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FORMATION OF 1,3,4,5,6-PENTACHLORO-4-METHOXYCYCLOHEXENE FROM THE CHLORINE CHLORINATION OF 4-CHLOROANISOLE

William David Watson*
The Dow Chemical Company
Organic Chemicals Production Research
Midland, Michigan 48640 U.S.A.

Jerry P. Heeschen
The Dow Chemical Company
Analytical Laboratories
Midland, Michigan 48640 U.S.A.

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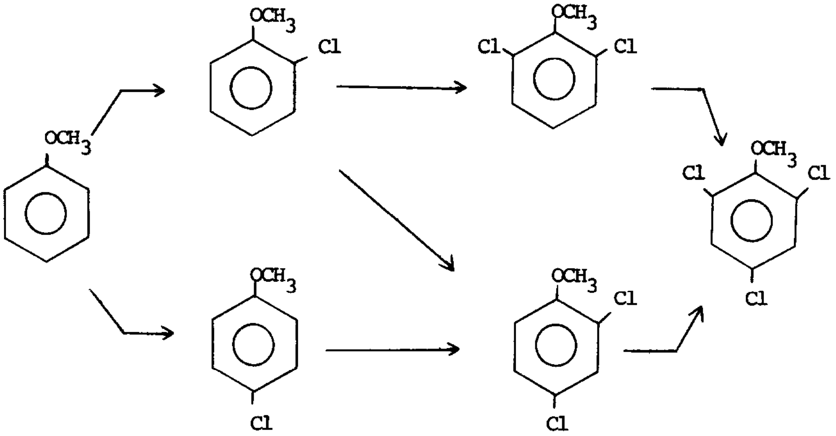
The chlorine chlorination of anisole[1-4] and 4-chloroanisole[5] has been previously reported. In general, conversions to the monochloroanisoles were kept low so that an accurate para/ortho ratio[1-4] or relative rate data[4,5] could be obtained. Relatively low temperature chlorine chlorinations of anisole have always been assumed to produce only electrophilic aromatic products via the following scheme.

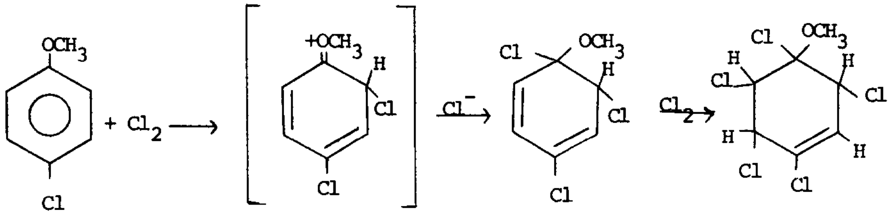


However, upon reinvestigating the chlorine chlorination of anisole at 35°C, it soon became apparent by analyzing the chlorination mixtures by nmr that non-aromatic compounds were being formed. As soon as chlorine was introduced, non-aromatic peaks appeared in the proton nmr spectrum, and according to integration of the methoxy protons a maximum of 28% of a new non-aromatic product was formed when dichlorination was maximized. At first these results were thought to occur via some photochemical process catalyzed by light or an impurity. However, when the reaction was rerun in the dark using purified reagents, the same results as above were obtained. Chlorination of 2-chloroanisole and 3-chloroanisole yielded no non-aromatic product whereas chlorination of 4-chloroanisole produced the non-aromatic species in 35% yield. Chlorination of 2,4-dichloroanisole and 2,6-dichloroanisole also yielded none of the non-aromatic species. Thus, it was established that this new product was produced only from 4-chloroanisole. Purification and isolation of the non-aromatic species was accomplished by first distilling the chloroanisoles from the reaction mixture (bp 90-100°C @ 5 mm Hg). The residue was chromatographed through a column packed with 80/200 mesh neutral alumina containing 5-7 wt. % water. Hexane was used as an eluent. In this fashion it was possible to obtain the new species in high purity as a viscous liquid that slowly solidified (mp 65.0-67.0°C). The compound has been identified as 1,3,4-5,6-pentachloro-4-methoxycyclohexene **2**.

The nmr spectra show a strong solvent dependence. The 100 MHz nmr spectra of purified material in CCl_4 and in benzene are described by the following first-order interpretation of the spectra as **2**. Chemical shifts, δ ppm, and splittings in CCl_4/benzene are: OCH_3 (3.54, s/3.02, s); H(2) (6.09, d of t/5.57, d of d); H(3) (4.98, d/4.09, d of d); [H(5) + H(6)] (4.55, d/-); H(5) (-/4.69,d); H(6) (-/4.5,d of d of d). In benzene solution the absorptions assigned to H(5) and H(6) are an obvious AB quartet with J(56)=8.2 Hz and with the upfield pair of lines being split further into doublets of 1.3 and 0.6 Hz. In CCl_4 solution the shift between H(5) and H(6) is so small that their combined pattern resembles the A part of an A_2X system where H(2) is the X nucleus. The following magnitudes of coupling constants, in Hz, describe the splittings observed in CCl_4/benzene solution: J(23)(6.4/6.6); J(25)(-/-(i.e.<0.5)); J(26)(-/1.3); (1/2)[J(25) + J(26)] (0.6/0.65); J(36)(-/0.6); J(56)(-/8.2). All spectral parameters are consistent with normal expectations for **2**. The relatively large coupling of 8.2 Hz between H(5) and H(6) implies that they are trans-axial to one another much of the time, since the alternative cis-eclipsed configuration in unlikely on steric grounds.

