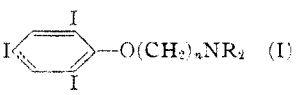
[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA, AND THE DEPARTMENT OF PHARMACOLOGY AND PHYSIOLOGY, DUKE UNIVERSITY MEDICAL SCHOOL]

Synthesis and Antitubercular Studies of Halogenated Phenyl Ethers

BY ALFRED BURGER, ELIZABETH L. WILSON,[1] C. O. BRINDLEY AND FREDERICK BERNHEIM

The tuberculostatic properties of 2,4,6-triiodophenol were first described by Carrasco,[2] who introduced bismuth salts of this compound under the name of *Neoform* into a short-lived therapeutic practice. More recently, Saz, Johnston, Burger and Bernheim[3] observed that triiodophenol itself is bacteriostatic, and some of its diethylaminoalkyl ethers are bactericidal in their action on human and bovine tubercle bacilli *in vitro*. Oxygen uptake by the bacilli was decreased, growth *in vitro* inhibited by several of the drugs tested, and the formation of tubercles in the omentum of infected guinea pigs was reduced. Based on this latter observation, an *in vivo* screening test was worked out which promised to accelerate considerably the initial evaluation of new antitubercular drugs as compared with the traditional laborious testing methods, and to reduce the quantity of the drug required in those tests.

In order to explore the significance of the diethylamino group in the ether chain of the active ethers, 1-(2,4,6-triiodophenoxy)-2-(4-morpholino)-ethane was tested, and, unexpectedly, found to be devoid of tuberculostatic activity. This led us to synthesize a number of dialkylaminoalkyl ethers of iodinated phenols with variations in the structure of the ether chain (I). In general,



chemotherapeutic activity was not restricted to compounds containing aliphatic amino groups; several ethers containing the 2-methylpiperidinopropyl radical were highly active. Activity, but also toxicity in guinea pigs, was usually greater in dialkylaminopropyl than in the corresponding dialkylamino ethyl ethers, while shortening of the ethylene group, in a trihalogenophenoxy diethylaminomethane derivative caused complete loss of antitubercular action. Replacement of the dibutylamino group in an active ether by the secondary monobutylamino group also abolished activity.

Replacement of nuclear iodine by other halogens did not lead to a definite pattern correlating chemical structure to antitubercular activity. Nuclear bromine had a slightly dystherapeutic effect while several of the polychloro derivatives rivaled analogous iodinated compounds. As the only tangible result of these variations, nuclear iodine does not appear superior to other halogens in the tuberculostatic activity of this series.

The basic aromatic ethers are listed in Table I. Although only a few non-halogenated dialkylaminoalkyl phenyl ethers have been tested it appears that such compounds lack antitubercular properties. Therefore, simpler non-basic phenyl alkyl ethers were not tested. However, several polyhalogenophenols and -anisoles exhibited an *in vitro* inhibition up to 85%. *In vivo* inhibition was negligible, perhaps owing to the low solubility of these derivatives. Lengthening the alkyl chain from one carbon atom in the bacteriostatic trihalogeno anisoles to twelve carbon atoms, in *n*-dodecoxy-2,4,6-triiodobenzene and its 3-methyl homolog, abolished this activity, probably because of the insolubility of these ethers in polar solvents. We had hoped that their high solubility in hydrocarbons would increase their chance of penetrating the lipid capsule of the acid-fast bacilli, and enable the "toxic" triiodophenoxy group to exert a more pronounced action on the organisms.

In the preparation of the starting materials, various commercially available phenols were iodinated in an ammoniacal medium. The anisoles were prepared from the corresponding sodium phenolates with dimethyl sulfate in aqueous solution while the dialkylaminoalkyl ethers were synthesized from the sodium phenolates and dialkylaminoalkyl halides in methanol solution by the Williamson reaction. The dialkylaminoalkyl halides were prepared from commercial dialkylamino alcohols with thionyl chloride.

The lauryl ethers listed in Table II were obtained from sodium triiodophenolate, and cresolate, respectively, and lauryl iodide in methanol solution.

2,4,5 - Trichlorophenoxy - diethylaminomethane was synthesized by condensation of diethylaminomethyl chloride hydrochloride[4] with sodium 2,4,5-trichlorophenolate in the presence of sodium methoxide.

