grafts of 56.6 days. The treatment with procarbazine caused a weight loss averaging 11.8 percent of the starting weight, although no mice died. The animals recovered their weights rather quickly.

The effect of both agents on the primary hemagglutinin response to sheep erythrocytes was also striking in tests made with small numbers of AKR mice, but procarbazine was somewhat superior to ALS in its immunosuppressant effect. Eight mice that received the long treatment with procarbazine had no circulating hemagglutinins when tested at day 13 (Table 2). Four of ten mice treated with ALS had no circulating hemagglutinins although the others produced appreciable, but reduced, amounts of antibody.

In the plaque-forming cell test (*5*), treatment with ALS (10 ml/kg intraperitoneally from day −2 to day 3) suppressed the plaque-forming cells to sheep erythrocytes by 94.4 percent, when compared to controls treated only with the normal rabbit serum, the test being done on day 4. In a dosage of 150 mg/kg from day −21 to day −17, 100 mg/kg from day −15 to day −4, and 50 mg/kg until day +3 (all doses being given intraperitoneally and totaling approximately 60 mg per mouse), procarbazine suppressed all (100 percent) the plaque-forming cells in the spleen at day 4.

Procarbazine is an active agent which suppresses both cell-mediated immunity, as judged by prolongation of skin-graft survivals, and humoral antibody. It appears to completely suppress circulating antibodies to sheep erythrocytes in mice. It is difficult to claim that procarbazine is better than ALS as an immunosuppressant, as the potency and effect of ALS varies from batch to batch. It is theoretically possible to produce an even more potent ALS than was used in this study. The advantages of a chemical ALS over a heterologous serum are self-evident. We did not attempt to determine the minimum effective dose of procarbazine; in fact, the dosage was the maximum tolerated.

There is no immediate explanation for the need for a long period of treatment. In an experiment in which 150 mg of procarbazine per kilogram of body weight was given from day −2 to day 6, all the mice had circulating hemagglutinins to sheep erythrocytes at day 7, although the titers were lower than the controls.

The mode of action of procarbazine, like that of ALS, is unknown. Weitzel *et al.* (*6*) reported that it inhibited the transport mechanism of nucleosides into lymphocytes. Floersheim (*2*) also found procarbazine specific for lymphocytes, in that the total number in the circulation was reduced approximately 70 percent after 4 weeks of treatment. Thus procarbazine apparently specifically depresses lymphoid tissue in the mouse.

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7. We thank Dr. F. K. Hess for making the procarbazine for this study, and M. Holeczek and Miss H. Baier for technical help.

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Photochemical Decomposition of DDT by a Free-Radical Mechanism

Abstract. *Both as a pure solid and in hexane solution, DDT readily decomposed when irradiated with ultraviolet light (2537 angstroms). Principal products identified by gas-liquid and thin-layer chromatography from irradiations of the solid phase were 1,1-dichloro-2,2-bis* (p-*chlorophenyl*) *ethane, 1,1-dichloro-2,2-bis*(p-*chlorophenyl*) *ethylene, and 4,4'-dichlorobenzophenone. 1,1-Dichloro-2,2-bis*(p-*chlorophenyl*) *ethane and hydrochloric acid were identified from irradiated solutions of DDT in hexane. On the basis of products obtained, quantum yields, scavenger experiments, and other chemical tests, a nonchain, free-radical mode of degradation is proposed.*

The resistance of DDT to degradation, as well as its effectiveness as an insecticide, is well known. The problem of DDT persistence in food products, soils, lakes, and the atmosphere is the result of the physical and chemical properties of the compound. We report here (i) the rate of ultraviolet degradation; (ii) the identification of the degradation products; and (iii) a proposed gross reaction mechanism of the photolysis.

Deposited as thin layers on the inside walls of quartz tubing, DDT was decomposed by ultraviolet light (2537 Å). After 48 hours of irradiation, 80 percent of the DDT was converted to a number of products including DDD, DDE, and DDC=O (*1*). To determine the mode of DDT decomposition, photochemical reactions were carried out in a quartz cell with DDT dissolved in *n*-hexane. Results from product identification, quantum yields, and radical-capturing compounds suggest that the photochemical degradation of DDT proceeded by a nonchain, free-radical mechanism.

Earlier work suggested that DDT could be decomposed by light. Lindquist *et al.* (*2*) reported that the insecticidal activity of DDT was reduced after a DDT solution was sprayed on surfaces exposed to sunlight. Wichmann *et al.* (*3*) found no effect of ultraviolet light on pure DDT, DDE, and DDC=O in the crystalline state. However, in benzene solution DDT decomposed and a yellow amorphic film was deposited after the solvent evaporated. Under the same conditions, DDE degraded more rapidly than DDT, but DDC=O was unaffected. Fleck (*4*) irradiated DDT in ethanol solutions and found that it decomposed to DDC=O in the presence of air. When the air was displaced from the cell with solution, a tetrakis (*1*) material was isolated.

