SOME CHLORO DERIVATIVES OF O-CRESOL

THESIS FOR THE DEGREE OF M. S.

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Thesis

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by

Wilbur S. Claus

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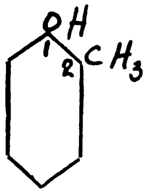
INTRODUCTION

In the subsequent investigation of the chloro derivatives of o-cresol, it was noticed that there is seemingly some confusion in the nomenclature of these derivatives. The 4 chloro-o-cresol is often labeled as 5 chloro-o-cresol; 3 chloro-o-cresol as 6 chloro-o-cresol; 3, 5 dichloro-o-cresol as 4, 6 dichloro-o-cresol. This is due to the fact that some investigators use the methyl group as number one, while others use the hydroxyl group as number one in their system of nomenclature.



This work uses the hydroxyl group as the ordinal group in all of the compounds listed, as shown above.

HISTORICAL

4 Chloro-o-cresol

Some of the early workers in this field were Claus and Jackson (J. prakt. chem., (2) 38, 328 (1888)) who prepared 4 chloro-o-cresol by the action of chlorine in an acetic acid solution in the presence of iron. They give the compound a melting point of 35°; boiling point, 220°.

In 1898, Peratoner and Condorelli (Gazz. chem. Ital., 28 I, 211) prepared the compound by the action of sulfuryl chloride on o-cresol.

It was in 1919 that Datta and Mitter (J. Am. Chem. Soc., 41, 2088 - 58) again prepared it by chlorinating the aqueous solution of the 4 - sulfonic acid derivative. They state that the chlorine replaces the sulfonic acid group with the formation of mineral acids. Their product melted at 47°. (This will be discussed in detail in Section III (Discussion) of this thesis.)

Morgan and Burstall (J. Chem. Soc., London 1928, 3260-70) obtained, by the interaction of selenium oxychloride on o-cresol in chloroform solution with progressive halogenation, this derivative as one of the many and varied products. Their compound method at 48°.

Th. de Crauw (Rec. Trav. Chem. Pays-Bas 50, 753-92; C. 1931, 4756) prepared 4 chloro-o-cresol by treating 2, - 5 dichlorotoluene with sodiummethylat which gave an impure product along with its isomer, 3 - methyl - 4 chloro phenol.

6 Chloro-o-cresol

The literature reveals meager and conflicting information concerning the preparation, properties, and proof of structure of this compound. This derivative with the chlorine atom ortho to the hydroxyl group is often confused with the derivative in which the chlorine atom is ortho to the methyl group (3 chloro-o-cresol).

Two - methyl - 6 - chlorophenol was first prepared, and then patented by Raschig (C. 1905 I, 1448: D. R. P. 160304). He states that by drying at 100° the o-chor-o-cresol - p-sulfonic acid, the desired product is obtained.

It was also prepared and patented by Fahlberg, List & Co., (D. R. P. 256345; C 1913 I, 866; Frdl. 8, 132: 11, 191). They give a boiling point of 185° (uncorr.).

Bures (Chem. Litzy, 21-22, 108, 142, 222, 261, (1927)) stated that ortho chloro and ortho bromo-o- and m-cresols are prepared by direct halogenation at 20°C. by slow addition of molar quantities of halogen to molar quantities of the cresol. The reaction is carried out without the aid of a catalyst. He, however, reports no properties or proof of structure of the desired compound.

Other references are Th. de Crauw (loc. cit.) and Anwers and Wittig (Ber., 57 B, 1270-5 (1924)) - neither of which give the method of preparation or properties of the listed o-chlor-o-cresol.

Many of the references in the literature pertaining to the 6 chloro-o-cresol deal with the preparation of the 3-chloro-o-cresol. It can be seen from the above that the information concerning the 6-chloro-o-cresol is unsatisfactory and incomplete, as revealed in the literature.

4, 6-dichloro-o-cresol

Zinke (A. 417, 206) prepared this compound by passing chlorine into a cold solution of o-cresol in carbon tetrachloride. He gives a melting point of 55° (out of benzene).

