New Syntheses of Aromatic Acid Chlorides from Trichloromethylarenes. 4. Ring Chlorination of *m*-Xylene, Isophthaloyl Chloride, and Hexachloro-*m*-xylene

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Monochlorination of *m*-xylene at 0–10 °C with Lewis acid catalysts gives a mixture of 25% 2-chloro- and 75% 4-chloro-*m*-xylene. Further chlorination gives 44% 2,4- and 56% 4,6-dichloro-*m*-xylene. The 4,6-dichloro isomer is preferentially trichlorinated. Photochlorination of the side-chain hydrogens in the monochloro-*m*-xylenes can be completed with difficulty, but complete side-chain chlorination of 4,6-dichloro-*m*-xylene is accompanied by extensive chlorinolysis. Isophthaloyl chloride is monochlorinated exclusively in the 5 position. The chief product of dichlorination is the 2,5 isomer, but the 4,5 isomer was also isolated. 1,3-Bis(trichloromethyl)benzene (hexachloro-*m*-xylene, HCMX) yields the 4-chloro- and 5-chloro-HCMX isomers in the ratio of 1:2, along with a little 2-chloro-HCMX. The various chloro-HCMX were converted to chlorinated isophthaloyl chlorides by heating at 250 °C with sulfur dioxide.

Conversion of trichloromethylarenes to aroyl chlorides by several new methods was described in the preceding papers.[1–3] Isophthaloyl chloride was the major target of this research, to be prepared from hexachloro-*m*-xylene (HCMX)[4] obtained by side-chain chlorination of *m*-xylene. Since HCMX was always accompanied by small amounts of ring-chlorinated derivatives, the ring-chloro-*m*-xylenes were studied in order to identify the impurities encountered during the main effort.

Chlorination of *m*-Xylene. *m*-Xylene is very reactive toward electrophilic ring chlorination, especially in the presence of small amounts (0.5–3.0%) of Lewis acids. Preparative ring chlorination is usually catalyzed by iodine, ferric chloride, or antimony trisulfide. Attempts to stop the reaction at the monochloro stage were unsuccessful, except by chlorinating to very low conversions. Substantial amounts of dichloro- and trichloro-*m*-xylenes were present even before the *m*-xylene had been completely consumed.

2-Chloro- and 4-chloro-*m*-xylene were formed in the ratio 1:3 with each of the catalysts mentioned, at 0–10 °C. Since there are two 4(6) positions, the reactivity ratio is 1:1.5, indicating that two methyl groups flanking the 2 position exert little more steric hindrance to chlorine introduction than does the single methyl groups adjacent to the 4(6) position. A patent claim[5] that use of antimony trisulfide as chlorination catalyst changed the 2- to 4- ratio to 1:9 could not be verified. Samples at various times during each chlorination always showed a 1:3 ratio.

With respect to the dichloroxylenes, the ratio was 44% of 2,4- to 56% of 4,6-dichloro-*m*-xylene early in the run, before trichlorination was detectable. This ratio agrees with that predicted (43% 4,6- and 57% 2,4-) from the relative reactivities of the 2 and 4(6) positions deduced above plus the assumption that the ratio is not altered by a chlorine atom. However, as chlorination was continued and trichlorination occurred, the ratio changed. As the last of the *m*-xylene disappeared, a sample contained 45% mono-, 45% di-, and 10% tri- and tetrachloroxylene. The 2,4- to 4,6- ratio was then 59:41, the reverse of the result at lower conversion, showing that the 4,6 isomer was preferentially trichlorinated. Further chlorination to two chlorines per molecule (average) gave a dichloro fraction containing 62% 2,4- and 38% 4,6-. The monochloro composition remained unchanged at 1:3.

The chlorination mixture was readily separated by fractional distillation into monochloro and dichloro fractions. The individual isomers could not be separated with the column at hand. However, about half of the 4,6-dichloro-*m*-xylene could be frozen out of the dichloroxylene fraction.

