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Selective Production of Diiodobenzene and Iodobenzene from Benzene

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Iodination of aromatic substances is an important step in the synthesis of many organic molecules including many pharmaceuticals and biochemicals. It is important to establish direct, simple, and selective methods to produce iodinated aromatics without the production of heavy metal iodides and other wastes often associated with these processes. Methods, such as the one described here, do not produce heavy metal waste nor use fluorinated solvents for environmental reasons. When iodine itself is used as a reagent, an additional benefit is derived if both iodine atoms from the molecular iodine are incorporated into the products rather than having one of the iodine atoms become waste as an iodide salt.

Recently, it was reported[1] that reaction mixtures of iodine, diiodine pentoxide (I_2O_5), activated or deactivated aromatic, and concd H_2SO_4 in acetic acid solvent selectively produce monoiodinated products in good yield. Trace amounts of diiodo products were seen in some cases, but usually no diiodo product was observed. However, both iodine atoms from molecular iodine appeared to be incorporated into the iodoaromatic product. While a large number of activated and deactivated aromatics were tested, iodination of benzene itself by this method was not attempted by these researchers.

In the current study, it has been found that when this method is used to iodinate benzene, diiodobenzene is selectively produced along with iodobenzene. Benzene is quantitatively reacted into these products when sufficient iodine is present. No other iodinated aromatic compounds are observed, even in the presence of high levels of iodine. These products are easily separated since 1,4-diiodobenzene is a crystalline solid at room temperature and 1,2-diiodobenzene and iodobenzene are liquids. None of the products was soluble in the aqueous acetic acid medium when water was added to stop the reaction. Additionally, I_2O_5, which oxidizes the molecular iodine, is not consumed during the reaction. The exact nature of the activated iodine is currently under investigation, but the ability of I_2O_5 to activate iodine without being consumed is a large advantage over other benzene iodination reactions which form diiodobenzene, since the oxidizing agents in these reactions are stoichiometrically consumed.[2−6] Also, many of these reactions involve corrosive reagents or the use of heavy metal oxidants or catalysts. The hazards associated with these reagents and their waste are eliminated in the current reaction system.

Other methods for benzene iodination reported in the literature result in the formation of iodobenzene[7−19] or mixtures of polyiodobenzenes.[3,20] A few reaction systems are reported[3,21] which can selectively regulate the number of iodine atoms substituted into the aromatic ring. However, these systems involve the use of fluorinated solvents[3] or thallium salts,[21] both of which pose environmental problems. Many reactions that produce 1,4-diiodobenzene also produce a substantial amount of tri- or tetraiodobenzene. Only iodobenzene and diiodobenzene are observed in the currently reported reaction.

For example, when 0.055 mol (4.3 g) of benzene, 0.022 mol (5.5 g) of iodine, 0.022 mol (7.3 g) of I_2O_5, and 60 μL of concd H_2SO_4 were reacted in 25 mL of glacial acetic acid at 60 °C for 40 h, the yield, based on benzene, of 1,4-diiodobenzene after purification was 8.7%; of 1,2-diiodobenzene, 1.5%; and of iodobenzene, 56%. If the amount of iodine was raised to 0.055 mol (14.0 g) while other conditions were kept constant, the yield of 1,4-diiodobenzene increased to 46%, that of 1,2-diiodobenzene increased to 8.0%, and the yield of iodobenzene decreased to 45%. Similar results were obtained with lower amounts of I_2O_5 and at temperatures between 50 and 70 °C, although no reaction was observed if I_2O_5 was absent.

In conclusion, a simple, safe, and effective method for the production of diiodobenzenes and iodobenzene in which the amount of each product can be regulated easily is presented. No heavy metals are used, thus eliminating the heavy metal salt waste normally associated with aromatic iodination reactions.

Experimental Section

General Comments. Iodine was obtained from Mallinckrodt, sulfuric acid and glacial acetic acid from Fisher Scientific, and I_2O_5 and benzene from Aldrich Chemical Co. All chemicals were used without further purification. NMR spectra were recorded at 300 MHz in acetic acid-d_4. FT-Raman spectra were obtained in glass cuvettes at 60 °C, using a NdYAG laser with a wavelength of 1064 nm. A wattage of only 500 mW was used because of the highly colored nature of the samples. Gas chromatography was obtained using a 5% phenylmethylsilicone column that is 30 m × 25 mm with a 0.25 μm film thickness. The injector temperature was 275 °C; the helium carrier gas held at 8 psi (1.03 mL/min initially through the column) with a

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(1) Keyes, A.; Johnson, D. R.; Soulen R. L. *CHED Newsletter,* **Fall 1994,** Abstract 72. Paper presented at the 208th National Meeting of the American Chemical Society, Washington, DC, August 21−25, 1994.