Claus and Rieman (Ber., 16, 1601) and Claus and Schweitzer (Ber., 19, 927) prepared the 4, 6 dichloro derivative by passing chlorine gas into a vigorous boiling solution of o-cresol. Their product melted at 55°.

Martini (Gazz. chem. Ital., 29 II, 60) obtained the desired product by the use of sulfuryl chloride on o-cresol.

Bures (loc. cit.) in his extensive survey of the chloro- and bromo-derivatives of o- and p - m - cresol gives a yield of 95 - 97%; mp. of 56°, and bp. of 226.5°.

Morikawa and Sakamoto (J. Chem. Soc., Japan 51, 275-7) (1930) : C. A. 26, 706 (1932) report that they were able to prepare the 4, 6-dichloro compound by passing chlorine into o-cresol in the presence of PCl_5 under direct sunlight and high temperature.

A recent patented procedure, Farbenind, (Fr. 724, 779 (Oct. 20, 1931) : C. A. 1932, 4827) stated that "cresols containing <u>n</u> cl atoms are prepared by treating a mixture of chlorotoluenes containing (n - 1) Cl atoms and chlorotoluenes containing <u>n</u> Cl atoms (the former largely predominating) with an alcoholic or aqueous alcoholi alkali hydroxide under pressure and at a temperature at which only the (n - 1) - chlorotoluene reacts. The amount of alkali hydroxide is calculated with respect to the (n - 1) - chlorotoluene".

DISCUSSION

The Sulfonation of o-Cresol

During the last few years a great deal of work has been done in this laboratory with the halogenation of phenol and phenolic compounds. Some of this investigation has been done by the method of sulfonation. However, some difficulty has been encountered in obtaining ortho halogen substitution. In most cases this has been done by protecting the para position or the para and one ortho position with sulfonic acid groups. Some of the important papers related to this problem are those of Peterson (Master's Thesis, 1933); Chen (J. Am. Chem. Soc., 55, 4214 (1933)); Hutchinson (J. Am. Chem. Soc., 54, 1504 (1932); and Ballard (Master's Thesis, 1932).

The halogenation of sulfonated phenol has been quite thoroughly discussed in Ballard's work. No attempt will be made to review that phase of sulphonation except inasmuch as it concerns o-cresol. The more important references are M. Tanaka and K. Jutani (J. Pharm. Soc., Japan 517, 247-252; C. A. 20, 2669); Datta and Bhoumick (J. Am. Chem. Soc., 43, 303, (1921)); Obermiller (Ber., 40, 3631, 3640) and Merck (Ber., 27, R 957).

Campbell (J. Chem. Soc., 121, 847-57 (1922)) stated in his study on the sulfonation of o-cresol that the speed of sulfonation is retarded by the methyl group to the hydroxyl group to the least extent at 20° (approximately one-third the degree of the para methyl group) and that as the temperature of sulfonation increases the retarding influence of the o-methyl group diminishes somewhat rapidly up to about 60°. Above this temperature the influence is only very slightly progressive.

Datta and Mitter (loc. cit.) stated that chlorine replaces the sulfonic acid group, wherein an aqueous solution, with the production of aromatic halogen derivatives. Later Datta and Bhoumick (loc. cit.) stated that frequently halogens not only replace the sulfonic acid groups, but that usually more halogens enter the ring with the formation of higher halogen derivatives. They believed this to be a good general method of preparation of halogen derivatives of pheolic compounds since they found that replacement of the sulfonic acid groups ($-SO_3H$) takes place readily at ordinary temperatures in the case of compounds having one or more hydroxyl groups attached to the nucleus.

Claus and Jackson (loc. cit.) found that by heating one part of o-cresol with one and one-half parts of concentrated sulfuric acid for 6 to 8 hours on a steam bath that the p-sulfonic acid derivative was prepared.

Engehardt and Latschinow (z. 1869, 621); Hautke, (Ber., 20, 3210); Neville and Winther (Ber., 13, 1946); Gerver (Ann. 169, 386); Hayduck (Ann. 172, 213); BASF, (D. R. P. 265, 415: C. 1913 II 150; Frdl 11, 189); and Datta and Mitter (loc. cit.) have also prepared the p-sulfonic acid derivative in similar ways.