Side-Chain Chlorination of Chloroxylenes. Pure 2-chloro-*m*-xylene was prepared from 2,6-dimethylaniline by the Sandmeyer reaction.[6] Photochlorination of the side chains at 100–120 °C proceeded rapidly until four chlorines had been introduced. Complete replacement of the side-chain hydrogens required prolonged treatment at 150 °C. The product, 2-chloro-HCMX, has been previously reported. Chlorination of the 1:3 mixture of 2- and 4-chloro-*m*-xylene was conducted in the same fashion. The mixture of 2-chloro- and 4-chloro-HCMX was separated by fractional distillation from 10–15% of chlorinolysis products (which included hexachlorobenzene and octachlorotoluene). The higher boiling 2-chloro-HCMX could be readily purified by crystallization. Pure 4-chloro-HCMX could not be obtained by this method, although it has been prepared by chlorination of pure 4-chloro-*m*-xylene.[7] The impure material could be converted to 4-chloroisophthaloyl chloride as described below.

Side-chain chlorination of 4,6-dichloro-*m*-xylene was extremely slow; after 44 h at 125–150 °C, when extensive chlorinolysis was evident, GC examination still showed the presence of hexa- and heptachloroxylene. No attempt was made to chlorinate 2,4-dichloro-*m*-xylene, since it is known that the prototype 2,6-dichlorotoluene cannot be carried beyond the 2,6-dichlorobenzal chloride[8] stage because of chlorinolysis to 1,2,3-trichlorobenzene.[9]

Chlorination of Isophthaloyl Chloride. Electrophilic chlorination (ferric chloride catalyst) is quite slow, even at 180 °C. After 23.5 h, the mixture contained 1.7% IPC, 67.6% 5-chloro-IPC, and 29.5% dichloro-IPC, and 4.3% unidentified material. Hexachlorobenzene crystallized in the head when this mixture was distilled. Pure 5-chloro-IPC[10] was separated by fractional distillation and shown to be free of the 2- or 4-chloro isomers by GC analysis of the methyl esters.

The major dichloro-IPC was the 2,5 isomer, which was separated from the dichloro cut by crystallization; it was identified by comparison to the product prepared from 2-chloro-*m*-xylene as described below, and by its single NMR peak. 4,5-Dichloro-IPC, isolated by repeated fractionation and crystallization, was identified by its AB_2 NMR pattern and by comparison to the material prepared below.

The small amount of trichloro-IPC was about half 4,5,6-trichloro-IPC, identical with that prepared below. The isomeric 2,4,5 isomer was not isolated.

Chlorination of Hexachloro-*m*-xylene (HCMX). Bradsher[7] obtained 5-chloro-HCMX by ferric chloride catalyzed chlorination of HCMX but did not mention any isomers. In our hands, the 4-chloro isomer was formed at about half the rate of the 5-chloro isomer, and a small amount of 2-chloro

Table I. Chloro-HCMX and Derived Isophthaloyl Chlorides, Dimethyl Esters, and Acids[k]

Mp, °C (registry no.)				
Cl_nHCMX	ICl	Ester	Acid	Formula
		2-Chloro Derivatives		
136–137[a] (36747-57-6)	74–77 (36747-58-7)	15 (60047-40-7)	223[b] (13049-16-6)	$C_8H_3Cl_3O_2$ $C_{10}H_9ClO_4$
		4-Chloro Derivatives		
<10[a] (27260-64-6)	<0[c]	51–52[c] (60047-41-8)	294[c] (2845-85-4)	
		5-Chloro Derivatives		
77–78[a] (60047-42-9)	<0[e]	80[a,e] (20330-90-9)	279–280[a,e] (2157-39-3)	
		2,5-Dichloro Derivatives		
112–113 (60047-43-0)	38–39 (60047-44-1)	108–109 (60047-45-2)	255–262 (60047-46-3)	$C_8H_2Cl_8$ $C_8H_4Cl_2O_4$
		4,5-Dichloro Derivatives		
64–65 (60047-47-4)	37–38 (60047-48-5)	79–80 (60047-49-6)	305–306[f] (6660-66-8)	$C_8H_2Cl_8$ $C_8H_2Cl_4O_2$ $C_{10}H_8Cl_2O_4$
		4,6-Dichloro Derivatives		
116–117[g] (25843-37-2)	76–77[g] (2855-01-8)	98–101[g] (60047-50-9)	353–356[g] (6660-65-7)	$C_8H_2Cl_8$
		Unidentified Dichloro-HCMX		
112–113[h]				$C_8H_2Cl_8$
		4,5,6-Trichloro Derivatives		
131–132 (60047-51-0)	73–75[i] (5002-45-9)	143–144[j] (20019-06-1)	>300[i] (5002-24-4)	C_8HCl_9 $C_{10}H_7Cl_3O_4$