Acknowledgment.—The authors are deeply grateful to Dr. Charles C. Haskell of Richmond, Virginia, for a generous grant which made these studies possible, and to the Duke University Research Council for funds used in this research. The technical assistance of Miss Joan Elliott and Mr. Edward Stanley-Brown in the preparation of some of the starting materials has been very helpful.

Experimental

Iodination of Phenols.—In general, 100 g. of the phenol was dissolved in a mixture of 800 cc. of 20% ammonium

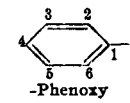
(1) Charles C. Haskell Fellow, University of Virginia, 1943-1944.

(2) Carrasco, *Boll. chim.-farm.*, **47**, 109 (1908); *Chem. Zentr.*, **79**, I, 1735 (1908).

(3) Saz, Johnston, Burger and Bernheim, *Am. Rev. Tuberc.*, **48**, 40 (1943).

(4) Prévost and de Mauny, *Compt. rend.*, **216**, 771 (1943); *C. A.*, **38**, 4563[6] (1944).

TABLE I



-Phenoxy	n	NR$_2$	Formula	M. p., °C. (d denotes decomp.)	Analyses, %	Calcd.	Found	n mg.% inhibited *in vitro* growth of tubercle bacillus y %		n mg./kg. reduced omental wt. per 100 g. guinea pig to x g. (control, y g.)			Av. wt. loss of animal in g.
								n	y	n	x	y	
2,4,6-Triiodo	2	NMe_2·HCl	$C_{10}H_{12}I_3NO$·HCl	226 d	C	20.72	21.01	3	90	100	0.73	0.83	80
					H	2.26	2.53						
2,4,6-Triiodo	2	$N(n\text{-Bu})_2$·HCl	$C_{16}H_{24}I_3NO$·HCl	192–194 d	Cl⁻	5.34	5.71			50	.66	.75	
2,4,6-Triiodo	2	Morpholino[a]·HCl[a]	$C_{12}H_{14}I_3NO_2$	130–131	N	2.39	2.67						
			$C_{12}H_{14}I_3NO_2$·HCl	240–242 d	N	2.25	2.41	5	00				
2,4,6-Triiodo	3	NEt_2·HCl	$C_{13}H_{18}I_3NO$·HCl	190–192 d	Cl⁻	5.71	6.37	3	96	30	.97	.98	70
2,6-Diiodo-4-bromo	2	NEt_2·HCl	$C_{12}H_{16}BrI_2NO$·HCl	174–177 d	Cl⁻	6.33	6.36	3	95				
2,6-Diiodo-4-chloro	2	NEt_2·HCl	$C_{12}H_{16}ClI_2NO$·HCl	182 d	Cl⁻	6.86	6.86	3	86				
2,4-Diiodo-6-chloro	2	NEt_2·HCl	$C_{12}H_{16}ClI_2NO$·HCl	155–156	Cl⁻	6.86	6.73			50	.58	.69	69
2,6-Diiodo-4-chloro	3	NEt_2·HCl	$C_{13}H_{18}ClI_2NO$·HCl	214 d	Cl⁻	6.70	6.63			50	.87	.95	124
2,4-Diiodo-6-chloro	3	NC_6H_{12}·HCl[d]	$C_{13}H_{20}ClI_2NO$·HCl	188 d	Cl⁻	6.38	6.30			50	.97	.93	149
2,6-Diiodo-4-phenyl	2	NEt_2·HCl	$C_{18}H_{21}I_2NO$·HCl	198–199 d	Cl⁻	6.36	6.58			50	.58	.69	39
2,6-Diiodo-4-methyl	2	NEt_2·HCl	$C_{13}H_{19}I_2NO$·HCl	166.5	Cl⁻	7.16	7.06	3	62	50	.71	.81	76
2,4-Diiodo-6-methyl	2	NEt_2·HCl	$C_{13}H_{19}I_2NO$·HCl	151–152	Cl⁻	7.16	7.23	3	88	50	.81	.81	113
2,4,6-Triiodo-3-methyl	2	NEt_2·HCl	$C_{13}H_{18}I_3NO$·HCl	173–174	C	25.24	25.20	5	95.4	50	1.1	1.1	54
					H	2.61	3.04	5	97.7				