The last two named authors stated that they were able to separate the insoluble o-sulfonic acid derivative from the soluble p-sulfonic acid derivative by pouring a cold sulfonated mixture of o-cresol into water. In repetition of this work, an innumerable number of trials failed to duplicate the results of these authors. To explain this discrepancy, it was assumed that the o-cresol used by the author was more pure (i.e. less contamination with the p-isomer) or that some important condition of the process as previously carried out had not been noticed or recorded.

The 4, 6-disulfonic acid derivative was prepared by the action of fuming sulfuric acid on o-cresol and heating on the steam bath by Claus and Jackson (ibid p. 334).

Haase (Ann. 230, 293): and Zehenter (Monatsh., 33, 345) also prepared the 4, 6-disulfonic acid derivatives from similar related compounds. Probably the most complete discussion of sulfonation, in general, with methods, examples, and procedures is given by Lassar-Cohn (Arbeits Methoden fur Organische Chemische Laborataorien, 5th ed., 919-980, (1923)).

Nitro-o-cresols

The nitro derivatives of o-cresol have been studied by a number of investigators. Those nitro derivatives especially related to this study are the 4 - nitro -, 6 nitro -, and the 4, 6-dinitro-o-cresols. Of the three mentioned nitro derivatives, the 4 nitro compound has a recorded melting point range of 79 to 95°. Some interesting facts were observed concerning these nitro compounds as prepared as intermediates of the chloro-o-cresols.

Schulta (Ber., 1907, 40, 4319) has reported one of the best procedures for mononitration. He records a 25 - 25% yield of the 6 nitro with about 75% formation of the 4 nitro-o-cresol by nitrating in the presence of benzene at 20°.

Neville and Winther (Ber., 1882, 15, 2978) reported that the 4 nitro derivative exists in either the anhydrous or the monohydrate form. They record the melting point of only the monohydrate as ranging from 30 - 40°.

Gibson (J. Chem. Soc., 127, 428) (1925)) stated that the 4 nitro derivative, when formed by action of HNO_3 on o-cresol in glacial acetic acid at 15°, and when recrystallized from hot benzene solution was deposited in fine yellow needles, which when touched or pressed became a powder. He gives a melting point of 96° of the anhydrous powder 4 - nitro derivative, stating that it melts as low as 75°, but depends upon the rapidity of heating. In repeating Gibson's work we obtained after many recrystallizations from hot benzene, the 4 nitro compound in light brown needles without the formation of the powder, having a constant melting point of

92 - 93.0°.

The 6 nitro-o-cresol used in the preparation of the 6 chloro-o-cresol was prepared by Gibson's method (loc. cit.), having a boiling point of 102 - 103°/9 mm. and melting point of 69.5 - 70°. He records a yield of 35% crude product.

Koetschet and Koetschet (Helv. Chemi. Acta 13, 474 - 82 (1930): C 1930 II, 1368) prepared it from o-toluidine. They give their maximum yield as 35%. Mp. 69 - 70°.

Veibel (Ber., 63, 2074-82 (1930)) has reported an exhaustive quantitative study of the preparation of the 6 nitro and 4 nitro compounds by using a mixture of HNO_3 and HNO_2.

The 4, 6-dinitro-o-cresol has been formed by the action of nitric acid on related compounds by Ullman and Sane (Ber., 1911, 44, 4730); Cain and Simonsen (J., 1914, 105, 156) Spiegel, Munblit, and Kaufmann (Ber., 1906, 39, 3240); Hofmann and Millar (Ber., 1881, 14, 568); Rapp (Ann., 1884, 224, 175); Wieland (Ber., 1921, 54, 1776); Hesse (Ber., 52, 1173); Ponzio (G., 46 II, 60); Robinson (J. Chem. Soc., London, 109, 1086); Kehrmann (Ber., 48, 2086); Datta and Varma (J. Am. Chem. Soc., 41, 2041); Frische (Ann., 224, 138); Oliveri-Fortorie (G., 28 I, 307); Noelting and Kohn (Ber., 17, 371) Noelting and De Salis (B., 14, 987); Claus and Jackson (loc. cit.); and Neville and Winther (Ber., 13, 1946).