[a] Reference 7. [b] G. Stapleton and A. I. White, *J. Am. Pharm. Assoc.*, **43,** 193 (1954). [c] German Patent 282 133; French Patent 820 697. [d] E. A. Leporskaya and A. A. Petrov, *Zh. Obshch. Khim.*, **28,** 1432 (1958); *Chem. Abstr.*, **53,** 1106 (1956). [e] Reference 10. [f] P. E. Hoch, *J. Org. Chem.*, **26,** 2066 (1961); U.S. Patent 3 235 586. [g] J. Pollak and Z. Rudich, *Monatsh. Chem.*, **43,** 209 (1922), report the respective melting points 113–114, 74–76, 97–98, and 279–281 °C. The agreement with the present results is good except for the acid. [h] This material depresses the melting point of the 2,5- and 4,6-dichloro-HCMX isomers. Ir did not permit a structural assignment. The NMR spectrum showed a single broadened peak at 7.62 ppm, compared to 7.69 and 9.02 ppm for the 4,6-Cl_2-HCMX. The sample contained 1.2% of an impurity (GC). It is not 2,5-dichloro-HCPX, known to melt at 202–204 °C (ref 11), although other melting points have been recorded in U.S. Patent 3 253 900 (198.5–199.5 °C) and U. S. Patent 2 814 648 (150 °C, clearly the wrong material). Reference 11 gives a rigorous structure proof. It may be 2,3-dichloro-HCPX from ipso substitution. [i] P. E. Hoch, U.S. Patent 3 221 044 mp 72–73 and >300 °C for the acid chloride and acid, respectively. [j] Needles from CCl_4. [k] All new compounds gave satisfactory microanalyses (±0.4%) for C, H, Cl: Ed.

isomer was also detected by GC. In other words, the 5 position is about four times as reactive as an individual 4(6) position. For preparative purposes, the chlorination at 110 °C was monitored by GC and stopped when the concentration of monochloro-HCMX had reached its maximum, but while considerable unreacted HCMX remained. The monochloro-HCMX fraction was readily separated from unchlorinated and dichlorinated HCMX by distillation, and a second distillation achieved a fair separation of the 4- and 5-chloro isomers. The latter was readily purified by crystallization from hexane. The liquid 4-chloro isomer was not obtained pure, but it was identified by the results of further chlorination.

Chlorination of 2-Chloro-HCMX. Chlorination in carbon tetrachloride was accompanied by extensive chlorinolysis. The neat material did not react with chlorine (ferric chloride) just above its melting point (137 °C), and higher temperatures merely caused more chlorinolysis. A second chlorine could be introduced with the Ballester–Silberrad reagent (sulfuryl chloride–disulfur dichloride–aluminum chloride)[11] exclusively in the 5 position. The isomeric 2,4-dichloro-HCMX could not be detected.

Chlorination of 4-Chloro-HCMX Ferric chloride catalyzed chlorination proceeded at a moderate rate at 125 °C; antimony pentachloride was inactive as catalyst. It is not selective, however, since trichloro-HCMX was observed long before the monochloro-HCMX had disappeared. When the starting material had been consumed, a substantial amount of hexachlorobenzene and octachlorotoluene had been formed. Neither 4,6- nor 2,4-dichloro-HCMX was isolated, though the former should be obtainable by fractionation of a large run. 4,5,6-Trichloro-HCMX was the only pure product isolated by distillation and crystallization; the isomeric 2,4,5- and 2,4,6-trichloro-HCMX were not definitely identified, but a GC peak about one-fourth the size of the 4,5,6 isomer peak is probably one of these. Preparative gas chromatography did not succeed in this case.

