have been observed, thirteen of which may be satisfactorily explained as binary combinations of the five Raman fundamentals. The remaining combination tone may be a binary combination involving the missing fundamental in the region of 260 cm.$^{-1}$.

OTTAWA, CANADA
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RECEIVED MARCH 21, 1949

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE SPRAGUE ELECTRIC COMPANY]

Some Reactions of Pentachlorobenzyl Chloride and Pentachlorobenzal Chloride; Steric Hindrance in the Alcoholysis of Pentachlorobenzal Chloride

BY SIDNEY D. ROSS AND MOUSHY MARKARIAN

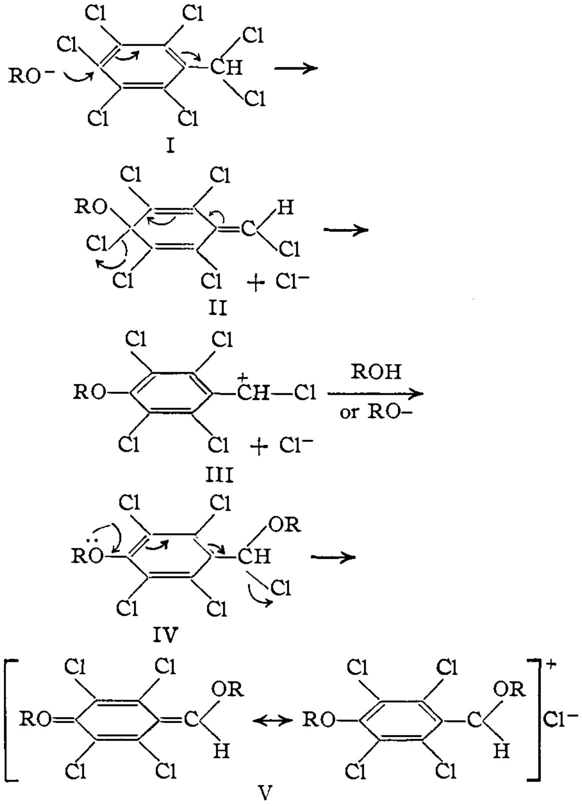
On the basis of earlier studies of substituted benzyl and benzal chlorides,[1] one would expect no great difference in the reactivity of pentachlorobenzyl and pentachlorobenzal chloride. However, the chlorine substituents at the 2- and 6-positions[2] might introduce steric effects, especially so in the case of the benzal derivative with its large $-CHCl_2$ group at the one position. The present work was undertaken to investigate the importance of such steric effects.

Pentachlorobenzyl chloride gave the expected products in the Friedel–Crafts reaction with benzene and in displacement reactions with alkoxide ions and acetate ion. With potassium hydroxide in aqueous acetone, dipentachlorobenzyl ether and 4-pentachlorophenyl-butanone-2 were obtained, and these products probably result from normal, nucleophilic displacements on the benzyl chloride by the conjugate bases of pentachlorobenzyl alcohol and acetone, respectively.

Pentachlorobenzal chloride reacts with benzene in the presence of aluminum chloride to give benzhydrylpentachlorobenzene, but this does not indicate an absence of steric hindrance, for the Friedel–Crafts alkylation involves a front side attack of the catalyst on the covalent carbon–chlorine bond.[3] More significantly, pentachlorobenzal chloride failed to react with either potassium acetate or silver acetate in acetic acid or with potassium hydroxide in aqueous acetone.

On reaction with sodium ethoxide in ethanol, pentachlorobenzal chloride gave, not the expected diethylacetal of pentachlorobenzaldehyde, but a product analyzing correctly for the diethylacetal of an ethoxytetrachlorobenzaldehyde, $C_{13}H_{16}O_3Cl_4$. Hydrolysis of this product gave an ethoxytetrachlorobenzaldehyde, $C_9H_6O_2Cl_4$, which differs from the known 2,4,5,6-tetrachloro-3-ethoxybenzaldehyde.[4] Similar results were obtained with sodium methoxide and sodium isopropoxide. On oxidation with fuming nitric acid the methoxytetrachlorobenzaldehyde gave chloranil, and we have, therefore, assigned 2,3,5,6-tetrachloro-4-alkoxybenzaldehyde structures to the three aldehydes.

The initial attack in the alcoholysis is probably on the para chlorine atom, since no acetals of pentachlorobenzaldehyde were isolated. If we assume such an initial attack, it is possible to rationalize the course of the reaction as



The carbonium ion, V, on reaction with alcohol or alkoxide ion, would give the final product. Such an attack on the para chlorine atom is probable only if there is appreciable steric hindrance about the one position.