Statement of Problem

This problem may be briefly stated as follows:

1. To prepare, identify and study the properties of some of the chloro derivatives of o-cresol.
    - a. 4 chloro-o-cresol.
    - b. 6 chloro-o-cresol.
    - c. 4, 6 dichloro-o-cresol.
2. To determine the properties and characteristics of the compounds formed.
3. To increase the yields of the 6 chloro-o-cresol.
4. To prepare their ester derivatives.

EXPERIMENTAL

The Preparation of 4 Chloro-o-cresol

In the preliminary work with the chloro-o-cresols, considerable difficulty was encountered in repeating Datta and Mitter's work (loc. cit.). They state that cold concentrated sulfuric acid was added to the o-cresol, care being taken to keep it cold, and then allowed to stand for "sometime". The whole of the syrupy liquid was then poured into water and the soluble portion containing the 4-sulfonic acid was separated from the insoluble oily 6-sulfonic acid derivative. The 4-sulfonic acid derivative was then diluted "with water" and chlorinated until the heavy oil which settles out was no longer formed. The oil was then separated by a separatory funnel and recrystallized from glacial acetic acid. On cooling and stirring, it yielded a white crystalline product melting at 47°.

After many repeated failures to prepare the 4-chloro-o-cresol by their method, it was decided to prepare it by Claus and Jackson's procedure (loc. cit.) as modified by Milligan (Master's Thesis, 1933). One modification was made in preparing the compound by his method; viz., the solution was cooled to 0° and below, by an ice and salt bath mixture. Milligan reported a yield never exceeding 30% while we obtained a yield of 40 - 42%. The procedure is as follows:

One hundred grams of freshly distilled o-cresol was dissolved in 300 grams of glacial acetic acid in a 500 ml. three-necked flask fitted with a mechanical stirrer, aspirator and thermometer. The solution was cooled below 0° in a ice and salt mixture into which dry chlorine gas was admitted at such a rate that the temperature did not exceed 5° above zero. When the theoretical amount of chlorine (by weight) was added, the acetic acid was removed by distillation at atmospheric pressure, and the remainder fractionated under reduced pressure. The product came over at 106-109/14 mm. pressure, and recrystallized from petroleum ether. It crystallized in the form of long, white needles, melting at 47.5° - 48.5°.

Anal. Calcd. for C_7H_7O Cl: Cl, 24.89. Found: Cl, 24.13.

Since halogenated phenolic compounds had been prepared in this laboratory by the fuming sulfuric acid method, it was suggested that this method be applied to the chlorination of o-cresol. Many preliminary runs were attempted, using small quantities of o-cresol, with variations in proportions of acid to o-cresol and conditions, in order to determine the optimum procedure for preparing these chloro derivatives. Below are listed the attempts as made:

o-Cresol Used	Fuming H_2SO_4 Used	Condition	Cl_2 Added	Observation
20 cc.	20 cc. (20%)	Room temp.	Very little	Viscous mass.
10 cc.	20 cc. (20%)	Room temp.	None	" "
18 cc.	72 cc. (20%)	Room temp.	Very little	" "
18 cc.	72 cc. (20%)	0°(40 cc. H_2O)	Some	" "
100 cc.	80 cc. (20%)	0°	Very little	" "
10 cc.	20 cc. (48%)	Room temp.	None	" "
54 cc.	25 cc. (48%)	0°	None	" "
54 cc.	25 cc. (48%)	0°(50 cc. H_2O)	Theo. am't.	Likely

From the results as observed above, it was noticed that in many cases sulfonation completely blocked halogenation. From the work of Datta and Mitter (loc. cit.) suggesting that chlorination takes place best in the cold or at ordinary temperatures, no preliminary attempts were made to determine the effect of heating the sulfonated cresols before chlorination. However, this was attempted and will be described in a latter part of this paper.

