TABLE V

GASEOUS PRODUCTS FROM IRON CATALYSTS[a]

Catalysts			Fused Fe_3O_4–MgO–K_2O Fe:MgO:K_2O = 100:6.8:0.83	Pptd. Fe_2O_3–CuO–K_2CO_3 Fe:Cu:K_2CO_3 = 100:10:0.5
Hydrocarbon products	C_1	g./cu. m.	13.8	6.2
	C_2	g./cu. m.	8.6	5.6
		olefin, %	22.1	41.0
	C_3	g./cu. m.	14.3	8.7
		olefin, %	76.8	82.4
	C_4	g./cu. m.	8.0	2.7
		olefin, %	79.4	77.4
	C_5	olefin, %	77.7	72.0

[a] Tests were made with 1 hydrogen to 1 carbon monoxide gas at 7.8 atmospheres and space velocity of 100. The average temperatures of testing of the fused catalyst and precipitated catalyst were 260 and 235°. The fused catalyst was reduced in hydrogen at 450° prior to use, and the precipitated catalyst was inducted in 1 hydrogen to 1 carbon monoxide gas at 235° and atmospheric pressure.

Thermodynamic Considerations

The products from the Fischer–Tropsch synthesis from both cobalt and iron catalysts are not present in amounts corresponding to thermodynamic equilibrium between products and their formation must result from the selectivity of the catalytic process. First, oxygenated compounds and olefins are thermodynamically unstable with respect to paraffins. Second, olefin isomers show a greater amount of alpha olefins than predicted from equilibria between olefin isomers, the isomers with internal double bonds usually being more stable than the alpha isomers. Third, branched paraffin and olefin isomers have a greater stability than corresponding normal isomers. Fourth, of paraffin molecules, the formation of methane is the most likely thermodynamically.

Acknowledgment.—We wish to acknowledge the help of Julian Feldman, Irving Wender and Dr. Milton Orchin for their extensive work in preparing the samples.

Summary

The distribution of Fischer–Tropsch synthesis products has been given from C_1 to C_{20} for precipitated cobalt catalysts, using 2 hydrogen to 1 carbon monoxide gas at atmospheric pressure and 190°. Quantitative analysis of C_5–C_8 paraffin isomers by mass spectrometery showed only the presence of monomethyl isomers. The predominant components, the straight-chain isomers, decreased with increasing molecular weight. Approximate analyses of olefins showed that internal double-bond olefins were the major constituents. Preliminary results on iron-catalyst products also are reported.

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[CONTRIBUTION FROM THE RESEARCH LABORATORY, DOMINION RUBBER CO., LTD.]

Derivatives of *p*-Chlorobenzenesulfonic Acid

BY MARSHALL KULKA

In the manufacture of DDT from chlorobenzene and chloral using sulfuric acid as condensing agent, *p*-chlorobenzenesulfonic acid is a by-product. Up to the present time, this by-product has found limited use in industry and has created a disposal problem. The purpose of this investigation was to prepare derivatives of *p*-chlorobenzenesulfonic acid to be tested as possible insecticides and fungicides. Several new sulfones, sulfonic esters and N-substituted sulfonamides were perpared and their properties noted.

The sodium salt of *p*-chlorobenzenesulfonic acid was converted to *p*-chlorobenzenesulfonyl chloride (I) and fluoride (II) by means of the corresponding halosulfonic acid in the presence of a chlorinated solvent and the optimum conditions for the conversion were developed. The use of chlorinated solvent made unnecessary the large excess of the halosulfonic acid usually employed in the preparation of various arylsulfonyl halides from sodium arylsulfonates.[1]

The sulfones (IV) were prepared by reducing (I) or (II) with excess aqueous sodium sulfite to *p*-chlorobenzenesulfinic acid (III) and condensing the sodium salt of (III) with suitable halogen derivatives. When the halogen compound employed was dichloroacetic acid, condensation and

$$p\text{-}ClC_6H_4SO_2X \xrightarrow{Na_2SO_3} p\text{-}ClC_6H_4SO_2H \xrightarrow[RCl]{NaOH} p\text{-}ClC_6H_4SO_2R$$