Experimental[5]

Pentachlorobenzyl Chloride.—Chlorine was added to molten pentachlorotoluene until the calculated gain in

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[1] The substituted benzyl chlorides have been extensively studied by Olivier (*Rec. trav. chim.*, **42**, 775 (1923); **49**, 697 (1930)) and the benzal chlorides by Asinger and Lock (*Monatsh.*, **62**, 323 (1930)). In both cases the rates of hydrolysis in acetone-water and alcohol-water were measured.

[2] Ross, THIS JOURNAL, **70**, 4039 (1948).

[3] Fairbrother, *Trans. Faraday Soc.*, **37**, 763 (1941).

[4] Biltz and Tammann, *Ber.*, **34**, 4118 (1901).

[5] The microanalyses are by Dr. Carl Tiedcke.

TABLE I

PENTACHLOROBENZYL ETHERS

Ether	Formula	Yield, %	M. p. or b. p. °C.	Mm.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
Methyl	$C_8H_5OCl_5$	65	100–102		32.60	32.30 32.12	1.70	1.49 1.70
Ethyl	$C_9H_7OCl_5$	75	65–66		35.10	35.40 35.18	2.29	2.12 1.98
n-Propyl	$C_{10}H_9OCl_5$	70	43–44		37.28	37.72 37.96	2.81	3.01 2.78
n-Butyl	$C_{11}H_{11}OCl_5$	66.5	139–139.5[a]	0.3	39.28	40.06 40.18	3.30	3.20 3.24

[a] $n^{20}{}_D = 1.5612$.

TABLE II

2,3,5,6-TETRACHLORO-4-ALKOXYBENZALDEHYDES

Aldehyde	Formula	Yield, %	M. p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
4-Methoxy	$C_8H_4O_2Cl_4$	32.8	119–120	35.08	34.80 34.61	1.46	1.56 1.41
2,4-Dinitrophenylhydrazone	$C_{14}H_{18}O_5N_4Cl_4$		248–250 dec.	37.02	36.70 36.51	1.78	1.89 2.01
4-Isopropoxy	$C_{10}H_8O_2Cl_4$	40	102–103	39.78	39.78 39.51	2.67	2.36 2.52
2,4-Dinitrophenylhydrazone	$C_{16}H_{12}O_5N_4Cl_4$		238–239 dec.	39.88	39.81 39.55	2.51	2.69 2.48

weight was attained. Distillation at 0.27 mm. (b. p. 134–136°) followed by crystallization from benzene–alcohol (1:1) gave 66.5% of product of m. p. 99–102°.

Benzylpentachlorobenzene.—Pentachlorobenzyl chloride (29.9 g., 0.1 mole) in benzene (150 cc.) was added dropwise at room temperature to a stirred suspension of aluminum chloride (1 g.) in benzene (100 cc.). The reaction mixture was maintained at 60° until no further hydrogen chloride was liberated and worked up in the usual manner. The product was crystallized from S. D. A. 30[6]-benzene; m. p. 113–114°; yield 19 g. (56%).

Anal. Calcd. for $C_{13}H_7Cl_5$: C, 45.87; H, 2.07. Found: C, 45.18, 45.35; H, 2.02, 1.88.

Benzhydrylpentachlorobenzene.—Pentachlorobenzal chloride (66.7 g., 0.2 mole) in benzene (150 cc.) was added to aluminum chloride (1.5 g.) in benzene (350 cc.) as above, and the mixture was stirred for twelve hours. The crude product, isolated by standard methods, was a red-brown solid, which tended to oil when crystallized from benzene–alcohol (1:3). The purified product was obtained both by decanting the mother liquor from the oil, and by distilling the combined mother liquor and oil from the crystallization at 1.7 mm. (b. p. 230–235°); yield 57 g. (69%); m. p. 128.5–129.5° after crystallization from benzene–alcohol. Benzhydrylpentachlorobenzene was also obtained, albeit in low yield, by adding benzene dropwise to a stirred suspension of pentachlorobenzaldehyde in 98% sulfuric acid.

Anal. Calcd. for $C_{19}H_{11}Cl_5$: C, 54.80; H, 2.66. Found: C, 55.15, 55.05; H, 2.75, 2.52.

Pentachlorobenzyl Acetate.—Pentachlorobenzyl chloride (29.9 g., 0.1 mole) was refluxed for twenty hours with potassium acetate (40 g., 0.4 mole) in glacial acetic acid. Addition of water, after most of the acetic acid was removed, gave the acetate; yield 32.2 g. (100%); m. p. 87–90° after three crystallizations from S. D. A. 30.

