[Contribution from the McPherson Chemical Laboratory, the Ohio State University

A STUDY OF THE ZINCKE AND SUHL REACTION

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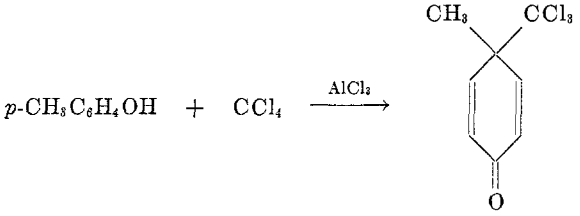
It has been shown that *p*-alkylated phenols may react with chloroform under alkaline conditions to yield 4,4-disubstituted-2,5-cyclohexadienones (1). Less well known is the reaction discovered by Zincke and Suhl in which *p*-cresol reacts with carbon tetrachloride in the presence of aluminum chloride to yield 4-methyl-4-trichloromethyl-2,5-cyclohexadienone, I (2).



I

We became interested in this reaction because of the fact that its generality has never been explored in spite of the fact that it affords a possibly general method for producing compounds containing a quarternary carbon atom and also because I has been shown to undergo a number of interesting reactions (3).

In Table I are listed a number of experiments which were carried out in order to obtain a better understanding of the reaction. Although we have not completed an exhaustive study of this reaction, we feel that a number of conclusions may be drawn.

In Zincke and Suhl's procedure, aluminum chloride was added to a solution of *p*-cresol in carbon tetrachloride. After a period of heating, the product (I) was isolated (after hydrolysis of the reaction mixture) in about 37–42% yield. We have checked this result and also shown that it is necessary to have an excess of aluminum chloride (calculated as $AlCl_3$) over *p*-cresol (note experiments 1 and 2, Table I). However, a 100% excess is little better than a 25% excess (note experiments 17 and 18). Boron trifluoride and anhydrous stannic chloride were ineffectual as catalysts.

A solvent other than carbon tetrachloride was needed if the reaction of other halides was to be studied. Nitrobenzene (experiments 11, 12, 13), chlorobenzene (experiment 3), and a saturated hydrocarbon, Skellysolve B, b.p. 65–70°, (experiments 14, 15, 16) were found to be improper solvents but carbon disulfide proved excellent. In this solvent yields of 56 to 60% were obtained (experiments 17, 18, 21, 22).

The Zincke and Suhl procedure of adding aluminum chloride to a solution

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[1] The material presented in this and the three accompanying papers was taken from the Ph.D. thesis of A. G. Pinkus (present address, Baylor University, Waco, Texas), Ohio State University, 1952.

TABLE I

YIELDS OBTAINED IN THE ZINCKE AND SUHL REACTION UNDER VARIOUS CONDITIONS

EXP.	*p*-Cresol (moles)	CCl_4 (moles)	$AlCl_3$ (moles)	SOLVENT (ml.)	TEMP.,[a] °C.	TIME (min.)	METHOD[b]	CRESOL RECOVERED	YIELD[c] of I, %
1	0.20	0.80	0.20	CCl_4	Reflux	120	1	Yes	0
2	.20	.40	.26	CCl_4	Reflux	120	1	No	40.0
3	.20	.25	.23	C_6H_5Cl (30)	Reflux	120	1	No	0
4	.20	.259	.23	CS_2 (50)	Reflux	120	1	No	51.2
5	.162	.187	.18	CS_2 (45)	Reflux	120	2	No	25.9
6	.20	.259	.23	CS_2 (100)	Reflux	120	1	No	53.0
7	.20	.259	.23	CS_2 (70)	Reflux	120	3	No	33.0
8	.20	.259	.23	CS_2 (50)	Reflux	25	4	Yes	2.0
9	.10	.120	.12	CS_2 (70)	Reflux	60	4	Yes	22.1
10	.10	.10	.11	CS_2 (40)	Reflux	90	5	Yes	46.7
11	.010	.010	.012	$C_6H_5NO_2$ (4)	50	90	6	Yes	0
12	.010	.010	.012	$C_6H_5NO_2$ (4)	60	150	6	Yes	0
13	.010	.010	.012	$C_6H_5NO_2$ (4)	85	120	6	Yes	0
14	.010	.010	.012	Skellysolve (4)	40	120	6	Yes	0
15	.050	.050	.063	Skellysolve (30)	50	120	6	Yes	0
16	.050	.050	.063	Skellysolve (30)	75	120	6	Yes	0
17	.050	.050	.10	CS_2 (25)	50	120	6	No	58.0
18	.050	.050	.063	CS_2 (25)	50	120	6	No	56.0
19	.050	.050	.063	CS_2 (25)	18	180	6	Yes	21.3
20	.050	.050	.063	CS_2 (25)	30	120	6	Yes	27.7
21	.10	.050	.14	CS_2 (25)	40	120	6	Yes	59.4[c]
22	.050	.050	.063	CS_2 (25)	45	120	6	No	60.3