(I, X = Cl) (II, X = F) (III) (IV) (R = alkyl or aralkyl)

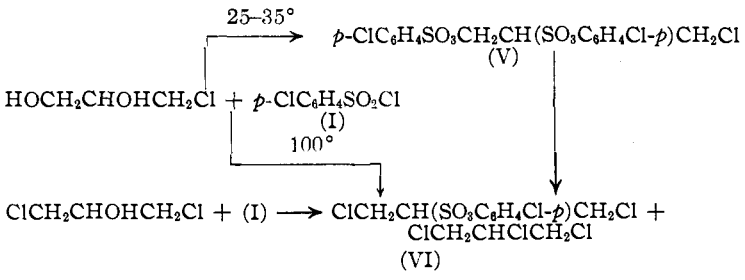
decarboxylation occurred simultaneously and the product was *p*-chlorophenyl chloromethyl sulfone.[2]

The esterification of primary alcohols with the sulfonyl halides (I) and (II) proceeded normally in the presence of sodium hydroxide or pyridine. However, when glycerol α-monochlorohydrin ($HOCH_2CHOHCH_2Cl$) was esterified with *p*-

(1) Green, Marsden and Scholfield, *J. Chem. Soc.*, **85**, 1432 (1904); Heumann and Köchlin, *Ber.*, **15**, 1118 (1882); Zincke and Kempf, *ibid.*, **44**, 418 (1911); Goldyrev and Postovsky, *J. Applied Chem., U. S. S. R.*, **11**, 316 (1938); *C. A.*, **32**, 5800 (1938).

(2) Smadel and Curtis, "Manufacture of Insecticides, Insect Repellents and Rodenticides," I. G. Farbenind., A. G. Leverkusen and Elberfeld, Combined Intelligence Objectives Sub-Committee Report No. XXIII-20 (PB Report No. 240, U. S. Department of Commerce).

chlorobenzenesulfonyl chloride (I) some irregularities were encountered. When the reaction was allowed to proceed at 25–35°, the diester, 3-chloropropyl bis-1,2-(*p*-chlorobenzenesulfonate) (V) was formed. At a higher temperature (100°) the reaction product was a mixture of 2-(1,3-dichloropropyl)-*p*-chlorobenzenesulfonate (VI) and 1,2,3-trichloropropane. The proportions of the two compounds occurring in the mixture depended upon the reaction time, prolonged heating favoring the formation of 1,2,3-trichloropropane. The identity of (VI) was established by comparison



with that synthesized from 1,3-dichloropropan-2-ol and (II). The diester (V) on heating at 100° with (I) and pyridine was also converted to a mixture of (VI) and 1,2,3-trichloropropane.

The N-substituted *p*-chlorobenzenesulfonamides were prepared in quantitative yields by condensing (I) with amines in the presence of sodium hydroxide.

An attempt to chlorinate (I) failed. Instead, the chlorosulfo group was replaced by chlorine and the main product was *p*-dichlorobenzene. Further chlorination of the dichlorobenzene also took place and some 1,2,3,5-tetrachlorobenzene was isolated. Under the same conditions of chlorination, the fluorosulfo group of (II) could not be replaced, (II) being recovered unchanged.

Experimental

p-Chlorobenzenesulfonyl Chloride (I).—To a suspension of dry, crude sodium *p*-chlorobenzenesulfonate (335 g.) in chloroform (700 cc.) was added with stirring, chlorosulfonic acid (370 g.) at such a rate that the temperature of the reaction mixture remained below 60° (about fifteen minutes). The thick slurry was stirred and heated at 55–60° for six hours, cooled and poured onto ice-water. The organic layer was separated, washed three times with cold water, dried over calcium chloride and the solvent removed. The residual oil distilled at 140° (12 mm.) and the distillate solidified on cooling; yield 293 g. or 89%; m. p. 52–53°. The melting point of (I) reported in the literature is the same.[3]

p-Chlorobenzenesulfonyl Fluoride (II). (a) from Chlorobenzene.—To mechanically-stirred fluorosulfonic acid (200 g.) in an aluminum beaker was added dropwise chlorobenzene (57 g.) over a period of three hours, the temperature of the reaction mixture being maintained at 48–50°. After stirring and heating for four hours more, the reaction mixture was poured cautiously into cold water. The organic layer was separated, washed with water and then steam distilled. The colorless oily distillate (70 g., 74%) solidified on cooling, m. p. 48–49°. The melting point of *p*-chlorobenzenesulfonyl fluoride reported in the literature[4] is 47–48°. The solid residue left after steam distillation consisted of 2.5 g. of bis-(*p*-chlorophenyl)-sulfone, m. p. 146–147°.