2,4,6-Triiodo-3-methyl	2	$N(n\text{-Bu})_2$·HCl	$C_{17}H_{26}I_3NO$·HCl	190–193 d	C	30.10	29.88	3	20				Too insol.
					H	4.02	4.05						
2,4,6-Triiodo-3,5-dimethyl	2	NEt_2·HCl	$C_{14}H_{20}I_3NO$·HCl	209 d	X	65.49	65.40						
2-Iodo-4-phenyl-6-bromo	2	NEt_2·HCl	$C_{18}H_{21}BrINO$·HCl	190–191 d	Cl⁻	6.93	6.82						
2,6-Diiodo-4-phenylazo	2	NEt_2·HCl	$C_{18}H_{21}I_2N_3O$·HCl	188–190 d	Cl⁻	6.05	6.40						
2,4,6-Tribromo	2	NMe_2·HCl	$C_{10}H_{12}Br_3NO$·HCl	194	Cl⁻	8.09	8.33	3	76.6	50	1.1	1.1	60
2,4,6-Tribromo	2	NEt_2·HCl	$C_{12}H_{16}Br_3NO$·HCl	149	Cl⁻	7.60	7.69	3	56.2	100	0.61	0.75	
										100	.82	.91	54
2,4,6-Trichloro	2	NMe_2	$C_{10}H_{12}Cl_3NO$	B. p. 131–133 (4 mm.)	[b]			5	95.5	100	.52	.75	
										50	.78	.91	39
		Picrate[c]	$C_{16}H_{15}Cl_3N_4O_8$	192–193	N	11.26	12.04						
2,4,6-Trichloro	2	NEt_2·HCl	$C_{12}H_{16}Cl_3NO$·HCl	160–162	Cl⁻	10.62	10.73	5	52.2	50	.79	.98	50
								5	82.6				
2,4,6-Trichloro	3	NC_6H_{12}·HCl[d]	$C_{13}H_{20}Cl_3NO$·HCl	156–157	Cl⁻	9.50	9.02			50	.83	.93	64
2,4,5-Trichloro	1	NEt_2·HCl	$C_{11}H_{14}Cl_3NO$·HCl	157–159 d	Cl⁻	11.09	11.10	5	00				
2,4,5-Trichloro	2	NMe_2·HCl	$C_{10}H_{13}Cl_3NO$·HCl	210–211	Cl⁻	11.59	11.70	3	92.1	50	.77	.91	60
2,4,5-Trichloro	2	NEt_2·HCl	$C_{12}H_{16}Cl_3NO$·HCl	183	Cl⁻	10.62	10.44	2	61.5	60	..	.63	All animals died
								5	67.2				
								5	72.1				
2,4,5-Trichloro	2	$N(n\text{-Bu})_2$·HCl	$C_{16}H_{24}Cl_3NO$·HCl	124	Cl⁻	9.11	9.26	3	97	50	.82	.98	65
2,4,5-Trichloro	3	NEt_2·HCl	$C_{13}H_{18}Cl_3NO$·HCl	179	Cl⁻	10.13	10.35			50	.82	.83	40
2,4,5-Trichloro	3	$N(n\text{-Bu})_2$	$C_{17}H_{26}Cl_3NO$	B. p. 180–190 (2 mm.)	[b]					50	.60	.69	55
		Picrate[c]	$C_{23}H_{23}Cl_3N_4O_8$	119–120	N	9.40	9.46						
2,4,5-Trichloro	3	NC_6H_{12}·HCl[d]	$C_{13}H_{20}Cl_3NO$·HCl	229–230	Cl⁻	9.50	9.87			50	.52	.69	100
2,4,5-Trichloro	2	$NH(n\text{-Bu})$·HCl	$C_{12}H_{16}Cl_3NO$·HCl	122	X	42.58	43.55			50	.68	.71	Very toxic
2,4-Dichloro	2	$N(n\text{-Bu})_2$·HCl	$C_{16}H_{25}Cl_2NO$·HCl	295–297	C	54.18	53.45			50	.83	.93	38
					H	7.39	8.87						
Pentachloro	3	NC_6H_{12}·HCl[d]	$C_{13}H_{15}Cl_6NO$·HCl	224 d	C	40.76	40.60			50	.93	.72	89
					H	4.33	4.36			50	.95	.62	5 pigs died
Unsubstituted	2	NEt_2·HCl	$C_{12}H_{19}NO$·HCl	137.5	C	62.73	62.77			50	.73	.83	42
					H	8.71	8.57						
4-*t*-Butyl	2	NEt_2·HCl	$C_{16}H_{27}NO$·HCl	158–160	Cl⁻	12.36	12.38			50	.88	.93	67
4-*t*-Amyl	2	NEt_2·HCl	$C_{17}H_{29}NO$·HCl	128–131	Cl⁻	11.82	11.84			50	.94	.83	52
3-Methyl	2	$N(n\text{-Bu})_2$	$C_{17}H_{29}NO$	B. p. 147–150 (1 mm.)	[b]					50	1.18	.95	84
3,5-Dimethyl	2	NEt_2·HCl	$C_{14}H_{23}NO$·HCl	132	Cl⁻	13.75	13.16			50	0.63	.68	52