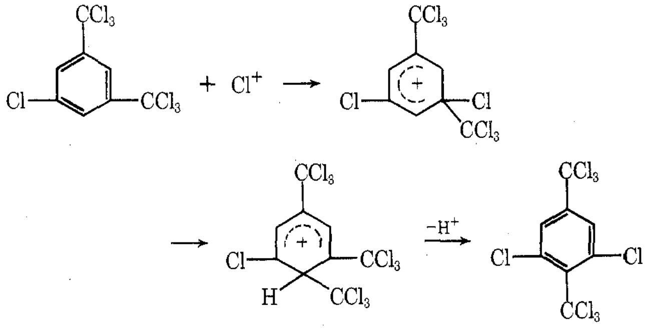
Chlorination of 5-Chloro-HCMX. This isomer was the least reactive toward chlorination, since all its open positions are ortho disubstituted. The literature implied that it would be impossible to introduce a chlorine atom between the two trichloromethyl groups. Indeed, about 80% of the product was the 4,5-dichloro isomer, but it was accompanied by 20% of the

2,5 isomer, identical with that obtained above. Thus an individual 4(6) position is only twice as reactive as the 2 position.

Chlorination of Dichloro-HCMX. The 2,5-dichloro isomer resisted further chlorination by the Ballester method, so iron-catalyzed chlorination was not attempted. The 4,5 isomer reacted very slowly at 145 °C with iron catalysis, and chlorinolysis was a major side reaction. 4,5,6-Trichloro-HCMX was the chief product, accompanied by an isomer peak (about one-fourth its size) which should be the 2,4,5-trichloro isomer.

The 4,6-dichloro isomer was not studied, since it would probably be even less reactive and more susceptible to chlorinolysis. The 4,5,6 isomer should be the only trichloro product, for the "buttressing" effect of the two ortho chlorines should push the two trichloromethyl groups over the 2 position, further restricting access by a chlorine atom.

Ipso Chlorination. Since many of the above reactions yielded unidentified GC peaks, frequently more peaks than isomers available, it is probable that a certain amount of ipso substitution occurred. It is illustrated with 5-chloro-HCMX.



No product derived from migration of a trichloromethyl group was positively identified, however.

Conversion of Chlorinated HCMX to Chlorinated Isophthaloyl Chlorides. The various chlorinated HCMX were transformed to the acid chlorides by heating with sulfur dioxide without catalyst.[1] Since the products were destined for another purpose, possible catalyst residues could not be tolerated. All of the chloro-HCMX, even the sterically unhindered 5-chloro-HCMX, reacted much more slowly with sulfur dioxide than did the parent HCMX. The retarding effect of electron-withdrawing groups on the sulfur dioxide reaction was noted previously with the chloro- and fluorobenzotrichlorides.[1] However, each was ultimately converted completely to the acid chloride, although prolonged treatment was required with the more hindered compounds.

The objective of this study, as noted above, was to identify the ring-chlorinated by-products of HCMX preparation by *m*-xylene chlorination. It was expected that chlorination conditions could then be modified so as to minimize ring chlorination. Accordingly, the residue from fractionating HCMX was examined. Its composition was 2-Cl, 20%; 4-Cl, 60%; 5-Cl, nil; 4,6-Cl_2, 10%; 2,5-Cl_2 (?), 3%; 4,5,6-Cl_2, 6%. Several unidentified trace components were also present. The absence of the 5-chloro isomer shows clearly that ring chlorination occurred early while *m*-xylene was still present, not later when extensive side-chain chlorination had occurred. Johnson in this laboratory then showed that α-chloro- and α,α'-dichloro-*m*-xylene were not ring chlorinated under photochlorination conditions. It was then simple to decrease ring chlorination from 10–13% to 3–4% by the device of reducing chlorine flow during the period while the last of the *m*-xylene was being monosubstituted, i.e., while the degree of substitution was 0.9–1.2 chlorines per molecule.

