



STUDIES ON THE MAJOR PHOTOLYTIC
PRODUCT OF ENDRIN

Thesis for the Degree of M. S.
MICHIGAN STATE UNIVERSITY
WENDEL LAURENCE BURTON
1968

THESIS



ABSTRACT
STUDIES ON THE MAJOR PHOTOLYTIC
PRODUCT OF ENDRIN

by Wendel L. Burton

The persistence, toxicity, and use of the chlorinated hydrocarbon insecticide endrin (A) has brought major concern not only to researchers but also to the public. The objective of the research described here was to determine to what degree endrin is reactive to irradiation particularly in the range of natural sunlight and atmospheric surface conditions and to study the nature of its photolytic products.

Indeed, endrin (A) was found to be converted cleanly in yields up to 80 per cent to an entirely new compound by irradiation at 2537Å in cyclohexane. The equivalent of dichloroacetylene was eliminated from endrin to yield 3,3,4,5R-tetrachloro-tetracyclo[5.2.1.0^{2,6}.0^{4,9}]decan-8-one (B), a ring system not previously reported.

Compound (B) was found to be highly resistant to the usual oxidation and reduction procedures, and to be insoluble in the common organic solvents used in chloro-insecticide analysis. Simple toxicity tests showed (B) to be three times as toxic to mice and five times as toxic to flies relative to endrin. However (B) did react quite specifically and cleanly in over 90 per cent yields through ring closure and homocyclization to

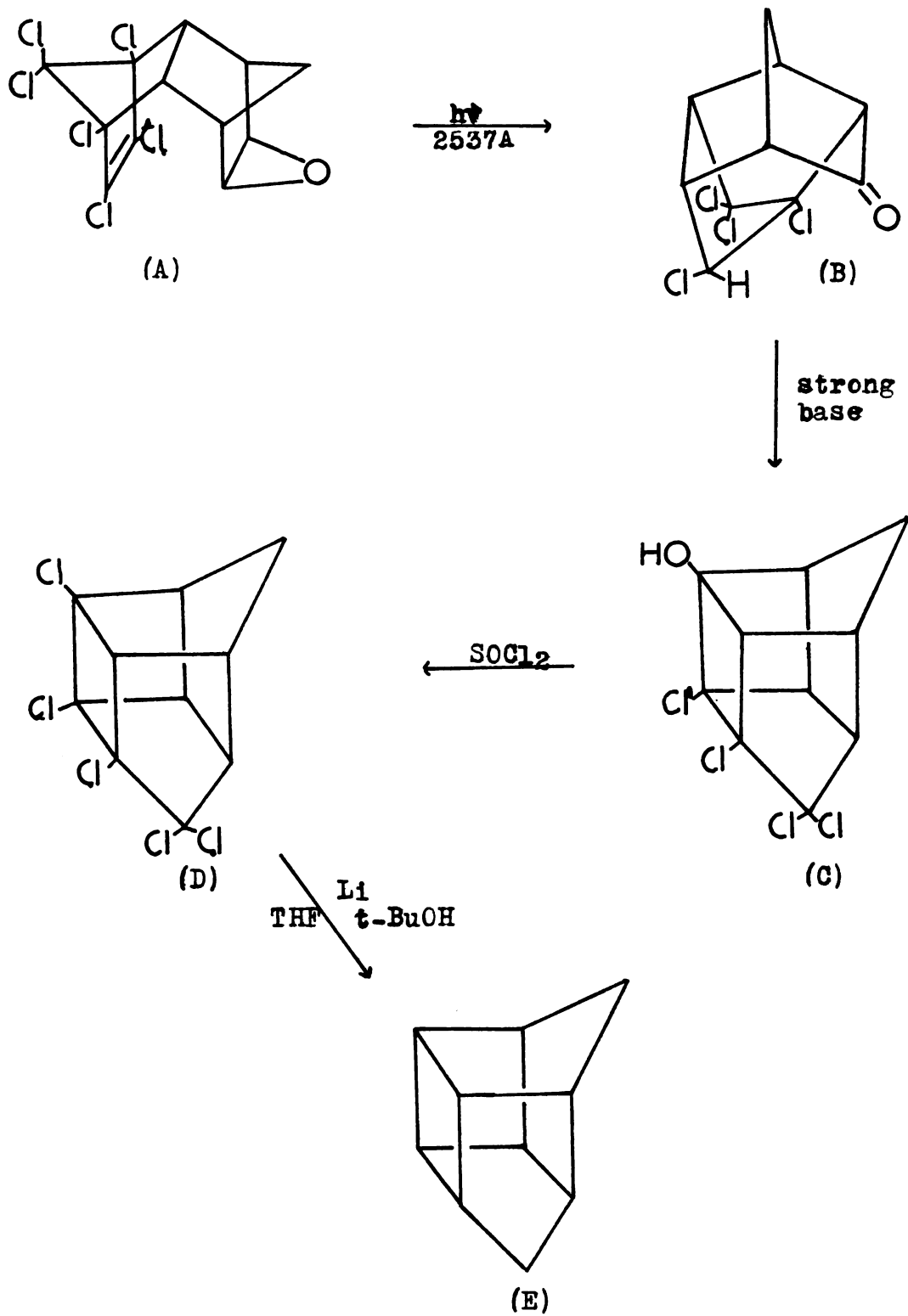
2,3,4,4-tetrachloro-pentacyclo [5.3.0.0^{2,6}.0^{3,10}.0^{5,9}] decanol (C).