It was noticed from the last preliminary attempt that dilution by water undoubtedly decreased the concentration of the acid enough to allow for chlorination. On this basis other attempts were made using those proportions and conditions. A typical run is as follows:

Fifty cc. of fuming sulfuric acid (49% SO_3) was placed in a three liter, three-necked flask fitted with a mechanical stirrer and thermometer and cooled by an ice-salt mixture. To the acid was added 1 mole (108 gm: 103 cc.) of o-cresol through a separatory funnel during 1 - 2 hours with constant stirring. Care was taken to keep the reacting mixture as close to zero as possible (allowing it to rise to 30° for the initial reaction). It was stirred for two more additional hours and then allowed to stand for 24 hours in the refrigerator. It was again placed in an ice-salt mixture and to it added 100 cc. of water during 1 hour, keeping the temperature below 10°. After stirring the mixture for 5 hours at room temperature, it was hydrolyzed by super-heated steam on an oil bath at 190 - 210°. The first portion of the distillate crystallized which was later found to be the 4, 6 dichloro derivative. The last portion of the distillate came over as a red oil, which was extracted with ethyl ether. The oil after five or more repeated fractionations gave the following fractions:

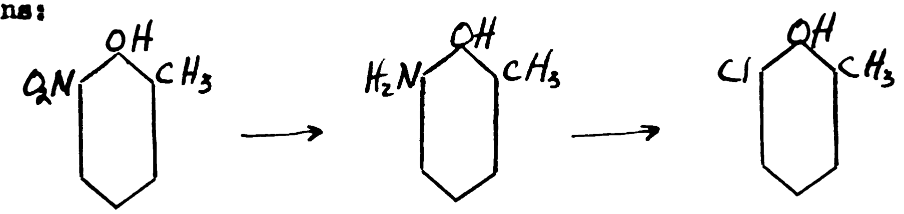
Up to 66°/9 mm.	2 gm.
66 - 72°/9 mm.	14.5 gm.
72 - 97°/9 mm.	29.0 gm.
97 - 102°/9 mm.	7.0 gm.
Residue about	3.0 gm.

The fraction between 66 - 72°/9 mm. was later found to be the 6 chloro isomer, while the 97 - 102°/9 mm. fraction, when cooled and seeded with 4 chloro needles prepared by the acetic acid method, proved to be 4 chloro product. The crystalline product (36 grams of crude product) when recrystallized from petroleum ether gave a constant melting point of 54.5 - 55° E. Bures (loc. cit.) gives a mp. of 56° for the 4, 6 dichloro derivative.

One similar run using two mole quantities gave an increased yield of the 6 chloro fraction (19.0%) with practically the same yield of the 4 chloro product (7%). No attempts were made to increase the yield of the 4 chloro product, for the main objective in using this fuming sulfuric acid method was to prepare the o-chloro-o-cresol derivative.

Preparation of 6 Chloro-o-cresol from 6 Amino-o-cresol

The 6 chloro-o-cresol was prepared by the following series of reactions:



For the preparation of the 6-nitro-o-cresol, the method of Gibson (loc. cit.) was used. A mixture of 107 cc. of HNO_3 (d. 1.42) and 300 cc. of glacial acetic acid was placed in a three liter three-necked flask, fitted with a mechanical stirrer and thermometer and cooled in an ice-salt bath mixture to -15°. To this solution was added 100 grams of o-cresol dissolved in 100 cc. of glacial acetic acid during a period of two hours. It was then allowed to stand for three hours in the freezing mixture after which it was poured into 5000 cc. of cold water and allowed to stand overnight. The product was filtered off at the suction pump and steam distilled. The distillate, while being collected in ice water, crystallized in yellow plates which was the crude 6-nitro product. Upon separation and fractionation it boiled at 102 - 3°/9 mm. and melted at 69 - 70°. Gibson reported a melting point of 70° and a yield of 35% of the crude 6-nitro product.

By using double amounts of the above and keeping the temperature below 0° during the addition of the o-cresol-acetic acid mixture during 2 - 3 hours, an increased yield of the crude product was obtained. The average yields with these modifications were 39 - 40% of the theoretical.