Anal. Calcd. for $C_9H_5O_2Cl_5$: C, 33.48; H, 1.55. Found: C, 33.56, 33.39; H, 1.60, 1.41.

Basic hydrolysis of the acetate gave the known pentachlorobenzyl alcohol[7]; yield 75%; m. p. 197–198° after crystallization from trichloroethylene.

Dipentachlorobenzyl Ether and 4-Pentachlorophenylbutanone-2.—A mixture of pentachlorobenzyl chloride (229 g., 1 mole), potassium hydroxide (112 g., 2 moles), acetone (1250 cc.) and water (500 cc.) was refluxed twelve hours, cooled and filtered to give a solid melting from 130–165°. Crystallization of this total product from benzene gave the ether; yield 129 g. (47.6%); m. p. 33–234° (dec.) after three crystallizations from benzene.

Anal. Calcd. for $C_{14}H_{14}OCl_{10}$: C, 30.98; H, 0.74. Found: C, 31.16, 31.00; H, 0.79, 0.92.

Concentration of the mother liquor from the above crystallization gave a first crop, which was discarded, and a second crop, which, after six crystallizations from ethanol containing a trace of benzene, yielded 12 g. of the ketone of m. p. 113–114°.

Anal. Calcd. for $C_{10}H_7OCl_5$: C, 37.52; H, 2.18. Found: C, 37.41, 37.22; H, 1.83, 2.01.

The ketone gave a 2,4-dinitrophenylhydrazone, which, after two crystallizations from glacial acetic acid, had m. p. 237° (dec.).

Anal. Calcd. for $C_{16}H_{11}O_4N_4Cl_5$: C, 38.41; H, 2.20. Found: C, 38.04, 38.20; H, 2.40, 2.34.

Pentachlorobenzyl Ethers.—The ethers shown in Table I were prepared by refluxing pentachlorobenzyl chloride in the appropriate alcohol with an excess of either sodium hydroxide or the appropriate sodium alkoxide.

2,3,5,6-Tetrachloro-4-ethoxybenzaldehyde Diethylacetal.—Pentachlorobenzal chloride (167 g., 0.5 mole) was refluxed twelve hours with sodium ethoxide (1.5 moles) in ethanol (1000 cc.). Most of the ethanol was removed, water was added, and the mixture was extracted with benzene. The benzene was removed, and the product was distilled to yield 136 g. (75%) of b. p. 128–138° at 0.12 mm. Fractionation at 0.4 mm. through a two-foot Vigreux column yielded 95 g. (52.4%) of product of b. p. 152° and $n^{20}{}_D$ 1.5350.

Anal. Calcd. for $C_{13}H_{16}O_3Cl_4$: C, 43.12; H, 4.45. Found: C, 43.40, 43.22; H, 4.06, 4.18.

2,3,5,6-Tetrachloro-4-ethoxybenzaldehyde.—A mixture of the diethylacetal (20 g., 0.055 mole), glacial acetic acid (180 cc.), water (20 cc.) and concentrated sulfuric acid (4 drops) was refluxed for five hours and then poured into water. This precipitated the crude aldehyde which was crystallized four times from ethanol; yield 9.5 g. (59.5%); m. p. 106–107.5°.

Anal. Calcd. for $C_9H_6O_2Cl_4$: C, 37.57; H, 2.10. Found: C, 37.51, 37.36; H, 2.02, 2.13.

The aldehyde gave a 2,4-dinitrophenylhydrazone which, after two crystallizations from glacial acetic acid, had m. p. 244–245°(dec.).

Anal. Calcd. for $C_{15}H_{10}O_5N_4Cl_4$: C, 38.50; H, 2.15. Found: C, 38.31, 38.49; H, 2.11, 2.08.

The two 2,3,5,6-tetrachloro-4-alkoxybenzaldehydes, shown in Table II, were obtained as above. The intermediate acetals were isolated by a single distillation. The 2,4-dinitrophenylhydrazones were crystallized from glacial acetic acid.

Oxidation of 2,3,5,6-Tetrachloro-4-methoxybenzaldehyde.—The aldehyde (3 g.) was heated for twenty hours with 200 cc. of fuming nitric acid. The reaction mixture

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(6) S. D. A. 30 is a specially denatured alcohol in which the denaturant is methanol.