[a] Prepared by Dr. K. C. Bass, Jr. [b] The free oily base was not analyzed. For physiological experimentation, it was dissolved in one mole of dilute hydrochloric acid. [c] The picrate was prepared in ethanol solution, and recrystallized from the same solvent. [d] NC_6H_{12} signifies the 2-methylpiperidino group.

hydroxide and 200 to 800 cc. of methanol with mechanical stirring at room temperature, and the calculated amount of an iodine solution, containing one part of iodine and two parts of potassium iodide in four parts of water, was added at such a rate that the brown color of iodine never persisted for any length of time. The iodine usually was absorbed rapidly in the beginning, and more slowly toward the end of the substitution. An occasional precipitate of nitrogen iodide which appeared in the reaction mixture went back into solution as absorption progressed. The reaction product precipitated directly from the mixture, or, in a few cases, was obtained on dilution with water. The iodinated phenols were recrystallized from methanol, methanol–water, or acetic acid. The yield of

TABLE II

Name	Formula	M. p., °C. (d denotes decomp.)	Analyses, % Calcd.	Found	*n* mg.% inhibited *in vitro* growth of tubercle bacillus *y* % *n*	*y*	*n* mg./kg./day reduced omental wt. from *y* g. (control) to *x* g. *n*	*x*	*y*	Av. wt. loss of animal, g. Remarks
2,4,6-Triiodoanisole	$C_7H_5I_3O$	99			2	25	60	0.60	0.63	54
					5	85.5				
2,4,6-Tribromoanisole	$C_7H_5Br_3O$	87			5	70.6				
					5	75.4				
2,4,6-Trichloroanisole	$C_7H_5Cl_3O$	65					60	.61	.63	00
2,4,5-Trichloroanisole	$C_7H_5Cl_3O$	76–77			5	95.4	50	.63	.75	00
					5	97.8				
2,6-Diiodo-4-chloroanisole	$C_7H_5ClI_2O$	65	Halogen		40	83	100	.81	.83	60
			73.33	72.85						
2,4-Diiodo-6-chloroanisole	$C_7H_5ClI_2O$	80					100	.81	.83	40
										3 deaths
2,4,6-Triiodo-*n*-dodecoxybenzene	$C_{18}H_{27}I_3O$	63–64	C, 33.77	33.56						
			H, 4.25	4.26						Too toxic
2,4,6-Triiodo-3-methyl-*n*-dodecoxybenzene[a]	$C_{19}H_{29}I_3O$	47–48	C, 34.88	34.62	5	6	75	1.1	1.1	Too insol.
			H, 4.47	4.44						
2,4,6-Triiodo-3,5-dimethylphenol	$C_8H_7I_3O$	175–177 d	I, 76.16	75.64	5	54.0				
					5	57.8				
2,4,6-Triiodo-3-methylphenol	$C_7H_5I_3O$	122			2	64.3	60	0.60	0.63	
					5	85.7	100	.77	.91	40
2,4-Diiodo-4-*t*-amylphenol	$C_{11}H_{14}I_2O$	62	I, 61.01	61.23						
2-Bromo-4-phenyl-6-iodophenol	$C_{12}H_8BrI$	86.5–88	Halogen							
			55.15	54.83						
2,4-Diiodo-4-*t*-butylphenol	$C_{10}H_{12}I_2O$	82	I, 63.14	63.41						

[a] Recrystallized from acetone.

the crude reaction product was above 90% but 5–20% of the material was usually lost during the purification.

The calculated amount of iodine was, in our experiments, the maximum number of moles of iodine needed to substitute all the available positions *ortho* and *para* to the phenolic hydroxyl group. We found that this amount of iodine was absorbed regardless of the nature, or the relative position of other substituents in the aromatic nucleus. The phenols serving as starting materials in these iodinations were obtained from the Eastman Kodak Co.