An attempt was made to prepare the 6 nitro product by using Peterson's method for obtaining 2-nitro-m-cresol (J. Am. Chem. Soc., 55, 3879 (1933); Gibson, J. Chem. Soc., 123, 1269; Hodgson and Beard, J. Chem. Soc., 127, 498 (1925)).

To a cold solution of 108 grams of o-cresol in 400 cc. of fuming sulfuric acid (20% SO_3), a mixture of 100 cc. of fuming H_2SO_4 (20% SO_3) and 46 cc. of conc. nitric acid (d. 1.5) was gradually added during one and one-half hours. The mixture was thus allowed to stand overnight. (A characteristic yellow nitro color was observed at the completion of the addition of the nitric acid solution, but a black colored solution was observed in the morning.) The liquid was diluted with 500 cc. of water and then steam distilled with super-heated steam. Only a small amount of product was collected in the distillate which when recrystallized from hot gasoline had a melting point of 85.5 - 86.5°. That this product was the 4, 6 di-nitro-o-cresol was proven by a mixed melting point with the 4, 6 di-nitro product produced by Gibson's method (p. 16). One other attempt was made using a 1:1 ratio of o-cresol to fuming H_2SO_4, but with similar results. It was deemed inadvisable to continue with this method for evidently both of the sulfonic acid groups were replaced by the nitro groups. The yields were too small to determine the presence of any of the 6 nitro product.

The 6 nitro was reduced to the 6 animo by the method of Proskouriakoff and Titherington (J. Am. Chem. Soc., 52, 3978 - 40 (1930)). Fifty grams of the 6 nitro product was dissolved in 1000 cc. of 3% NaOH solution and placed in a 2 l. three-necked flask equipped with a mechanical stirrer and thermometer. The solution was heated to 90° wherewith the heat was discontinued while about 190 grams of sodium hydrosulfite ($Na_2S_2O_4$) were added with constant stirring. (Care must be taken to keep the temperature below 100°.) Invariably, the reduction was completed when a straw-colored solution was obtained on the addition of the sodium hydrosulfite. Ten grams of norit were added and the temperature maintained at 90 - 95°. The solution was filtered while hot and the filtrate cooled at the tap. The crystallized product was filtered and dried in an oven at 40°. The crude dry product was recrystallized from hot CCl_4 which gave a constant melting point of 88 - 89°. (The yield averaged 40 - 42% of the theoretical.)

The 6 animo-o-cresol was treated with hydrochloric acid, diazotized and converted into the corresponding chlorine compound as modified by Marvel and McAlvain for the preparation of o- and p- chlorotoluene (Organic Syntheses, Wiley and Sons, Vol. III, 33).

The cuprous chloride solution was prepared by dissolving 156 grams of crystallized copper sulfate and 40.5 grams of sodium chloride in 500 cc. of water to which was added a solution of 33 grams of sodium sulfite and 21.8 grams of NaOH dissolved in 150 cc. of water. The mixture was stirred continually during the addition of the sodium sulfite solution and was then allowed to cool to room temperature. The solution was decanted and washed several times with cold water, after which it was dissolved with 165 cc. of HCl (d. 1.14).

Sixty-two and one-half grams of the 6-animo product was dissolved in 200 cc. of HCl (d. 1.14), care being taken to insure complete salt formation. The mixture was cooled to 0° by adding cracked ice, to which was added a solution of sodium nitrite (35 grams dissolved in 100 cc.

water) keeping the temperature at 0°. The diagotized solution was then poured into the well stirred cold cuprous chloride solution (0°). The solution became somewhat thick due to the separation of the addition product between the diagonium salt and the cuprous chloride. Stirring was continued for two hours after which it was allowed to warm up to room temperature by standing overnight. (When warmed on the steam bath, no escaping nitrogen was observed.)