(2) Rozen, S.; Zamir, D. *J. Org. Chem.* **1990,** *55,* 3552−3555.

(3) Barluenga, J.; González, J. M.; Garcia-Martín, M. A.; Campos, P. J. *Tetrahedron Lett.* **1993,** *34,* 3893−3896.

(4) Rozen, S.; Zamir, D.; Menachem, Y.; Brand, M. *J. Org. Chem.* **1988,** *53,* 1123−1125.

(5) Kurgane, D.; Neilands, O.; Tilika, V. *Otkrytiya, Izobret., Prom. Obraztsy, Tovarnye Znaki* **1978,** *55,* 68.

(6) Eglitis, J.; Brinkmanis, R. *Otkrytiya, Izobret., Prom. Obraztsy, Tovarnye Znaki,* **1979,** *56,* 114−115.

(7) Muathen, H. A. *J. Chem. Res., Synop.* **1994,** 405.

(8) Bachki, A.; Foubelo, F.; Miguel, Y. *Tetrahedron* **1994,** *50,* 5139−5146.

(9) Barluenga, J.; González, J. M.; Garcia-Martín, M. A.; Campos, P. J.; Asenio, G. *J. Chem. Soc., Chem. Commun.* **1992,** 1016−1017.

(10) Sy, W.-W.; Lodge, B. A.; By, A. W. *Synth. Commun.* **1990,** *20,* 877−880.

(11) Shono, R.; Matsummuar, Y.; Katoh, S.; Ishida, K.; Kamada, T. *Tetrahedron Lett.* **1989,** *30,* 1649−1650.

(12) Makhon'kov, D. I.; Cheprakov, A. V.; Beletskaya, I. P. *Zh. Org. Khim.* **1988,** *24,* 2251−2258.

(13) Htihot'ev, M. G.; Buketova, I. A.; Polevshchikov, P. F. *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.* **1987,** *30,* 22−24.

(14) Makhon'kov, D. I.; Cheprakov, A. V.; Rodkin, M. A.; Beletskaya, I. P. *Zh. Org. Khim.* **1986,** *22,* 1117−1120.

(15) Shimizu, A.; Yamataka, K.; Isoya, T. *Bull. Chem. Soc. Jpn.* **1985,** *58,* 1611−1612.

(16) Eckelman, W. C.; Adams, H. R.; Paik, C. H. *Int. J. Nucl. Med. Biol.* **1984,** *11,* 163−166.

(17) Sugita, T.; Idei, M.; Ishibashi, Y.; Takegami, Y. *Chem. Lett.* **1982,** 1481−1484.

(18) Merkushev, E. B.; Yudina, N. D. *Zh. Org. Khim.* **1981,** *17,* 2598−2601.

(19) Ogata, Y.; Nakajima, K. *Tetrahedron* **1964,** *20,* 43−57.

(20) Mattern D. L. *J. Org. Chem.* **1984,** *49,* 3051−3053.

(21) Ishikawa, N.; Sekiya, A. *Bull. Chem. Soc. Jpn.* **1974,** *47,* 1680−1682.

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100 mL/min split flow. The temperature program starts at 50 °C for 3 min and then heats at 30 °C/min to 260 °C where it is held for 5 min. The transfer line to the mass selective detector is held at 280 °C.

General Procedure for Synthesis of Diiodobenzene and Iodobenzene. In a representative experimental procedure, iodine, I_2O_5, and concd H_2SO_4 in glacial acetic acid were heated under nitrogen in a three-necked flask with constant stirring. When the desired temperature was reached, benzene was added to the mixture, and the reaction mixture was heated and stirred. The red iodine color became fainter or disappeared after time. The reaction mixture was cooled, and distilled water was added to dissolve the I_2O_5. At this point, the 1,2-diiodobenzene and iodobenzene also separated from the aqueous layer. Filtration separated the 1,4-diiodobenzene from a biphasic filtrate containing 1,2-diiodobenzene and iodobenzene in an oily layer. These compounds were purified as described previously.[22] The 1,4-diiodobenzene was recrystallized from ethanol.

Products were identified by NMR, GC−MS, and FT-Raman of their acetic acid solutions. The melting point of 1,4-diiodobenzene was also obtained. In all cases, data matched those for authentic samples obtained from Aldrich Chemical Co. FT-Raman (CH_3COOH): 1,4-diiodobenzene 1051 (m), 684 (m); 1,2-diiodobenzene 1045 (m), 317 (m); iodobenzene 1017 (m), 996 (s), 657 (m), 266 (s).

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[22] Ogata, Y.; Nakajima, K. *Tetrahedron* **1964,** *20,* 2751−2754.