Preparation of Dialkylaminoalkyl Chlorides.—One mole of thionyl chloride, dissolved in twice its volume of dry benzene, or in chloroform,[5] was added dropwise, and with stirring, at −5° to a solution of one mole of the freshly distilled dialkylamino alkanol in twice its volume of one of the solvents mentioned above. The addition required one to two hours. The mixture was refluxed with stirring on a steam-bath for three to five hours and allowed to cool. The crystalline dialkylaminoalkyl chloride hydrochloride was filtered, washed with acetone, and recrystallized from ethanol–ether. When chloroform was used as a solvent, it had to be removed under reduced pressure to permit crystallization of the crude hydrochloride. The yields were 80–90%. None of the pure salts used by us was appreciably hygroscopic.

In order to obtain β-di-*n*-butylaminoethyl chloride hydrochloride, the solvent (either benzene or chloroform) had to be removed, and the crystalline salt was recrystallized from benzene–ether. It was extremely soluble in acetone, and not hygroscopic when pure. The crude hygroscopic salt did not always crystallize readily but had to stand at 4° for several days in a number of runs.

β-*n*-Butylaminoethyl chloride hydrochloride was prepared in an analogous manner.

Dimethyl- and diethylaminoethanol and morpholinoethanol were furnished by Carbide and Carbon Chemicals Corp.; mono- and dibutylaminoethanol by Sharples Chemicals.

3-(2-Methylpiperidino)-propanol-1 was supplied generously by the Lilly Research Laboratories, while the other dialkylamino alcohols were purchased from Eastman Kodak Co.

Preparation of Dialkylaminoalkyl Aryl Ethers.—In most of these experiments, 0.1 mole of the phenol was dissolved in a solution of 0.2 mole of sodium in methanol[6] (about 10 cc. per g. of phenol) at 30–50°. Twelve hundredths of a mole of the dialkylaminoalkyl chloride hydrochloride was added in one batch, and the mixture refluxed for five to twelve hours. Sodium chloride precipitated immediately, and bumping could be reduced by frequent shaking or stirring.

Since the dialkylaminoalkyl chlorides, especially the dialkylaminoethyl chlorides, have a tendency to polymerize, their reaction with the sodium phenolates was accelerated by addition of 0.1 mole of sodium iodide to the reaction mixtures. However, the yields of the basic ethers were not improved appreciably by this procedure.

The precipitated sodium chloride was filtered, the solution evaporated under reduced pressure, the gummy semi-solid residue extracted with ether and water, and the ether solution washed repeatedly with 25% sodium hydroxide solution and with water. Insoluble precipitates of recovered sodium polyhalogenophenolates frequently appeared at the interphase.

The ether solution was dried over sodium sulfate, the solvent removed, and the oily base converted to the hydrochloride in acetone–ether solution. In a few cases, the hydrochlorides did not crystallize; the basic ethers were distilled at 1–3 mm., and the oily distillates used directly, or in solution in one equivalent of dilute hydrochloric acid, for the bacteriostatic tests. No attempt was made to distil

(5) The preferential use of this solvent was recommended to us by Mr. H. A. Shonle, Lilly Research Laboratories, Indianapolis, Ind.

(6) Methanol was used for all iodinated phenols while ethanol gave equally good, or better, yields of ethers containing halogens other than iodine.

ethers containing iodine. The hydrochlorides were recrystallized from methanol, ethanol, methanol–ether, acetone, or ethyl acetate–ether.

The yields in the Williamson reactions averaged 25–35%. Low yields, sometimes below 5%, were obtained in several preparations involving dimethylaminoethyl chloride. Dialkylaminopropyl chlorides usually rendered the corresponding aryl ethers in yields of 50–90%. However, the optimum conditions have not been determined in all cases.

1-(2,4,5-Trichlorophenoxy)-2-*n*-butylaminoethane was prepared from *n*-butylaminoethyl chloride in an analogous manner. The yield was 18%.

2,4,5-Trichlorophenoxy Diethylaminomethane.—Diethylaminomethyl chloride hydrochloride was obtained in 81% yield by the direction of Prévost and de Mauny[4] and condensed with sodium 2,4,5-trichlorophenolate according to the procedure outlined above. The yield was 5%.

Chemical Analysis.—Most of the hydrochlorides listed in Table I were titrated in water or dilute alcohol solution with 0.05 *N* potassium hydroxide solution to a phenolphthalein end-point.