The chemistry of (C) proved interesting as it underwent cleanly and in excellent yields replacement of the hydroxy group by a chlorine by reaction with either thionyl chloride or phosphorus pentachloride to give 1,2,3,4,4-pentachloro-pentacyclo [5.3.0.0^{2,6}.0^{3,10}.0^{5,9}] decane (D).

Reduction with lithium metal, tertiary butyl alcohol in tetrahydrofuran of (D) gave a known compound pentacyclo [5.3.0.0^{2,6}.0^{3,9}.0^{5,8}] decane (E) established by direct comparison with an authentic sample.

Nuclear magnetic resonance spectroscopy proved to be the most singularly important tool in the structure determination of photolytic products of endrin, although infrared, ultraviolet, and mass spectroscopy, and gas, thin layer, and column chromatography were also utilized.

It might be concluded that the photolytic product (B) may well be the real species causing the persistency and toxicity instead of its parent (A), especially in view of the fact that photolysis at 3600Å (which is the ultraviolet radiation in sunlight at earth's surface) yielded results essentially similar to those obtained at the shorter wavelength 2537Å.



STUDIES ON THE MAJOR PHOTOLYTIC
PRODUCT OF ENDRIN

By

Wendel Laurence Burton

A THESIS

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

MASTER OF SCIENCE

Department of Chemistry

1968

650117
7-11-68

ACKNOWLEDGMENT

Sincere thanks should be extended to Professors
R.D. Schuetz and M.J. Zabik whose friendship and
insight have encompassed more than just chemistry.

TABLE OF CONTENTS

	Page
ACKNOWLEDGMENTS	ii
LIST OF FIGURES	v
LIST OF TABLES	vi
BACKGROUND	1
RESULTS AND DISCUSSION	6
EXPERIMENTAL	18
Photolysis	19
Preparations	22
2,3,4,4-Tetrachloro-Pentacyclo [5.3.0.0 ^{2,6} . 0 ^{3,10} .0 ^{5,9}] Decanol	22
1,2,3,4,4-Pentachloro-Pentacyclo [5.3.0. 0 ^{2,6} .0 ^{3,10} .0 ^{5,9}] Decane	24
Pentacyclo [5.3.0.0 ^{2,6} .0 ^{3,9} .0 ^{5,8}] Decane .	25
Pentacyclo [5.3.0.0 ^{2,6} .0 ^{3,10} .0 ^{5,9}] Decanol	27
Attempted Preparations	29
Dehalogenation of Photoproduct IV . . .	29
Tosyl Hydrazone Formation of Photoproduct IV	30
Hydrazone Formation of Photoproduct IV .	30
Wolff-Kishner Reduction of Photoproduct IV	31
Clemmensen Reduction of Photoproduct IV	32
Thio Ketal Reduction of Photoproduct IV	33

TABLE OF CONTENTS (CONTINUED)