(b). **From Sodium p-Chlorobenzenesulfonate.**—A mixture of dry crude sodium *p*-chlorobenzenesulfonate (100 g.), fluorosulfonic acid (200 g.) and carbon tetrachloride (150 cc.) in a covered aluminum beaker was stirred and heated at 70–75° for twenty-four hours. The acid layer was separated, washed twice with carbon tetrachloride and then heated and stirred with fresh solvent for another twenty-four hours. This operation was repeated once more. The carbon tetrachloride extracts from each of the twenty-four hour runs were washed with water, the solvent removed, the last traces under vacuum, and then steam distilled. The yields of *p*-chlorobenzenesulfonyl fluoride from the three successive twenty-four hour treatments were 50 g., 19 g., and 7 g. or a total yield of 76 g., 85%.

3-Nitro-4-chlorobenzenesulfonyl Fluoride.—To a solution of fuming nitric acid (d. 1.5, 125 cc.) and concentrated sulfuric acid (50 cc.) heated at 60° was added *p*-chlorobenzenesulfonyl fluoride (50 g.) over a period of ten minutes with good stirring. The reaction mixture was then stirred and heated at 65° for one and one-quarter hours and poured into cold water. The oily material which separated was washed well with warm water and then fractionally distilled in order to separate off the unnitrated material (about 10 g.). The fraction b. p. 165–166° (17 mm.) (41 g., 67%) solidified quickly and on crystallization from ethanol or ether yielded prisms melting at 51–52°. *Anal.* Calcd. for $C_6H_3ClFNSO_4$: C, 30.06; H, 1.25. Found: C, 30.56, 30.88; H, 1.88, 1.68. This compound (2 g.) when treated with liquid ammonia gave a yellow solid which when recrystallized from ethanol yielded needles (1.7 g., 85%) m. p. 175–176°. The melting point of 3-nitro-4-chlorobenzenesulfonamide recorded in the literature is 175–176°.[5]

***p*-Chlorobenzenesulfinic Acid (III).**—To a vigorously-stirred solution of sodium sulfite (300 g.) in 1000 cc. of water warmed to 70° was added *p*-chlorobenzenesulfonyl fluoride (100 g.). The reaction mixture was kept at a temperature of 70–80° for five hours, then heated at 100° for a few minutes, strongly acidified with concentrated hydrochloric acid, cooled and filtered. The white precipitate was recrystallized from water yielding *p*-chlorobenzenesulfinic acid, m. p. 98–99° (72.8 g., 81%) in three successive crops. When one mole of *p*-chlorobenzenesulfonyl chloride was reduced at a temperature of 55–60° with two liters of 28.5% aqueous solution of sodium sulfite, a 60% yield of *p*-chlorobenzenesulfinic acid was obtained, and when two liters of a 31.5% solution of sodium sulfite was employed, the yield was 80%.

3,4-Dichlorobenzyl Chloride.[2]—A mixture of *o*-dichlorobenzene (2 l.), zinc chloride (625 g.) and trioxymethylene (150 g.) was stirred and heated at 65–70° for twenty-four hours during which time dry hydrogen chloride gas was bubbled in slowly. The separated organic layer was washed with water, with a solution of sodium bicarbonate and with water and then distilled. The fraction boiling at 110–130° (14 mm.) was collected, yield 200 g. or 22%. This colorless liquid on slow redistillation boiled mostly at 122–124° (14 mm.) and on oxidation with alkaline 3% potassium permanganate yielded a white solid melting at 206–207° after two recrystallizations from benzene. The melting point of 3,4-dichlorobenzoic acid is 209°.[6]

***p*-Chlorophenyl 3,4-Dichlorobenzyl Sulfone.**—A solution of *p*-chlorobenzenesulfinic acid (27 g.), sodium hydroxide (6.2 g.) and a little water was taken to dryness under reduced pressure. The sodium salt was dissolved in hot ethanol (150 cc.), 3,4-dichlorobenzyl chloride (35 g.) added, and the solution heated under reflux for eight hours.