[a] Temperatures reported are those of an electrically-heated oil-bath. [b] Methods: 1. Adding aluminum chloride to the solution of *p*-cresol in carbon tetrachloride. 2. Reacting aluminum chloride and *p*-cresol in carbon disulfide, then adding carbon tetrachloride dropwise to the refluxing mixture. 3. Reverse order of addition: adding a solution of aluminum dichloride *p*-cresoxide in carbon disulfide dropwise to a refluxing mixture of carbon tetrachloride and aluminum chloride in carbon disulfide. 4. A solution of *p*-cresol in carbon disulfide added to the refluxing mixture of carbon tetrachloride, aluminum chloride, and carbon disulfide. 5. A solution of *p*-cresol in carbon tetrachloride added dropwise to a refluxing suspension of aluminum chloride in carbon disulfide. 6. Carbon tetrachloride added at once to the solution of aluminum dichloride *p*-cresoxide in carbon disulfide and then heating the mixture. [c] Yields are based on *p*-cresol except in experiment 21 in which it is based on carbon tetrachloride since *p*-cresol is in excess.

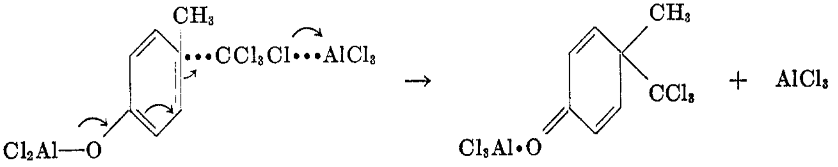
of *p*-cresol in carbon tetrachloride was found to be less effective than that in which a solution of *p*-cresol in carbon disulfide was added to a suspension of aluminum chloride in carbon disulfide. Hydrogen chloride was evolved and the chloroaluminum salt of *p*-cresol formed was soluble. After the completion of this step, the carbon tetrachloride was added and the mixture was heated in the range 40–50° for two hours (experiments 17, 18, 21, 22). Examination of Table I will reveal the other variables studied.

In addition to the 56–60% of I obtained in the best experiments there was also formed dark polymeric material. No *p*-cresol was recoverable. Two experiments showed that the polymer was not being formed from I. In the first I was heated with aluminum chloride in carbon tetrachloride. An orange complex was formed but after hydrolysis and steam-distillation 97% of I was recovered. In the second I was heated with *p*-cresol and 2.25 moles of aluminum chloride in carbon disulfide to reflux. Both I and *p*-cresol were recovered in high yield. A possible explanation for the formation of polymer will be presented in the discussion of mechanism of the reaction.

Having found a suitable solvent we were interested in exploring the generality of the reaction by using halides other than carbon tetrachloride and phenols other than *p*-cresol. Although exhaustive studies in each case were not performed we were unable to obtain products comparable to I with *p*-cresol and methyl chloride, methyl iodide, methylene chloride, chloroform, and hexachloroethane. With 1,1,1-trichloroethane, a 1.6% yield of a 2,4-dinitrophenylhydrazone having an analysis in agreement with that expected for a compound similar to I was obtained but the parent ketone was not obtained. When 2,6-dibromo-4-methylphenol and 2,6-dichloro-4-methylphenol were reacted with carbon tetrachloride 9% and 36% yields of the expected dieneones analogous to I were obtained. However, all attempts to introduce an angular trichloromethyl group into 5,6,7,8-tetrahydro-2-naphthol failed (1).