For several hydrochlorides, and water-insoluble derivatives, the total halogen content was determined by the method of Schwenk, Papa and Ginsberg,[7] using samples of 30–80 mg. and correspondingly small amounts of the required reagents. The silver nitrate and potassium thiocyanate solutions were 0.05 *N*. Reliable results were obtained on this semi-micro scale with most of the compounds; those derivatives analyzed for carbon, hydrogen or nitrogen did not give consistent halogen values by reduction with Raney nickel alloy.

Summary

A number of alkyl and dialkylaminoalkyl ethers of phenol and halogenated phenols with various substituents has been described. It has been found that nuclear iodine is not a prerequisite for the antitubercular action of such compounds.

(7) Schwenk, Papa and Ginsberg, *Ind. Eng. Chem., Anal. Ed.*, **15**, 576 (1943).

CHARLOTTESVILLE, VA.
DURHAM, N. C. RECEIVED APRIL 25, 1945

NOTES

Isolation of Rutin from *Hydrangea Paniculata*, Var. *Grandiflora Sieb.*

BY JAMES F. COUCH AND JOSEPH NAGHSKI

Rutin, 3,5,7,3′,4′-pentahydroxyflavone-3-rutinoside, has recently assumed some prominence in the treatment of increased capillary fragility associated with hypertension[1,2] and is promising as a remedy for certain other diseases resulting from capillary breakdown. Rutin has been found in thirty-three species of plants and is, thus, one of the most widely distributed of the glucosides. This paper reports the isolation and identification of rutin in the flowers of a common garden species of *Hydrangea*. Previous chemical examinations of the roots of white-flowered species of *Hydrangea* have been reported.[3,4,5] Hashimoto and Kawana[6] extracted the dried flowers of *H. paniculata* with benzene and obtained a phenolic substance, $C_9H_6O_3$, but they do not mention rutin. The presence of rutin in relatively large quantities in the flowers has not previously been reported.

Experimental.—Fresh blossoms (67.5 g., moisture, 83.6%) were digested with alcohol (300 ml.) for several hours. The solvent was removed from the filtered extract. The residue was freed from fats and resins with benzene and the insoluble matters were extracted with boiling water. On cooling and standing, 0.4 g. of rutin crystallized, m. p. 183–185°; raised by recrystallization from boiling water to 190–192°. A further crop, 0.05 g., was obtained by re-extracting the insoluble matters with boiling water; yield, 0.45 g. or 4.06% of the moisture-free plant.

Anal.[7] Calcd. for $C_{27}H_{30}O_{16}$: C, 53.10; H, 4.95. Found: C, 53.34; H, 5.09.

The substance gave the usual tests for the identification of rutin. These data were confirmed on a larger sample (1.6 kg.) of fresh flowers.

(1) J. Q. Griffith, J. F. Couch and M. A. Lindauer, *Proc. Soc. Exp. Med. Biol.*, **55**, 228–229 (1944).

(2) J. F. Couch and C. F. Krewson, United States Department of Agriculture, Mimeograph Circular AIC-52, July, 1944.

(3) C. S. Bondurant, *Am. J. Pharm.*, **59**, 122–124 (1887).

(4) A. G. Leubert, *ibid.*, **70**, 550–552 (1898).

(5) H. J. M. Schroeter, *ibid.*, **61**, 117–118 (1889).

(6) A. Hashimoto and T. Kawana, *J. Pharm. Soc. Japan*, **55**, 183–186 (1935); *C. A.*, **29**, 5112 (1935).

(7) C and H determinations by C. L. Ogg.

AGRICULTURAL RESEARCH ADMINISTRATION
BUREAU OF AGRICULTURAL AND INDUSTRIAL CHEMISTRY
UNITED STATES DEPARTMENT OF AGRICULTURE
EASTERN REGIONAL RESEARCH LABORATORY
PHILADELPHIA, PA. RECEIVED MARCH 26, 1945

sym-Tetraphenylethane from DDT and Related Compounds[1]

BY ELMER E. FLECK, ROBERT K. PRESTON AND H. L. HALLER

During an investigation of the effect of various solvents on the dehydrochlorination of 1-trichloro-2,2-bis-(*p*-chlorophenyl)-ethane (known as DDT),[2] it was noted that an abnormal reaction took place in the presence of anhydrous aluminum chloride and benzene. When one mole of anhydrous aluminum chloride was used with a large

(1) Some of the work reported was done under a transfer of funds, recommended by the Committee on Medical Research, from the office of Scientific Research and Development to the Bureau of Entomology and Plant Quarantine.

(2) Fleck and Haller, THIS JOURNAL, **66**, 2095 (1944).