(3) Pummerer, *Ber.*, **42**, 1803 (1909).

(4) Davies and Dick, *J. Chem. Soc.*, 2104 (1931).

(5) Fischer, *Ber.*, **24**, 3187 (1891).

(6) Kraay, *Rec. trav. chim.*, **49**, 1082 (1930).

The cooled reaction mixture was filtered and the white precipitate washed with cold ethanol, and with hot water and dried, yield 35 g. or 68%, m. p. 116–120°, recrystallized from ethyl acetate or ethanol white needles, m. p. 135–136°. *Anal.* Calcd. for $C_{13}H_9Cl_3SO_2$: C, 46.50; H, 2.68. Found: C, 46.77, 46.66; H, 3.17, 3.19.

***p*-Xylylene Bis-*p*-chlorophenyl Disulfone.**—A solution of *p*-chlorobenzenesulfinic acid (26.5 g.), sodium hydroxide (6 g.) in a little water was taken to dryness under reduced pressure. The sodium salt was dissolved in hot ethanol (300 cc.) and a solution of *p*-xylylene dichloride (13.2 g.) in hot ethanol (100 cc.) was added. The reaction mixture was heated under reflux for eight hours, cooled and filtered. The white precipitate was washed with cold ethanol and hot water and dried, yield 26 g. or 78%, m. p. 315–317° (uncor.). Recrystallization from tetrachloroethane yielded microscopic crystals, m. p. 335–337°. *Anal.* Calcd. for $C_{20}H_{16}Cl_2S_2O_4$: C, 52.75; H, 3.52. Found: C, 52.79, 52.68; H, 4.02, 4.13.

***p*-Chlorophenyl Chloromethyl Sulfone.**[2]—To a solution of *p*-chlorobenzenesulfinic acid (72 g.), water (900 cc.) and sodium carbonate (45 g.) was added dichloroacetic acid (61 g.) and the solution heated on the steam-bath for forty-four hours. The precipitated white needles (60.5 g. or 65%) were filtered, washed with water and recrystallized from ethanol, m. p. 120–121°. *Anal.* Calcd. for $C_7H_6Cl_2SO_2$: C, 37.33; H, 2.67. Found: C, 37.40, 37.37; H, 2.79, 3.06.

2-Chloroethyl *p*-Chlorobenzenesulfonate.—To a solution of *p*-chlorobenzenesulfonyl fluoride (25 g.) and ethylene chlorohydrin (35 cc.) was added sodium hydroxide (7 g.) and the temperature of the stirred reaction mixture was maintained at 20–25° (cooling was necessary at first) for three hours. The excess ethylene chlorohydrin was distilled off under reduced pressure, the residue dissolved in chloroform, washed with water, the solvent removed and then distilled, b. p. 197° (13 mm.), $n^{20}D$ 1.5465. The yield of the colorless, viscous liquid was 30.5 g. or 93%. *Anal.* Calcd. for $C_8H_8Cl_2SO_3$: C, 37.65; H, 3.14. Found: C, 37.87, 38.00; H, 3.49, 3.33. This ester was also prepared by heating under reflux for five hours a solution of *p*-chlorobenzenesulfonyl chloride and excess ethylene chlorohydrin, yield 74%.

2,2,2-Trichloroethyl *p*-Chlorobenzenesulfonate.—To a solution of *p*-chlorobenzenesulfonyl fluoride (13 g.), trichloroethanol (10 g.) and dry ether (40 cc.) was added sodium hydroxide (3 g.) and the temperature of the stirred reaction mixture maintained at 20–25° for three hours. The ether was removed, the white residue washed with water and recrystallized from methanol, plates, m. p. 73–74°, yield 18.9 g. or 87%. *Anal.* Calcd. for $C_8H_6O_3SCl_4$: C, 29.63; H, 1.85. Found: C, 29.83, 30.03; H, 2.27, 2.32.