To see whether the material could be converted to a polychloro-IPC useful as a monomer for flame-retardant polymers, the above chloro-HCMX residue was chlorinated with ferric chloride catalyst until extensive chlorinolysis became apparent. The product was treated exhaustively with sulfur dioxide until GC analysis showed no further change. The product contained small amounts of 2-Cl and 4-Cl, mostly a mixture of 4,5- and 4,6-Cl_2, and some 4,5,6-trichloroisophthaloyl chloride. The presence of small amounts of 2,5-Cl_2 and isomeric Cl_3 isophthaloyl chlorides was inferred from the GC analyses of both the Cl-HCMX and the acid chloride mixtures. Numerous small unidentified peaks were also present.

Tabular Survey of Physical Properties of Chlorinated HCMX and Isophthaloyl Chlorides. Identification of the many compounds discussed above was facilitated by comparison of their physical properties. These are collected in Table I. In addition, infrared and NMR spectra were consistent with the structures assigned.

Experimental Section

Chlorinations were conducted by passing cylinder chlorine through an empty trap into the liquid maintained at the temperature mentioned in the text. The effluent hydrogen chloride and excess chlorine escaped through the condenser past an empty trap into a caustic scrubber. Electrophilic chlorinations were conducted in the presence of 0.5–3.0% (w/w) of anhydrous ferric chloride, 1.0% of iodine, or 2.0% of antimony trisulfide.[5] For side-chain chlorination, the catalyst was omitted and the flask was irradiated with two Westinghouse 275-W sunlamps. The course of the reaction was monitored by GC analysis on 20% SE-30.[1]

The catalyst was removed by washing the product with warm 6 N hydrochloric acid containing sodium bisulfite, followed by a water wash. The product was dried either with calcium chloride or, for viscous materials, by vacuum pumping.

Occasionally the mixture was first distilled rapidly at 0.1 mm in simple apparatus to detar it. The product was then fractionally distilled through a 1-m precision column packed with Helipak (Podbelniak Co.) loose packing; both nickel and Hastelloy B were resistant to corrosion, but stainless steel (304) was slowly corroded and darkened the product.

The reactions with sulfur dioxide were conducted in a 240-ml Hastelloy C shaker tube at about 250 °C, as described previously.[1] If GC analysis of the product showed that conversion was incomplete, it was returned to the bomb with an equal weight of thionyl chloride, a large excess of sulfur dioxide was added, and the mixture was again heated at 250 °C for several hours. No attempt was made to find optimum conditions for single-pass conversion.

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Registry No.—*m*-Xylene, 108-38-3; isophthaloyl chloride, 99-63-8; hexachloro-*m*-xylene, 881-99-2.

References and Notes

(1) Part 1: C. S. Rondestvedt, Jr., *J. Org. Chem.*, accompanying paper in this issue.
(2) Part 2: C. S. Rondestvedt, Jr., *J. Org. Chem.*, accompanying paper in this issue.
(3) Part 3: C. S. Rondestvedt, Jr., *J. Org. Chem.*, preceding paper in this issue.
(4) See footnote 7 of ref 1 for a discussion of the abbreviations used in these papers.
(5) British Patent 778 642 (1951).
(6) British Patent 822 717 (1959).
(7) C. K. Bradsher, P. M. Gross, M. E. Hobbs, R. S. Kittila, L. Rapoport, P. Tarrant, and G. West, *J. Am. Chem. Soc.*, **70**, 1317 (1948).
(8) The *Chemical Abstracts* name is 2,6,α,α-tetrachlorotoluene.
(9) German Patent 1 237 552 (1967); French Patent 1 343 178 (1963); H. E. Fierz-David and L. Blangey, "Fundamental Processes of Dye Chemistry", 7th ed, Interscience, New York, N.Y., 1949, p 162.
(10) N. Rabjohn, *J. Am. Chem. Soc.*, **70**, 3518 (1948); Belgian Patent 620 385 (1963).
(11) M. Ballester and C. Molinet, *Chem. Ind. (London)*, 1290 (1954); M. Ballester, C. Molinet, and J. Castaner, *J. Am. Chem. Soc.*, **82**, 4254 (1960).