To determine the extent of decomposition by ultraviolet light, uniformly ring-labeled ^{14}C and unlabeled carrier DDT were used. A standard solution of DDT (0.1 mg with a ^{14}C activity of 1.1 μc in glass-distilled benzene) was coated onto the inside surface of a quartz tube (2 by 35 cm). The solvent was removed by evaporation in a stream of dry air. The tube was sealed with serum caps, and flushed continuously with helium for 8 to 10 hours. The sample was then irradiated by four 15-watt germicidal, low-pressure, ultraviolet lamps (2537 Å). A yellow polymeric material which rapidly formed on the surface of the DDT (a phenomenon commonly occurring in photochemical reactions) eventually stopped further decomposition. In order to continue the reaction, the reaction mixture was dissolved with a small amount of diethyl ether. To evenly distribute the mixture over the

Table 1. Effect of irradiation on the decomposition of DDT, DDE, and DDD, and the intensity of unknown products as determined by gas-liquid chromatography (initial concentration of the compound was 40 mg per 100 ml of *n*-hexane; diluted 1 to 100). Retention time is retention time on the gas chromatograph.

Original compound	Length of irradiation (hours)	Original composition remaining (%)	Peak heights of unknown products at retention time (minutes)					DDD (%)
			1.49	2.29	2.60	2.76	3.30	
DDT	0.25	57	0	33	1	23	0	1
DDT	1.0	30	13	15	3	86	0	5
DDT	4.0	3	22	29	0	60	0	4
DDD	0.25	96	0	0	0	0	0	0
DDD	1.0	77	0	15	0	0	0	
DDD	4.0	8	0	19	0	0	0	
DDE	0.25	56	0	21	21	0	10	0
DDE	1.0	8	0	33	44	0	31	0
DDE	4.0	0	0	15	46	0	4	0

inside surface of the tube, the tube was rotated while dry air was passed over the surface to remove the solvent. In addition, helium was passed through the tube for 10 hours to purge any additional traces of solvent prior to the next irradiation period.

After irradiation, the solid sample was eluted from the reaction tube with ether and concentrated to 2 ml for thin-layer chromatography. A portion (75 μl) was applied to an aluminum oxide plate, and the reaction mixture was separated with two different solvent systems. Confirmation of the presence of DDT, DDD, DDE, and DDC=O was made by gas-liquid chromatography and thin-layer chromatography (*5*). Of the applied DDT, 80 percent had decomposed after exposure to ultraviolet light for 48 hours. The principal products separated by two-direction thin-layer chromatography from the reaction mixture were DDD, DDC=O, and DDE, comprising 7.7, 7.2, and 7.8 percent of the initial activity, respectively. Fifty percent of the ^{14}C activity remained on the original spot (R_F=0) of the thin-layer plate. With a thin-layer chromatography technique used to detect acid products (*5*), we found that DDA and BA comprised 4.4 and 3.8 percent, respectively, of the reaction mixture.

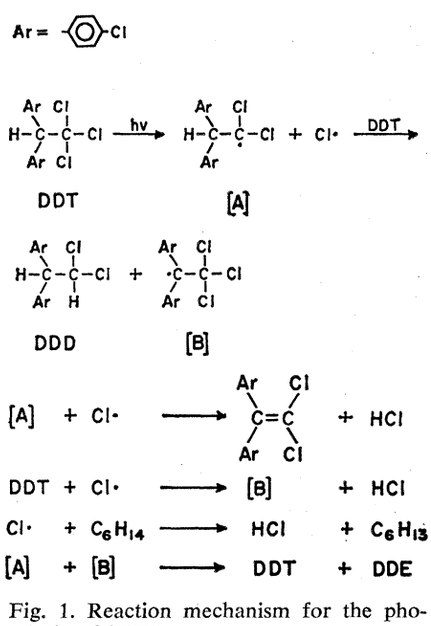

Fig. 1. Reaction mechanism for the photolysis of DDT.

Hexane solutions of DDT in quartz cylindrical cells were exposed to 2537-Å light at 30°C. A holder was fixed to the bottom of the irradiation chamber to maintain the reaction cell exactly 11 cm from the lamps. After irradiation, DDD and HCl were identified, and a number of other compounds were isolated by gas-liquid chromatography (Table 1). An irradiation cell containing 30 ml (8.45 μmole of DDT) was irradiated for 5 hours, and the results showed that 1.31 μmole of DDT had reacted and 1.12 μmole of HCl had formed.