(7) Beilstein and Kuhlberg, *Ann.*, **152**, 246 (1849).

into ice and water, yielding 1.5 g. (58%)
il of m. p. 265–280°. Recrystallization
ave golden yellow crystals of m. p. 285°.
e product with phenylhydrazine in eth-
crystals of m. p. 229–230°.[8]

Summary

enzyl chloride reacts with benzene
of aluminum chloride to give ben-
benzene, with potassium acetate in
ive pentachlorobenzyl acetate, and
ydroxide or sodium alkoxides in al-
ethers. With sodium hydroxide in aqueous acetone, dipentachlorobenzyl ether and small amounts of 4-pentachlorophenylbutanone-2 were obtained.

Pentachlorobenzal chloride undergoes the Friedel–Crafts alkylation to give benzhydrylpentachlorobenzene. It does not react with potassium acetate or silver acetate in acetic acid or with potassium hydroxide in aqueous acetone. With sodium alkoxides in alcohols acetals of 2,3,5,6-tetrachloro-4-alkoxybenzaldehydes are obtained. These on hydrolysis give the corresponding aldehydes.

NORTH ADAMS, MASS. RECEIVED SEPTEMBER 8, 1948

Combie, *J. Chem. Soc.*, **103**, 220 (1913).

RIBUTION FROM CHEMISTRY DEPARTMENT, NORTHWESTERN UNIVERSITY MEDICAL SCHOOL]

Peptic Hydrolysis of Egg Albumin. I. Kinetic Studies

BY HENRY B. BULL AND BYRON T. CURRIE

been the subject of exhaustive
does not appear, however, that the
hydrolysis of a purified protein by
n studied in detail. We have inves-
ion of crystalline pepsin on crystal-
in as a function of substrate con-
hydrogen ion concentration and of
An interpretation of these data is
the Michaelis–Menten[2] formula-
extended to include the influence of
and the formation of an activated

Experimental

il to Armour and Company for the crys-
Its activity as determined by us was 0.19
of nitrogen. The egg albumin was pre-
hen's eggs by the method of Kekwick and

the action of pepsin on egg albumin was
he amount of egg albumin which cannot
ed at its isoelectric point. The technique
The egg albumin solution was brought to
by the cautious addition of hydrochloric
ion was placed in the reaction vessel and
perature in a thermostated bath. The
of solution containing sufficient pepsin
pepsin per 100 cc. of reaction mixture
lowly stirred. A glass electrode was in-
eaction mixture and the *p*H maintained
bling hydrochloric acid gas through the
. A small amount of caprylic alcohol
vent foaming. Ten-cc. samples were re-
als to 50-cc. Pyrex volumetric flasks and
ately to the isoelectric point of egg albu-
lition of acetate buffer. These samples
a glycerol bath to boiling, cooled and
ne, filtered, and the total nitrogen of an
iltrate determined with micro-Kjeldahl.
as expressed in terms of protein and is
lubilized protein.

Results

cal values are so extensive that it is not practical to report them in detail, and we are characterizing our data by means of the Michaelis–Menten constants. These constants were obtained by plotting the reciprocal of the initial rate of reaction against the reciprocal of the egg albumin concentration. The intercept of the straight lines on the *y*-axis gave the reciprocal of the maximum velocity (V), and the slopes of the straight lines yielded the ratio of the dissociation constant (K_m) of the Michaelis–Menten complex to the maximum velocity. The initial reaction rates were obtained from the slope of the line at zero time when the amount of solubilized protein was plotted against time. At 30° these plots gave essentially straight lines up to one hour, while at 45° the extent of reaction was so much greater that gentle curves were obtained. Three to four determinations for each protein concentration at various time intervals were needed to evaluate the initial rate, and four to five protein concentra-

TABLE I

MOLE-SECOND MICHAELIS–MENTEN CONSTANTS FOR THE DIGESTION OF EGG ALBUMIN BY PEPSIN AT 30°

*p*H	*V*	K_m
1.34	0.092	0.67×10^{-4}
1.60	.092	1.78×10^{-4}
1.80	.074	2.44×10^{-4}
2.00	.077	3.40×10^{-4}
2.40	.038	4.45×10^{-4}
2.60	.030	5.95×10^{-4}
2.80	.013	7.35×10^{-4}

TABLE II

MOLE-SECOND MICHAELIS–MENTEN CONSTANTS FOR THE DIGESTION OF EGG ALBUMIN BY PEPSIN AT 45°

*p*H	*V*	K_m
2.00	0.48	3.94×10^{-4}
2.30	.37	4.45×10^{-4}
2.63	.16	5.07×10^{-4}
2.85	.09	5.82×10^{-4}

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