Baeyer Villiger Oxidation of Photoproduct IV	Page 34
Photolysis of Compound II, 1,9,10,10,11, exo -12-Hexachloro Pentacyclo [7.2.1.0 ^{2,6} . 0 ^{4,8} .0 ^{7,11}]Dodecan-3-one	35
BIBLIOGRAPHY	44

LIST OF FIGURES

Figure		Page
I.	The Infrared Spectrum of 3,3,4,5R-Tetrachloro-Tetracyclo [5.2.1.0 ^{2,6} .0 ^{4,9}]Decan-8-one in KBr	37
II.	The Infrared Spectrum of 2,3,4,4-Tetrachloro-Pentacyclo [5.3.0.0 ^{2,6} .0 ^{3,10} .0 ^{5,9}]Decanol in KBr	38
IIa.	The Infrared Spectrum of 2,3,4,4-Tetrachloro-Pentacyclo [5.3.0.0 ^{2,6} .0 ^{3,10} .0 ^{5,9}]Decanol in Carbontetrachloride	39
III.	The Infrared Spectrum of 1,2,3,4,4-Pentachloro-Pentacyclo [5.3.0.0 ^{2,6} .0 ^{3,10} .0 ^{5,9}]Decane Concentrate in Carbontetrachloride	40
IV.	The Infrared Spectrum of Pentacyclo [5.3.0.0 ^{2,6} .0 ^{3,9} .0 ^{5,8}]Decane Superimposed on a Known Authentic Sample in KBr	41
V.	The Infrared Spectrum of Pentacyclo [5.3.0.0 ^{2,6} .0 ^{3,10} .0 ^{5,9}]Decanol in KBr	42

LIST OF TABLES

Table		Page
I.	Nuclear Magnetic Resonance Data	43

BACKGROUND

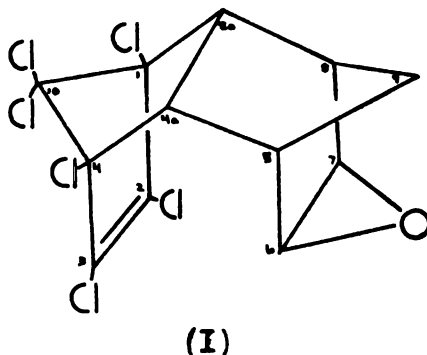
The fate and persistence of organic pesticides has been given considerable attention recently. The wide spread application of pesticides has preceded their in depth studies of the potential long range effects as health hazards to man and his environment. Studies have been made on the half lifes, residue levels, drift, runoff, and toxicities of the various pesticides. However, the chemical nature, especially under field conditions, of the pesticides and their potential photolytic decomposition products is still unknown. The need and importance for such research is dramatic when one considers the unexplored risks of the present applications of organic pesticides to our environment. For example, last year over 800 million pounds were applied in the United States alone and this level increases 35 million pounds a year.(1)

A major portion of these pesticides belong to a group known as the chlorinated hydrocarbon insecticides. This group of insecticides recently has been getting greater publicity because of the events like the Colorado River fish kill and the fire ant fiasco.

The chlorinated hydrocarbon insecticides are applied yearly in the United States on the 150 million

pound scale. They have developed and hold this market because of their broad spectrum and low cost. It is because of this broad spectrum and its supposed ability to remain active for long periods of time that has stimulated research interest in these materials here at Michigan State University.

A widely used member of the chlorinated hydrocarbon insecticides is endrin. Interest in endrin (1,2,3,4,10,10-hexachloro-6,7 epoxy-1,4,4a,5,6,7,8,8a octahydro-1,4-endo endo-5,8 dimethanonaphthalene), I, has arisen



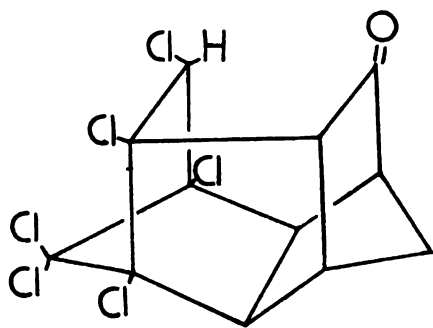
from two reasons. The first is its wide use as an effective broad spectrum and low cost pesticide. The second is its unique stereochemistry which allows it to undergo a variety of reactions from simple addition to complex transannular rearrangements. (2-8)