With the addition of steam, during steam distillation, an oily layer separated on top which volatized with the steam. The light brown oil in the distillate was extracted with petroleum ether and dried over anhydrous $CaCl_2$. The ether was distilled off and the oil fractionated three times under reduced pressure. The fraction between 66 - 68°/9 mm. (27.5 grams) was the desired product. The almost colorless oil failed to crystallize. The proof of its structure was identified by chlorinating this fraction of 6 chloro-o-cresol in a cold chloroform solution with one mole of chlorine. mp. 54 - 55°. The analysis of the liquid was as follows:

Anal. Calcd. for C_7H_7OCl: Cl, 24.89. Found: Cl, 24.54.

6 Chloro-o-cresol by the Fuming Sulfuric Acid Method

It has been reported (Peterson and Chen, loc. cit.) that ortho halogenated phenolic compounds can be prepared directly by halogenation in fuming sulfuric acid. This method, previously mentioned (p. 13), had as its objective the preparation of this o-chlor-o-cresol.

By sulfonating and chlorinating in the cold (p. 13) a maximum yield of 19% was obtained for the 6 chloro derivative. Sulfonation was then attempted at room temperature with the subsequent procedure the same as in above case. The yield of the o-chloro product was 21.0 grams for the one mole quantity used (yield 14.8%). Another sulfonation carried out this time by heating the o-cresol and fuming sulfuric acid (in the same proportions as above) with the same subsequent procedure gave a yield of only 5.0%. No duplicate results were made as checks since the procedure was carefully adhered to in each trial run.

It is generally believed that by heating a sulfonated mixture that some of the o-sulfonic acid is changed to the p-sulfonic isomer. If this be true, then with heating there should be an increased amount of p- sulfonic acid formed and an increased amount of the 6 chloro product formed. However, it was noticed in the above runs that there was a decrease in the amount of the 6 chloro formed by heating the sulfonated mixtures and a corresponding increase in the amount of the 4, 6 dichloro product formed. The explanation of this phenomenon is largely conjectural.

Chlorination of the 6 chloro fraction (66 - 72°/9 mm.) in a cold chloroform solution with one mole of chlorine gave a dichloro product (mp. 54 - 55°) which gave a mixed melting point of the same with the 4, 6 dichloro product formed from 6 animo o-cresol.

Anal. Calcd. for $C_7H_6OCl_2$: Cl, 40.08. Found : Cl, 39.91.

The Method Reported by Huston and Ballard

A series of attempts were made to prepare the 6 chloro derivative by the method reported by Huston and Ballard (Organic Syntheses, Wiley and Sons, Vol. XIV, 14) for the preparation of o-bromophenol. Since Claus and Jackson (loc. cit.) reported that the p- sulfonic acid derivative was prepared by heating one part of cresol to one and one-half parts of conc. sulfuric acid for 6 - 8 hours on the steam bath, it seemed reasonable that with the formation of the sodium salt of this p- sulfonic acid, that on chlorination, chlorine should enter the ortho position, giving then on neutralization, acidification and hydrolysis, the desired 6 chloro-o-cresol.

The above authors' method was followed rigorously using the above method for the preparation of the p- sulfonic acid derivative. The amount of NaOH necessary for this method was calculated to be four moles (Ballard, Master's Thesis, 1932, p. 27). It was necessary to omit one step of their procedure; viz., the concentration and evaporation of the solution on an oil bath, which greatly interfered with the subsequent acidifying and steam distillation. If the solution was concentrated and evaported, there was excessive foaming up and charring of the product during the steam distillation. A typical run is as follows:

One part of o-cresol and one and one-half part of conc. sulfuric acid were placed in a one liter three-necked flask and heated on the steam bath for 6 hours. When cooled to room temperature, the calculated amount of NaOH was added with stirring and the temperature kept below 40°. The solution was then chlorinated (below 40°) till the theoretical amount, by weight, had been absorbed. (The solution must be alkaline after chlorination.) The product was then transferred to a 5 l. round bottomed flask to which was added 350 cc. of conc. sulfuric acid with frequent cooling and shaking. (Excessive acid caused decomposition and charring.) The flask was then fitted for steam distillation, which was carefully controlled to prevent some foaming up due to an excess of the liberated hydrogen chloride. Steam distillation required about an hour, after which the product was extracted with ethyl ether. The oil obtained was then slowly fractionated in a one and one-half foot small side arm Claisen flask, collecting the fraction between 66 - 72°/9 mm. as the 6 chloro product.