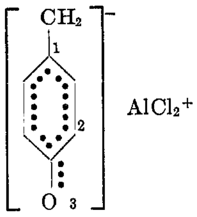
When the reaction was carried out using benzotrichloride instead of carbon tetrachloride two new reactions were discovered. The description of this work is given in the accompanying paper (4).

Our concept of the mechanism of the Zincke and Suhl reaction has aluminum chloride playing a dual role: it first reacts with *p*-cresol to form a chloroaluminum salt (II) with loss of hydrogen chloride; and it also activates a molecule of carbon tetrachloride by forming a loose complex, III. This complex is subject to a nucleophilic attack on carbon by the chloroaluminum salt, as shown. The chloride ion displaced combines with the $AlCl_2^+$ ion to produce aluminum chloride which remains complexed with the product (IV).



II III IV

The salt II may react at three positions: on the *para* carbon, 1, to give the



II

Zincke and Suhl product (I); at the *ortho* carbon, 2, to give compounds which in the present case are probably the precursors of the polymers formed (see below) and in the case of the reactions involving benzotrichloride (4) afford ketones and dioxocins; and on the oxygen, 3, to form the carbonates which have been isolated previously (2) in the case where 2,3,5,6-tetrabromo-*p*-cresol was used in place of *p*-cresol.

In support of this mechanism, a number of facts may be cited. When *p*-cresol in carbon disulfide is allowed to react with aluminum chloride (mole for mole), all of the aluminum chloride goes into solution and one equivalent of hydrogen chloride is evolved. (The chloroaluminum salt (II) formed is probably not monomeric (5) but for simpler representation the monomeric form is used.) When the solvent was removed *in vacuo*, a colorless crystalline salt remained which, on treatment with water, yielded *p*-cresol. A similar type of compound has been reported for phenol (6).

The only evidence we have for a complex (III) between carbon tetrachloride and aluminum chloride is the formation of a yellow color on the aluminum chloride when heated with carbon tetrachloride. When the carbon tetrachloride was removed *in vacuo*, the color disappeared. The interaction of alkyl halides and aluminum halides has frequently been demonstrated (7).

Possibly, the Zincke and Suhl reaction fails in nitrobenzene (see experiments 11, 12, 13, Table I) and in chlorobenzene (experiment 3) because the solvents inactivate the aluminum chloride toward complexing with carbon tetrachloride. When pure I is treated with aluminum chloride, an orange complex is formed. In the Zincke and Suhl reaction, the reaction mixture (both before and after hydrolysis) is dark-colored. This dark color is due to the byproducts formed. We believe these byproducts arise from reaction intermediates in which a trichloromethyl group is introduced in a position *ortho* to the phenolic group. In such a compound the chlorine atoms are activated by the ring and undergo further condensation leading to the polymers. The deep color is probably due to the presence of triarylmethyl type dyes (8).

EXPERIMENTAL

General. Melting points were determined in a Hershberg type (9) melting point apparatus using Anschütz total immersion thermometers. Boiling points are uncorrected. All solvents were redistilled in addition to further purification wherever noted. All analyses are by Clark Microanalytical Laboratories, Urbana, Illinois.

We wish to thank Mrs. Alfred Brooks, Robert Lieberman, and Albert C. Antoine for the infrared spectrograms which were taken on a Baird double beam recording spectrophotometer using sodium chloride optics.