Endrin's major use has been in protecting the cotton plants from bollworms, cabbage looppers, and numerous other pests. (9) It also is supposed to be

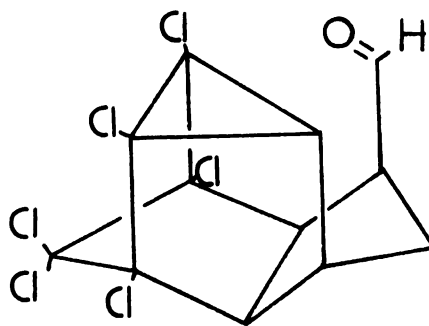
highly toxic and stable for long periods of time under field conditions. For example, in comparison to DDT endrin is fifteen times as toxic to mammals, thirty times as poisonous to fish(10), 300 times as toxic to some birds, and has been found to kill at least fifty per cent of the shrimp in as low concentration as one half part per billion.(11) This toxicity level, combined with data like the residues found in vegetables treated with insecticides (2,420-4,370 parts per billion DDT in spinach)(12), or the runoff of surface waters on sprayed fields (0.36 parts per billion in furrow water from cotton field sprayed with 0.4 lbs/acre or roughly 400 ppb/acre)(9), or that of the endrin spray applied ten feet above the ground in three mile per hour wind the ten micron size drifted one mile whereas the two micron size was found as far as twenty one miles away(12) gives one some indication of its potential hazard to human environment. Half life studies have indicated that endrin is one of the more persistent insecticides with a half life of over seven years in the field.

While endrin is moderately persistent, it does however disappear through some avenue other than the general routes like runoff, leaching, and translocation. A reasonable avenue for its removal is by photochemical reactions and chemical rearrangements into other chemical compounds as a result of irradiation by sunlight, most probably in the range below 3600Å. Roburn (13) reported

qualitatively that endrin was partially converted to new compounds by irradiation of the deposited solid at 2537Å. Rosen and Sutherland (14) isolated the previously reported (6) ketone II and aldehyde III in



(II)



(III)

thirty seven and nine per cent yield respectively following irradiation of endrin at 2537Å using hexane; acetone as the extracting solvent. Compounds II and III were found to be nontoxic to the housefly and mosquito at concentrations 0.24 µg/fly and 96 ppb, respectively.

Yields of thirty seven and nine per cent does not explain what is the fate to even one half of the endrin applied. A better initial approach would be to study the photolysis of endrin in solution. More exacting conditions can be attained in solution versus solid irradiation; and since the usual application of endrin is in the form of a twenty per cent active ingredients in a hydrocarbon solvent, two such inert solvents were

chosen: hexane and cyclohexane. Therefore, photolysis experiments were carried out in these laboratories to ascertain whether endrin does undergo photochemical rearrangements in solution.

RESULTS AND DISCUSSION

Endrin, indeed, underwent photochemical reaction in solution. In varying the percent of endrin from 0.3 to 8.9 percent by weight (or 0.0063 to 0.1000 molar) the rate of disappearance of endrin was found to be nearly complete within eight hours. At concentrations greater than one per cent, precipitation occurred during the photoreaction, probably due to the insolubility of some of the photolytic products. After an initial photolytic lag phase of one hour, precipitation commenced and continued until, at the end of the second hour of photolysis the reaction had to be stopped due to the density of the product(s). Up to an 80% yield of a pure white crystalline material was recovered from such photolysis reactions. Simple toxicity tests (19) showed this major photolytic product, IV, to be three times as toxic to mice and five times as toxic to flies relative to I, endrin.

Compound IV became of immediate interest for several reasons. (1.) The initial product IV was found to be insoluble in most of the common organic solvents used for the detection of organo-chloride pesticides. For example, no change was noticed in IV by refluxing it in ethanol, benzene, carbon tetrachloride, chloroform,

petroleum hydrocarbons, ether or dimethyl sulfoxide. It was soluble only in methylene chloride. However, when IV was ground to a very fine powder it became readily soluble in hot absolute ethanol and chloroform. (2.) IV's retention time, using two types of columns and different temperatures on the gas chromatograph, was nearly identical to its parent compound I, and could not be distinguished from the latter. Either material or a mixture of the two gave only a single peak with a proportional increase of area as one increased the concentration. (3.) Its infrared absorption spectrum was nearly superimposable on that of compound II above 1350K*.