An ultraviolet absorption spectrum of DDT in *n*-hexane was obtained. The spectrum of DDT showed maximums at 2700 and 2400 Å, with molar extinction coefficients of 846 and 8460, respectively. Both bands presumably correspond to the formation of a π^* singlet electronic state.

To discern the reaction mechanism involved, the quantum yield for the disappearance of DDT was estimated. The intensity of the lamps was determined by the potassium ferrioxalate actinometer method (*6*). At 2537 Å, the actinometer absorbed 100 percent of the 5.01×10^{16} quanta/sec of light striking it. From this value, the quantum yield for DDT, which also absorbed approximately 100 percent of the light striking it, was calculated to be 0.16. Such a value indicated that the reaction proceeded by a nonchain process in that an efficient chain reaction should consume many molecules per quantum of light absorbed.

Iodine (*7*) and *n*-butylmercaptan (*8*) scavengers were used to gain further information about the reaction. These two compounds react efficiently with free radicals and are commonly used radical "traps." Irradiation of DDT (40 mg/100 ml) in hexane for an hour without a scavenger resulted in 5 percent conversion of DDT to DDD. During this period, 70 percent of the DDT was decomposed. After 1 hour of irradiation with both *n*-butylmercaptan (0.1 ml/100 ml) and DDT (40 mg/100 ml) in solution, 12 percent of the original material existed as DDD. The disappearance of DDT (70 percent decomposition) was not inhibited by the mercaptan. The enhancement of DDD formation is presumably due to the lability of the hydrogen attached to the sulfur of the mercaptan and suggests that the free radical [A] is an intermediate in DDT photolysis and a precursor of DDD.

$$\underset{\text{(DDT)}}{Ar_2CH{-}CCl_3} + h\nu \rightarrow \underset{\text{[A]}}{Ar_2CH{-}CCl_2^{\bullet}} + Cl^{\bullet}$$

$$[A] + CH_3CH_2CH_2CH_2SH \rightarrow \underset{\text{(DDD)}}{Ar_2CH{-}CHCl_2} + C_4H_9S^{\bullet}$$

$$2\ C_4H_9S^{\bullet} \rightarrow C_4H_9S{-}SC_4H_9$$

With iodine (40 mg/100 ml) as a scavenger with DDT (40 mg/100 ml) and irradiating for 1 hour, only 1 percent of the DDT was converted to DDD, with 47 percent of the DDT being degraded. The two scavengers may trap the free radical [A] in the same manner—that is, the mercaptan donates a hydrogen atom to form DDD and the iodine scavenger may donate one iodine atom to form the corresponding iodine-containing compound rather that DDD.

The intermediacy of [A] can, furthermore, explain the other photolysis products (Fig. 1). This mechanistic scheme involves production of a free radical [A] and a chlorine atom. The [A] radical and the chlorine radical may recombine to form DDT, the chlorine may abstract the aliphatic hydrogen from [A] to form DDE, or [A] may abstract a hydrogen from the *n*-hexane solvent or a DDT molecule to form DDD and the [B] radical. DDD was isolatable from the DDT reaction mixture because it is comparatively stable

(disappearance quantum yield of 0.04). DDE was not detected as an irradiation product of DDT in hexane, possibly because it reacts as rapidly as it is formed (disappearance quantum yield of 0.26).

These initial products, DDD and DDE, absorb ultraviolet light and react to form a number of secondary products which were identified only by retention times on the gas-liquid chromatograph (Table 1). To determine the photolytic products resulting from DDE and DDD, each compound was irradiated separately in *n*-hexane solution and the reaction mixture was analyzed by gas-liquid chromatography. Irradiation of DDD produced only one major peak at R_F of 2.76 minutes. Products from DDE irradiations had R_F values of 2.29, 2.60, and 3.30 minutes. Irradiation of DDT yielded a mixture with the major products having R_F values of 1.49, 2.29, 2.60, 2.76, and 4.40 minutes (DDD). It is possible, therefore, that the DDT products with R_F values of 2.29 and 2.60 resulted from initial DDE formation, and the product with R_F value of 2.76 originated from DDD photolysis.

To determine the effect of HCl on the reaction process, sufficient *n*-butylamine was added to the DDT solution to neutralize the HCl produced. In the presence of *n*-butylamine, no change in the rate of either DDT disappearance or DDD formation was observed. These observations indicated that the progress of the reaction was not dependent upon HCl production.