The yield of this ester was 63% when *p*-chlorobenzenesulfonyl chloride was heated under reflux with excess trichloroethanol for eight hours.

2-(1,3-Dichloropropyl) *p*-Chlorobenzenesulfonate (VI). (a)—This ester was prepared from *p*-chlorobenzenesulfonyl fluoride and 1,3-dichloropropanol-2 as described above. The product was distilled and the fraction distilling at 190–200° (14 mm.) was collected. It solidified on cooling and scratching. Recrystallizations from methanol containing a little water gave white plates (yield 25%), m. p. 53–54°. *Anal.* Calcd. for $C_9H_9Cl_3SO_3$: C, 35.58; H, 2.17. Found: C, 35.69, 35.84; H, 3.50, 3.60.

(b)—To a solution of *p*-chlorobenzenesulfonyl chloride (106 g.) in dry pyridine (50 cc.) was added glycerol α-monochlorohydrin ($HOCH_2CHOHCH_2Cl$) (28 g.) over a period of a few minutes. The temperature of the reaction mixture was kept below 100° by cooling occasionally on a water-bath. Then the reaction mixture was heated on the steam-bath for one hour, cooled and poured into water. The oily material was extracted with chloroform and the solvent removed from the extract. The residual oil was distilled yielding colorless distillate, b. p. 70–80° (20 mm.), $n^{20}D$ 1.4840 (9 g.), and residue which solidified on scratching and cooling (38 g.); crystallized from ethanol, m. p. 51–52°; no depression of m. p. when mixed with (VI) prepared in (a).

The distillate boiled at 155–158° and analysis agreed closely with that of 1,2,3-trichloropropane.

3-Chloropropyl Bis-1,2-(*p*-chlorobenzenesulfonate) (V).—To a solution of *p*-chlorobenzenesulfonyl chloride (106 g.) in dry pyridine (50 cc.) was added glycerol α-monochlorohydrin ($HOCH_2CHOHCH_2Cl$) (28 g.) dropwise with stirring over a period of fifteen minutes. The temperature of the reaction mixture was kept at 25–35° by cooling. The thick slurry was stirred and the temperature kept at 30–35° by occasional cooling for another half hour. Finally it was allowed to stand at room temperature for four hours and then poured into water. The organic layer was extracted with chloroform and the extract washed with water. The solvent was removed and the thick sirupy residue (96 g. or 84%) on cooling and treatment with a little ethanol solidified; crystallized from ethanol, m. p. 66–67°. *Anal.* Calcd. for $C_{15}H_{13}O_6Cl_3S$: C, 39.17; H, 2.82; Cl, 23.11. Found: C, 39.35, 39.59; H, 3.20, 3.16; Cl, 23.11.

This compound on heating with *p*-chlorobenzenesulfonyl chloride and pyridine at 100° yielded a mixture of (VI) and 1,2,3-trichloropropane.

2,4-Dichlorophenyl *p*-Chlorobenzenesulfonate.—To a solution of 2,4-dichlorophenol (16.3 g.) and sodium hydroxide (4 g.) in water (40 cc.) was added *p*-chlorobenzenesulfonyl fluoride (19.5 g.) and the reaction mixture stirred and heated at 50–60° for two hours. The semi-solid reaction mixture was filtered, washed with hot water and dried; yield of white solid was 29 g. or 85%, m. p. 110–115°, recrystallized from ethanol or ethyl acetate, m. p. 119–120°, rhombohedra. *Anal.* Calcd. for $C_{12}H_7Cl_3SO_3$; C, 42.67; H, 2.07. Found: C, 42.67, 42.87; H, 2.06, 2.23.