Preparation of 4-methyl-4-trichloromethyl-2,5-cyclohexadienone (I). In the best procedure developed, a solution of 5.41 g. (0.050 mole) of redistilled *p*-cresol in 5 ml. of carbon disulfide was added dropwise to a stirred suspension of 8.33 g. (0.063 mole) of powdered anhydrous aluminum chloride in 25 ml. of purified carbon disulfide. During this addition (10–15 minutes) hydrogen chloride was evolved and about one equivalent of the aluminum chloride went into solution. Redistilled carbon tetrachloride (7.70 g., 0.050 mole) was added in one portion and the mixture was then heated by an oil-bath at 45°. The color darkened and more hydrogen chloride was evolved. This additional hydrogen chloride is undoubtedly that formed by attack at the *ortho* position in the side reactions leading to tar formation. As the reaction proceeded, a dark brown tarry mass collected on the sides of the flask. After two hours of heating, the solvent was removed *in vacuo* and the mixture was decomposed by the dropwise addition of water. The use of dilute hydrochloric acid in place of water had no noticeable effect on the yield. The dienone (I) was obtained crystalline in 6.91-g. yield by steam-distillation. A dark tar remained in the flask. Recrystallization of the product from petroleum ether (Skellysolve B, b.p. 65–70°) afforded 6.79 g. (60.3% yield) of I, m.p. 103.8–104.2°, carbonyl band at 5.95 μ (taken in mineral oil, Nujol, mull). When 7.5 g. (0.0563 mole) of aluminum chloride was added to a solution of 11.30 g. (0.050 mole) of I in 25 ml. of carbon disulfide, an orange-yellow complex formed. After two hours at reflux followed by decomposition with 10% hydrochloric acid, I was recovered in 96.6% yield (10.91 g.). It is notable that no dark tarry material was formed in this experiment.

Attempted reaction of I and p-cresol. Using a procedure similar to that in the preparation of I, a mixture of 15.0 g. (0.11 mole) of aluminum chloride, 5.41 g. of *p*-cresol, 11.28 g. of I, and 90 ml. of carbon disulfide was heated at reflux for two hours. There was no formation of a dark color during this time. The solvent was removed *in vacuo* and the mixture was decomposed by the cautious addition of water. The organic layer was taken into ether-benzene and washed with water, 10% sodium hydroxide (see below), water, and saturated sodium chloride solution, and filtered through anhydrous sodium sulfate. Removal of the solvent and recrystallization from Skellysolve B afforded 9.10 g. of I (80.8% recovery). A complete recovery of I from the mother liquors was not attempted. From the above alkaline extract was obtained 4.02 g. (74.3% recovery) of *p*-cresol, b.p. 88–91.5° at 10–12 mm.

2,6-Dibromo-4-methyl-4-trichloromethyl-2,5-cyclohexadienone. The reaction was run in the previously described manner using 5.0 g. (0.038 mole) of aluminum chloride, 4.0 g. (0.026 mole) of carbon tetrachloride, 40 ml. of carbon disulfide, and 6.7 g. (0.025 mole) of 2,6-dibromo-*p*-cresol [m.p. 47.0–48.0° prepared in 91.3% yield by bromination of *p*-cresol in acetic acid (10)]. The typical dark color formed a few minutes after heating at 40°. After decomposition, the mixture was taken up in benzene-ether and worked up in the usual manner. After removing some of the solvent by distillation and cooling, colorless crystals were formed. They were collected (see below for filtrate), washed with ether, and dried *in vacuo*. Attempted recrystallization of this product (0.6 g., m.p. 189–192°) from various mixtures of solvents gave only white amorphous material. The compound left no residue on ignition, contained halogen, did not form a phenylhydrazone by the usual procedure (11), and was not further investigated. The benzene-ether filtrate from above was extracted with 10% sodium hydroxide and the organic layer, which had taken on a bright orange-red color, was treated in the usual manner. Removal of solvent left 6.4 g. of a gummy solid which was extracted several times with ether to give a colored ether solution (see below) and 0.70 g. of a white crystalline solid, m.p. 160–165° and a second crop, 0.21 g., m.p. 159–166°, totaling 0.91 g. (9.4%) of crude 2,6-dibromo-4-methyl-4-trichloromethyl-2,5-cyclohexadienone. Sublimation at 1 mm. gave white crystals, m.p. 168.7–169.5° (carbonyl absorption at 5.95 μ, Nujol mull). Positive tests (12) for chlorine and bromine were obtained.

Anal. Calc'd for $C_8H_5Br_2Cl_3O$: C, 25.1; H, 1.3.
Found: C, 25.3; H, 1.2.

We were unable to prepare a phenylhydrazone confirming the previous report (3). The mixture melting point with a sample of the compound prepared by the bromination of I (3) was not depressed.

No pure compound was obtained from any other fraction of this reaction mixture.

