. 34～36°C.

Found: C, 43.77; H, 4.48. Calcd. for $C_9H_{11}I$: C, 43.92; H, 4.51%.

sym-Triethylbenzene.—To *sym*-triethylbenzene (24.3 g., 0.15 mol.), *o*-iodoanisole (23.4 g., 0.1 mol.) and sulfuric acid (15 g., 0.15 mol.) were added at 30～32°C over a 1.5 hr. period. Little iodine was liberated. After standing overnight, the mixture was worked up as usual. The fractionation of the oil gave unchanged triethylbenzene (12.7 g., b. p. 115～117°C/29 mmHg), *o*-iodoanisole (4.5 g., b. p. 112～115°C/18 mmHg), a monoiodinated fraction (17.9 g., b. p. 150～153°C/16 mmHg), and a residue (ca. 0.5 g.). The redistillation of the monoiodinated fraction gave 17.1 g. of monoiodo-*sym*-triethylbenzene (b. p. 169～170°C/31 mmHg).

Found: C, 49.74; H, 6.00. Calcd. for $C_{12}H_{11}I$: C, 50.01; H, 5.95%.

sym-Triisopropylbenzene.—*sym*-Triisopropylbenzene (20.4 g., 0.1 mol.) was iodinated with *o*-iodoanisole (15.6 g., 0.07 mol.) and sulfuric acid (10 g., 0.1 mol.) at 35～38°C by the same method used above. After 3 hours agitation, the mixture was left to stand overnight. Working up as usual and the distillation of the residual oil gave the starting materials unchanged (20.0 g., b. p. 114～120°C/18 mmHg), iodine containing a higher boiling fraction (6.5 g., b. p. 130～180°C/18 mmHg), and a residue (ca. 2.0 g.). This high boiling fraction was chromatographed on a short column to remove 2,4-diiodoanisole. It yielded 5.9 g. of monoiodo-*sym*-triisopropylbenzene, b. p. 173～175°C/28 mmHg.

Found: C, 54.06; H, 7.02. Calcd. for $C_{15}H_{23}I$: C, 54.56; H, 7.02%.

4) **Tetraalkylbenzenes.**—*Durene* (*sym-Tetramethylbenzene*).—Durene (4.0 g., 0.03 mol.) was dissolved in cyclohexane (5 ml.) and then iodinated with *o*-iodoanisole (11.7 g., 0.05 mol.) and sulfuric acid (7 g., 0.07 mol.) at 30～35°C. Little iodine was liberated. After 4 hr., the mixture was, diluted with water and extracted with cyclohexane. The evaporation of the solvent, followed by the chromatography of the residual oil on an alumina column, gave unchanged durene (ca. 0.5 g.) and monoiododurene (5.2 g., m. p. 80～81°C). A mixed melting point determination with an authentic specimen showed no depression.

Found: C, 46.29; H, 5.10. Calcd. for $C_{10}H_{13}I$: C, 46.16; H, 5.04%.

sym-Tetraethylbenzene. — *sym*-Tetraethylbenzene (28.5 g., 0.15 mol.) was iodinated by using *o*-iodoanisole (23.4 g., 0.1 mol.) and sulfuric acid (15 g., 0.15 mol.) at 30～33°C. After 4 hr., the mixture was treated as usual. The distillation of the oily product gave the starting materials unchanged (23.5 g., b. p. 105～135°C/19 mmHg), an iodinated products fraction (15.5 g., b. p. 155～175°C/19 mmHg), and a residue (ca. 2.0 g). To remove 2,4-diiodoanisole, the iodinated products fraction was chromatographed on an alumina column with petroleum ether. The redistillation of the resulting oily material yielded 13.5 g. of modoiodo-*sym*-tetraethylbenzene, b. p. 186～188°C/26 mmHg.

Found: C, 52.60; H, 6.57. Calcd. for $C_{14}H_{21}I$: C, 53.17; H, 6.70%.

sym-Tetraisopropylbenzene.—Attempts to iodinate this compound gave only the starting material unchanged and 2,4-diiodoanisole. A large amount of free iodine was liberated, and the disproportion of *o*-iodoanisole was the only reaction that proceeded.

5) **Pentamethylbenzene.**—To the stirred solution of pentamethylbenzene (7.4 g., 0.05 mol.) in cyclohexane (10 ml.), *o*-iodoanisole (15.2 g., 0.07 mol.) and sulfuric acid (10 g., 0.1 mol.) were added at 34～36°C over a 1.5 hr. period. After 4 hr., the mixture was worked up as usual. The chromatography of the crystalline residue on an alumina column gave unchanged pentamethylbenzene (ca. 1.0 g., m. p. 51～53°C), iodopentamethylbenzene (7.9 g., m. p. 141～142°C), and a small amount of 2,4-diiodoanisole. The melting point of our iodopentamethylbenzene differs from that of Töhl (m. p. 129°C)[5] by 12°C.

Found: C, 48.22; H, 5.59. Calcd. for $C_{11}H_{15}I$: C, 48.18; H, 5.52%.

Summary

A method has been developed for the direct iodination of certain polyalkylbenzenes by the transfer of an iodine atom of iodoanisole. It consists of the simultaneous addition of iodoanisole and sulfuric acid to the polyalkylbenzene to which the transfer is to be made. In this way, iodo compounds have been prepared from eight polyalkylbenzenes.

The authors wish to acknowledge the valuable suggestions of Professor Sango Kunichika.

Institute for Chemical Research
Kyoto University
Takatsuki, Osaka