β-Chloroethyl 3,4-Dichlorobenzenesulfonate.—To a solution of ethylene chlorohydrin (20 cc.) and 3,4-dichlorobenzenesulfonyl chloride (50 g.) (prepared from *o*-dichlorobenzene and excess chlorosulfonic acid), was added dry pyridine (17 g.) dropwise over a period of one-half hour, the temperature being kept at 10–15° by cooling. The reaction mixture was stirred at 10–15° for an additional hour and then allowed to stand at 5° for two hours. The solid reaction mixture was dissolved in chloroform and the solution washed well with water. Removal of the solvent left a solid residue; crystallized from eth-

TABLE I

p-CHLOROBENZENESULFONAMIDES PREPARED

p-Chlorobenzenesulfonamide	M. p., °C.	Analyses, %	C	H	N
N,N-Dimethyl-	79–80	Found	44.16	4.55	6.46
			44.19	4.59	
		Calcd.	43.74	4.56	6.38
N,N-Diethyl-	37–38	Found	48.39	5.28	5.44
			48.32	5.53	5.25
		Calcd.	48.49	5.65	5.65
N-Isopropyl-	85–86	Found	45.87	4.81	7.38
			45.71	4.62	7.00
		Calcd.	46.25	5.13	6.00
N-Butyl	50–51	Found	48.51	5.36	5.85
			48.26	5.41	5.69
		Calcd.	48.49	5.65	5.65
N-(*p*-Chlorobenzenesulfonyl)-morpholine	148–149	Found	45.45	4.38	5.29
			45.36	4.50	5.55
		Calcd.	45.90	4.59	5.34
N-(β-Hydroxyethyl)-	104–105	Found	40.16	4.04	6.32
			40.28	3.96	6.43
		Calcd.	40.77	4.24	5.94
N,N'-Bis-(*p*-chlorobenzenesulfonyl)-1,2-diaminopropane	141–142	Found	42.83	4.02	6.82
			42.83	3.77	6.74
		Calcd.	42.56	3.78	6.62

anol, yield 48 g. or 81%, m. p. 69–70°, colorless rhombohedra. *Anal.* Calcd. for $C_8H_7O_3Cl_3S$: C, 33.16; H, 2.42; Cl, 36.79. Found: C, 33.53, 33.26; H, 2.78, 2.55; Cl, 36.68.

An attempt to prepare this compound by heating 3,4-dichlorobenzenesulfonyl chloride and excess ethylene chlorohydrin under reflux resulted in only poor yield of the ester.

Preparation of the *p*-Chlorobenzenesulfonamides.—To a stirred solution of *p*-chlorobenzenesulfonyl chloride (1 mole) in chloroform was added dropwise the amine (1 mole) (free amine or aq. solution) over a period about one-half hour. The reaction mixture was kept below 40° by cooling. Then an aqueous solution of sodium hydroxide (1 mole) was added dropwise with cooling and stirring. After stirring for an additional half-hour, the reaction mixture was allowed to separate. The organic layer was washed with water and the solvent removed. Yields of the white *p*-chlorobenzenesulfonamides were quantitative. They were crystallized from ethanol or petroleum ether.

N-(β-Chloroethyl) *p*-Chlorobenzenesulfonamide.—To N-(β-hydroxyethyl) *p*-chlorobenzenesulfonamide (5 g.) was added thionyl chloride (10 cc.) and the solution heated under reflux for two hours. The reaction mixture was stirred with water to decompose excess thionyl chloride and the precipitated white solid (3.0 g. 58%) was filtered, washed with water and dried. Crystallization from ethanol or ethyl acetate yielded white plates (2.0 g.), m. p. 152–153°. *Anal.* Calcd. for $C_8H_9O_2SNCl_2$: C, 37.80; H, 3.54; N, 5.51. Found: C, 36.80, 36.97; H, 3.25, 3.38; N, 5.35, 5.89.

The Action of Chlorine on *p*-Chlorobenzenesulfonyl Chloride.—*p*-Chlorobenzenesulfonyl chloride (50 g.) and a trace of ferric sulfate was heated in a flask equipped with a condenser and a gas inlet tube at 175–180° while a rapid stream of chlorine gas was passed in for one hour. The white solid (12.5 g.) which sublimed into the condenser melted at 52–54° and did not depress the melting point of *p*-dichlorobenzene. The material left in the pot on distillation yielded 10.5 g. more of *p*-dichlorobenzene, total yield 22.5 g. or 63%, b. p. 172–180° and a fraction (9 g.) b. p. (12 mm.) 125–130°; crystallized from ethanol, m. p. 50–52° (4 g.) (the melting point of 1,2,3,5-tetrachlorobenzene is 51°). The oily product left in the mother liquors is probably a mixture of the three isomeric tetrachlorobenzenes.