2,6-Dichloro-4-trichloromethyl-2,5-cyclohexadienone. The reaction was run in the usual manner using 5.0 g. (0.038 mole) of aluminum chloride, 4.68 g. (0.03 mole) of carbon tetrachloride, 60 ml. of carbon disulfide, and 5.31 g. (0.030 mole) of 2,6-dichloro-*p*-cresol [m.p. 36.0–37.0°, prepared in 31.1% yield by chlorination of *p*-cresol in carbon tetrachloride (13)]. On adding the carbon tetrachloride, no color change was observed after stirring for ten minutes at room temperature. The typical dark color formed when the mixture was heated by an oil-bath at 50°. After two hours of stirring at this temperature, the solvent was removed *in vacuo* and the mixture was decomposed by the cautious addition of water with cooling. The mixture was taken up in benzene-ether, extracted twice with 10% sodium hydroxide, and worked up in the usual manner. Removal of solvent gave a yellow solid, which on recrystallization from cyclohexane, yielded 3.41 g. (35.5%) of 2,6-dichloro-4-methyl-4-trichloromethyl-2,5-cyclohexadienone as white prisms in two crops, m.p. 165.4–166.0° and 163.5–164.5° (carbonyl absorption at 5.93 μ, Nujol mull). This compound was previously prepared (3) by chlorination of the Zincke and Suhl ketone.

Methyl chloroform and p-cresol. The reaction was run in the usual manner at room temperature using 16.0 g. (0.1205 mole) of aluminum chloride, 10.81 g. (0.10 mole) of *p*-cresol, 40 ml. of carbon disulfide, and 14.0 g. (0.105 mole) of methyl chloroform [b.p. 74–74.5°, obtained through the generosity of the Dow Chemical Co., Freeport, Texas]. Extraction of the steam distillate with sodium hydroxide left a small quantity of an insoluble yellow oil which could not be crystallized. This residue was dissolved in 95% alcohol and about 0.5 g. of 2,4-dinitrophenylhydrazine was added, the mixture being heated to effect solution. An amorphous orange precipitate which formed immediately was collected, washed with alcohol-water, and dried *in vacuo*, (0.02 g., m.p. 272–273°). This product did not contain halogen and was not further investigated. The filtrate was heated to boiling and one ml. of concentrated hydrochloric acid was added dropwise. On cooling, 0.60 g. of red crystals, m.p. 151–152°, separated. An analytical sample, m.p. 151.5–152.0°, was obtained by recrystallization from 95% ethanol. The compound contained chlorine inert to alcoholic silver nitrate.

Anal. Calc'd for $C_{15}H_{14}Cl_2N_4O_4$: C, 46.8; H, 3.7; N, 14.6.
Found: C, 47.1; H, 3.6; N, 14.7.

Accordingly this compound is probably the 2,4-dinitrophenylhydrazone of 4-(1,1-dichloroethyl)-4-methyl-2,5-cyclohexadienone. Attempts to improve the yield in this reaction showed that more polymer was formed at higher temperatures whereas no condensation occurred at temperatures around 0°.

SUMMARY

1. The yield of 4-methyl-4-trichloromethyl-2,5-cyclohexadienone in the Zincke and Suhl reaction has been increased to 60% (a gain of 20%) by the use of an improved method.

2. A mechanism has been presented for the Zincke and Suhl reaction.

3. The following compounds have been synthesized by means of the Zincke and Suhl reaction: 2,6-dibromo-4-methyl-4-trichloromethyl-2,5-cyclohexadienone, 2,6-dichloro-4-methyl-4-trichloromethyl-2,5-cyclohexadienone, and 4-(1,1-dichloroethyl)-4-methyl-2,5-cyclohexadienone, the latter compound being isolated as the 2,4-dinitrophenylhydrazone.

4. Attempts to use the following compounds in the Zincke and Suhl reaction with *p*-cresol were unsuccessful: hexachloroethane, chloroform, methylene chloride, methyl chloride, and methyl iodide.

5. Attempts to introduce an angular trichloromethyl group into 5,6,7,8-tetrahydro-2-naphthol by means of the Zincke and Suhl reaction were unsuccessful.

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