A series of such runs were made using varying percentage strength of NaOH solution, with all other conditions remaining the same. Tabulated below are the results, using a 1:1½ ratio of cresol to acid (heating on steam bath for 6 hours) in one-half mole quantities of the cresol:

% NaOH Used	Gm. of NaOH/cc. of H_2O	Fraction: 66-72°/9 mm.	% Yield
30	80 g/267 cc.	5.0 gm.	7
40*	80 g/200 cc.	10.0 "	14
50	80 g/160 cc.	10.0 "	14
60*	80 g/133 cc.	8.0 "	11.2
70	80 g/114 cc.	8.0 "	11.2
80	80 g/100 cc.	9.5 "	13.4

* Checks were made with practically identical yields.

A series of runs were also made using a 1:2 ratio of cresol to conc. sulfuric acid and heating on the steam bath for 3 hours. The amount of NaOH was calculated to be 5 moles. The tabulated results are as follows: (The yields are based on 1/2 mole quantities used.)

% NaOH Used	Gm. of NaOH/cc. of H_2O	Fraction: 66-72°/9 mm.	% Yield
40	100 g/250 cc.	5.5 gm.	7.8
50	100 g/200 cc.	8.0 "	11.2
60	100 g/166 cc.	6.0 "	8.4
70*	100 g/143 cc.	5.5 "	7.8
80	100 g/125 cc.	Solidified before complete chlorination.	

* Repeated with practically the same yield.

It appears from the above results that an excess of conc. sulfuric acid on sulfonation partially blocks chlorination, while with an increase in the concentration of the NaOH solution beyond 50% causes a decrease in the amount of the 6 chloro formed. The best yields were obtained by using a $1:1\frac{1}{2}$ ratio of cresol to acid, and a 40 or 50% NaOH solution for the formation of the sodium salt.

Derivatives and Analyses of Derivatives

4 Chloro-o-cresol

Esters	Crystalline form	Mp.	Chlorine	
			Cal.	Found
Benzoyl	Small white needles	71.5-72°	14.42	14.29
Benzene sulfonyl	Small white crystals	60.5-61.5°	12.57	12.62
p- tolyl sulfonyl	Short flat needles	96.5-97.5°	11.98	11.19

6 Chloro-o-cresol

Benzoyl	Viscous liquid (bp)	131-133°/1 mm.	14.42	13.91
Benzene sulfonyl	Light green colored liquid (bp)	70-72°/1 mm.	12.57	12.65
p- tolyl sulfonyl	Small flat needles	50.5-51.5°	11.98	11.27

4, 6 Dichloro-o-cresol

Benzoyl	Oily liquid	130-132°/1 mm.	25.25	23.94

The esters were prepared by the method of Einhorn and Holland (Am., 301, 95 (1898)) and recrystallized from ethyl alcohol.

The p- nitro benzyl ether of the 6 chloro derivative was prepared according to Kamm (Qualitative Organic Analysis, 2nd ed., 1932, p. 165; Reid (J. Am. Chem. Soc., 39, 304 (1917)). It recrystallized from ethyl alcohol in fine needles, mp. 87 - 88°.

Anal. Calcd. for $C_{14}H_{12}O_3N$ Cl: Cl, 12.73. Found: Cl, 12.80.

SUMMARY

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1. Chlorination of o-cresol in fuming sulfuric acid gave rise to the 4 chloro-, 6 chloro-, and 4, 6 dichloro-o-cresols.
2. The structure of the 6 chloro-o-cresol was definitely established.
3. The 6 chloro-o-cresol was prepared by method reported by Huston and Ballard.
4. The benzoyl, benzene sulfonyl and p- tolyl sulfonyl esters of the 4 and 6 chloro-o-cresols were prepared. The p- nitro benzyl ether of the 6 chloro derivative was also prepared.