The infrared spectra of **2** in CCl_4 and CS_2 show bands at 3008, 1649, and 790 cm^{-1} which support the trisubstituted double bond, bands at 2938, 2835, 1188, 1160, and 1038 cm^{-1} which support a saturated methyl ether group, and bands at 742, 717, 645, 620, and 590 cm^{-1} which support the carbon chlorine bonds.[6] Other major absorbances were observed at 1210, 1140, 975, and 868 cm^{-1}. The mass spectrum shows a weak molecular ion (M^+) at 282 (5Cl). Other major fragments and their tentative identification are 247 (M^+-Cl), 211 (M^+-Cl-HCl), 210 (M^+-2HCl), 195 (3Cl), 176 (2Cl), 133 ($C_5H_3Cl_2^+$), and 126 ($CH_3OCClCHCl^+$, most intense). The molecular weight of **2** was determined to be approximately 274 by ebullioscopy which is consistent with the assignment of 282 as the molecular ion. In addition to the above data, elemental analysis showed the following results: found C, 30.0; H, 2.45; Cl, 62.7 (calculated for $C_7H_7Cl_5O$: C, 29.5; H, 2.46; Cl, 62.4).

2 is formed from the addition of two molecules of chlorine to 4-chloroanisole. A possible pathway to form **2** could be the 1,2-addition of chlorine to form **1** (1,4-addition across the 2,5-position is also possible) and then either 1,2- or 1,4- addition of chlorine to the unsubstituted double bond of diene **1** to form **2**.[7]

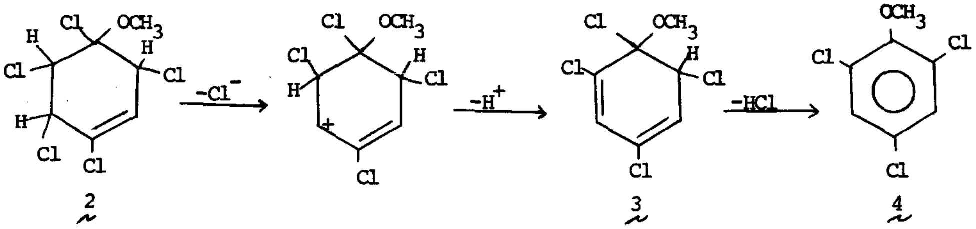


1

2

Under the reaction conditions **2** is not further chlorinated to the cyclohexane derivative; trisubstituted double bonds with one electron withdrawing group are known to be unreactive.[8] It is unexplained at present why 4-chloroanisole forms an addition product while 2- and 3-chloroanisole do not.

2 has been examined chemically on a limited basis. Pyrolysis in a glc column at 250°C led to a variety of products including chloromethane, various chloroanisoles, and chlorophenols. When **2** was eluted with hexane through a column of dry alumina or silica gel, 2,4,6-trichloroanisole **4** was isolated in quantitative yield. **4** was identified by proton nmr spectrum, mass spectrum, ir spectrum, and the mp (60.0-61.0°C) which were identical to an authentic sample of **4** prepared by the reaction of sodium 2,4,6-trichlorophenate and dimethylsulfate. **4** was also formed by the slow thermal decomposition of **2** at 150°C. The aromatization of **2** to form exclusively **4** could occur by an E1 mechanism[9] where the first step would be the loss of chloride ion from C-6 to form the allylic carbocation. Then loss of a proton would yield diene **3** which would readily lose HCl to form **4**.



The formation of **4** from **2** further verifies our structural assignment of **2** since the other pentachloromethoxycyclohexene isomers that would yield **4** on aromatization are not consistant with the spectral data.

Unusual reaction products from electrophilic attack of alkyl aryl ethers have been previously reported. Nitration of 4-haloanisoles in acetic acid results in a 28-40% yield of 4-nitroanisole due to attack at the ipso position (i.e., the position bearing the substituent).[10] Recently, de la Mare[11] has reported the isolation of chlorinated cyclohexanones and cyclohexadienones from the chlorination of 3,4-dimethyl anisole. However, in this work no keto products were obtained as evidenced by a lack of carbonyl absorbances in the ir.

The reaction described in this paper appears to be a general one for aryl ethers since phenetole and diphenyl ether[12] give similar results. These and other substituted aryl ethers are presently under investigation.

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