All three reasons lead to the same conclusion. The most widely used methods today for the detection of pesticides and their residues could have been missing the identification of IV. Also IV might be the persistent and toxic residue that is now attributed to endrin.

The problem, therefore, was to identify compound IV and ascertain if its chemical properties justified the above possibilities.

IV's physical data was encouraging in this direction. The melting point was not sharp but rather indefinite, melting from 215-218° with some prior softening and close to the reported 220°^a for its parent compound I. The infrared spectra showed a strong absorption at 1745K and no absorption at 1420K which could be attributed to a carbonyl in a five membered ring with no alpha

*K, Kaysers or reciprocal centimeters

methylene groups. A medium intensity absorption at 1465K can be ascribed to a methylene group. The weak lines at 2960K and 2890K could be ascribed to the carbon-hydrogen stretching frequency of a five membered ring and a tertiary carbon hydrogen stretching respectively by extending the near superimposability of its infrared to the known compound II. Multiple bonding frequencies were absent from the spectrum which was also confirmed by the lack of absorption in its visible and ultraviolet spectrums. Finally absorption frequencies below 1400K were too numerous and strong to be of much value in assigning the presence of functional groups.

The elemental analysis of IV established that the equivalent of dichloroacetylene had been eliminated during the photodecomposition of endrin. Calculated for $C_{10}H_8Cl_4O$: C, 42.00; H, 2.82; Cl, 49.59 and found C, 42.09, 41.93; H, 2.79, 2.88; Cl, 49.64, 49.55. Mass spectra and vapor phase osmometry placed the molecular weight at 286 g/mole.

Nuclear magnetic resonance (nmr) spectrometry revealed at least four chemically distinct types of protons based on the observed chemical shifts. The first type was attributed to the protons of a methylene group at tau 8.2. This group showed a solvent effect with increasing dielectric constant of the solvent. In carbon tetrachloride (τ 8.2) the methylene group appeared

as a singlet. In methylene chloride ($\epsilon=9.1$) there appeared an AB type quartet with area integration of 1:5:5:1, $J=7.2$ cps, and $\Delta\nu=7.4$ cps. In dimethylformamide ($\epsilon=36.7$), the AB type quartet had an integration of 1:1.6:1.6:1 with $\Delta\nu=16.6$ cps.

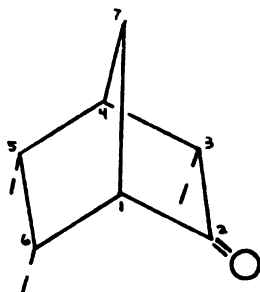
The second distinct type of proton was attributed to a tertiary hydrogen. It appeared as a broad symmetrical multiplet at tau 7.2.

The third type of proton was also attributed to tertiary hydrogens. Total integration assigned four protons to this region of tau 6.7-6.9. The coupling in this region did not allow satisfactory resolution to assign J and $\Delta\nu$ values from the spectrum.

The fourth type of proton was attributed to a hydrogen bonded to the same carbon as a chlorine with a chlorine atom located on one of the adjacent carbon atoms. It appeared as a sharp singlet at tau 5.4. Spin decoupling techniques failed to alter the spectra.

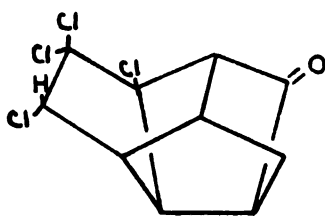
From the physical data alone a number of possible working models were constructed to serve as a guide to develop experimental procedures to distinguish between the models and to finally arrive at a known structure or system for IV.

The hydrocarbon portion of endrin was assumed to be left intact as supported by the nmr data and the three known thermolysis derivatives of endrin. The positioning of the carbonyl on either side where the epoxide could

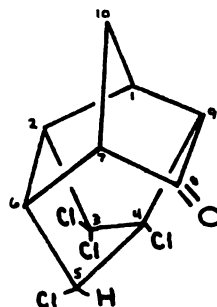


open was not important so long as a new carbon-carbon bond was formed on the other side to meet the condition of no alpha methylene groups to the carbonyl. This new carbon bond at carbon three would necessarily be endo to the norbornyl system identical to the supposedly unreacted linkages at carbons five and six.