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1. Abbreviations are: DDT, 1,1,1-trichloro-2, 2-bis (*p*-chlorophenyl) ethane; DDE, 1,1-dichloro-2, 2-bis (*p*-chlorophenyl) ethylene; DDD, 1,1-dichloro-2, 2-bis (*p*-chlorophenyl) ethane; DDC=O, 4,4′-dichlorobenzophenone; BA, *p*-chlorobenzoic acid; DDA, bis (*p*-chlorophenyl) ethanoic acid; tetrakis, 2,3-dichloro-1,1,4,4-tetrakis (*p*-chlorophenyl) butene.
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Relation of Pharmacological and Behavioral Effects of a Hallucinogenic Amphetamine to Distribution in Cat Brain

Abstract. *The hallucinogen 2,5-dimethoxy-4-methylamphetamine, also known as STP, accumulates in specific areas of cat brains. The unchanged compound was detected in the brain for at least 6 hours, whereas its behavioral effects lasted for about 4 hours. The coincidental pharmacological and behavioral effects of the compound apparently indicate a relation between the anatomical distribution and action.*

The hallucinogenic agent 2,5-dimethoxy-4-methylamphetamine, also called either DOM or STP, has, in humans, psychedelic effects which are about 60 to 100 times more potent than those of mescaline, but it is 30 to 50 times less active than lysergic acid diethylamide (LSD) (*1*). In rabbits this drug provokes an abnormal electroencephalogram by a mechanism different from that provoked by *d*-amphetamine (*2*).

We have studied the tissue distribution and elimination of STP-H^3 in mice, rats, rabbits, and cats (*3*) and have synthesized the analogs of STP to test the chemical structure on animal behavior (*3*). We also report on the correlation of the behavioral and pharmacological effects of STP to its sites of accumulation in the cat brain.

By a trituim-hydrogen exchange reaction (*4*), STP was synthesized and labeled with tritium in positions 3 and 6. Labile tritium atoms were removed until a constant specific activity of 360 μc/mg was achieved. The chemical and radiochemical purity of the compound was ascertained by thin-layer chromatography (silica gel G) and by its infrared spectrum. The chromatograms were developed in chloroform and methanol (1 : 1); butanol, acetic acid, and water (4 : 1 : 1); and isopropanol, butanol, acetic acid, and water (10 : 1 : 1 : 1). Autoradiograms and ultraviolet fluorescence were used to detect STP-H^3 on the plates.

Six cats (one female) (1.8 to 3.0 kg) were anesthetized with ether, and STP-H^3 (10 mg/kg; 3.6 mc/kg) was

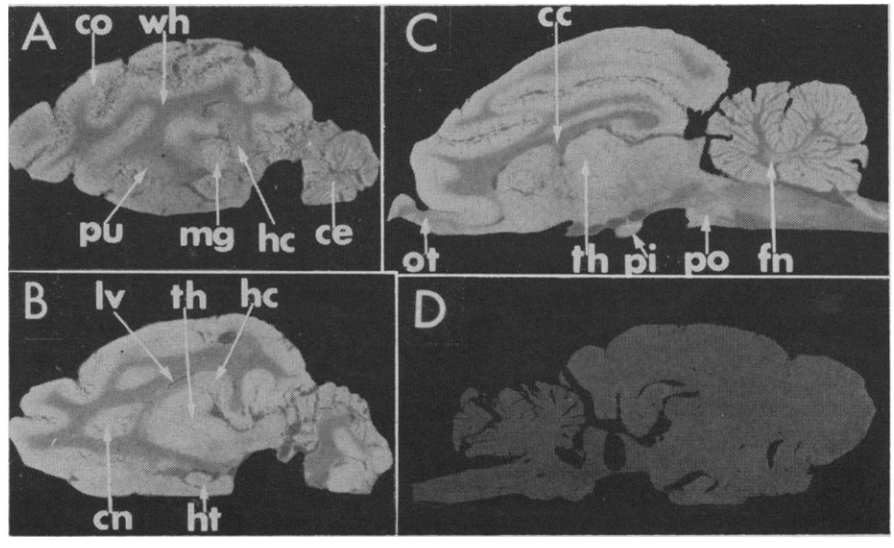

Fig. 1. Distribution of the radioactivity (light areas) in cat brains 15 minutes (A–C) and 6 hours (D) after injection of STP-H^3 intravenously. Abbrevations: *cc*, corpus callosum; *ce*, cerebellum; *cn*, caudate nucleus; *co*, cortex; *fn*, fastigial nucleus; *hc*, hippocampus; *ht*, hypothalamus; *lv*, lateral ventricle; *mg*, medial geniculate nucleus; *ot*, olfactory tract; *pi*, pituitary; *po*, pons; *th*, thalamus; and *wh*, white matter.