Summary

p-Chlorobenzenesulfonic acid was converted to *p*-chlorobenzenesulfonyl chloride and fluoride and from these several new sulfones, sulfonic esters and N-substituted sulfonamides were prepared.

The esterification of glycerol α-monochlorohydrin with *p*-chlorobenzenesulfonyl chloride resulted in 3-chloropropyl bis-1,2-(*p*-chlorobenzenesulfonate), 2-(1,3-dichloropropyl)-*p*-chlorobenzenesulfonate and 1,2,3-trichloropropane.

The reaction of chlorine with *p*-chlorobenzenesulfonyl chloride yielded *p*-dichlorobenzene.

GUELPH, ONTARIO, CANADA RECEIVED AUGUST 24, 1949

[CONTRIBUTION FROM THE MALLINCKRODT CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Dimethylgermanium Oxide. Toxicity and Effect on Blood Composition

BY EUGENE G. ROCHOW AND BERNICE M. SINDLER

Early work on the biological effects of germanium indicated that the subcutaneous administration of germanium dioxide or sodium germanate had a distinct erythropoietic action[1] and so was useful in the treatment of secondary and pernicious anemias. A later study indicated that a temporary increase in the number of erythrocytes per unit volume might be due merely to dehydration following the injection of large doses of colloidal GeO_2,[2] although this was before a clarification of the polymorphism of GeO_2[3] so that it is not known whether the soluble (hexagonal) or insoluble (tetragonal) form was administered in this or the earlier work. A single subcutaneous administration of 10.5 mg. of germanium/kg. (as GeO_2) has been shown not to be toxic, nor is a single intravenous injection of 12.6 mg. germanium/kg.,[4] but "excessive amounts" cause a marked drop in blood pressure and "toxic doses" cause a rise in *p*H of the blood and massive brown deposits in the organs.[1a]

(1) (a) L. Kast, H. M. Croll and H. W. Schmitz, *J. Lab. Clin. Med.*, **7**, 643 (1922); (b) J. L. Lenker, *Penn. Med. J.*, **26**, 86 (1922); (c) R. M. Parr, *Trans. Ill. Acad. Sci.*, **21**, 194 (1928); U. S. Patent 1,909,070.

(2) W. C. Hueper, *Am. J. Med. Sci.*, **181**, 820 (1931).

(3) A. W. Laubengayer and D. S. Morton, THIS JOURNAL, **54**, 2303 (1932).

(4) G. C. Harrold, S. F. Meck and C. P. McCord, *Ind. Med.*, **18**, 236 (1944).

The relatively easy preparation of organogermanium halides by the direct synthesis[5] has led to the synthesis of polymeric dimethylgermanium oxide,[6] which has a surprisingly high solubility in water in comparison with ethyl or phenylgermanium oxides. The immediate questions which arise are (1) does the $(CH_3)_2Ge<$ group undergo hydrolysis or oxidation *in vivo*, resulting in the liberation of toxic methyl groups, and (2) if the $(CH_3)_2Ge<$ group is stable under body conditions, does it exert a stimulating influence on red blood cell formation as does germanium ion? Complete answers to these questions would involve elaborate and exhaustive studies with separate groups of experimental animals in large number, but it was felt that some preliminary information might be gained by subcutaneous injection of an aqueous solution of dimethylgermanium oxide in experimental animals. In the absence of gross toxicity, the effect of the substance on blood composition could be followed by periodic determination of hemoglobin level and red cell count on the same group of animals.

Experimental

Dimethylgermanium oxide was prepared from dichloride,[6] distilled as the tetramer, and dissolved in water to a

(5) Rochow, THIS JOURNAL, **69**, 1729 (1947); **70**, 436 (1948).

(6) Rochow, *ibid.*, **70**, 1801 (1948).