Using the adage that five membered rings were preferred as photolytic products, two such models could be suggested, (IVa and IVb).



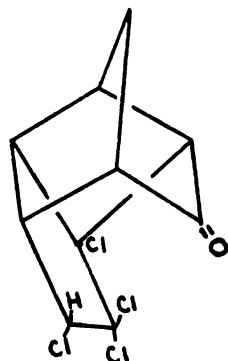
(IVa)



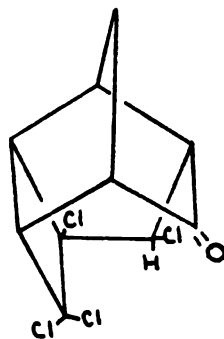
(IVb)

Models with four membered rings were also possibilities. (IVc, IVd, and IVe).

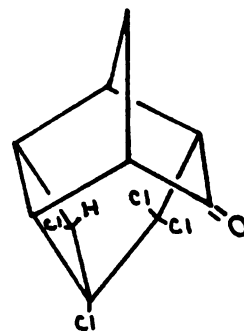
Three membered rings were unlikely as indicated by the lack of characteristic absorptions in both the infrared and nmr spectras.



(IVc)



(IVd)



(IVe)

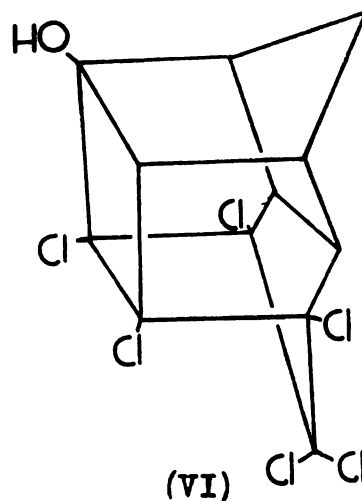
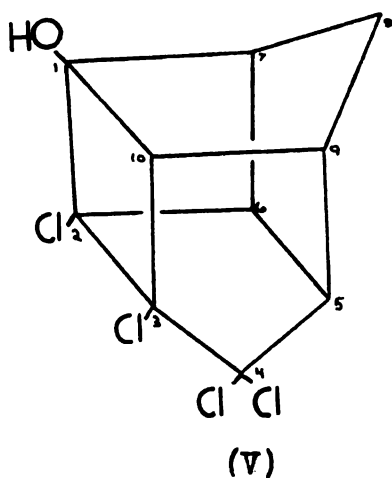
The most apparent difference between the models was that IVa and IVc should be capable of olefin formation whereas IVb,d,e should not. Such olefin formation could be easily detected by a very sharp characteristic band at 1600K for a mono- or dihalo- ethylene in the infrared. Application of Attenburrow's dehalogenation procedure to IV resulted in only starting material being recovered.(15) Dehydrohalogenation using alcoholic potassium hydroxide also failed to produce any olefin; however, reaction did occur and a new product was formed which exhibited a hydroxyl band in the infrared spectrum.

Since the ring systems for the models have not been reported in the literature, chemical studies were begun to attempt to convert IV into a known compound. Initial efforts were directed at the carbonyl group. However it was quickly discovered that IV was quite unreactive. Attempts to prepare the tosyl hydrazone and hydrazone

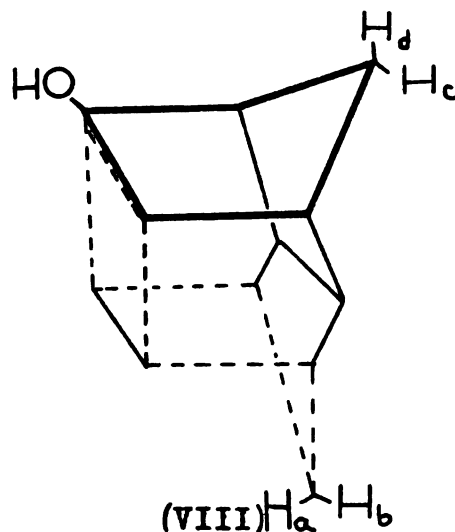
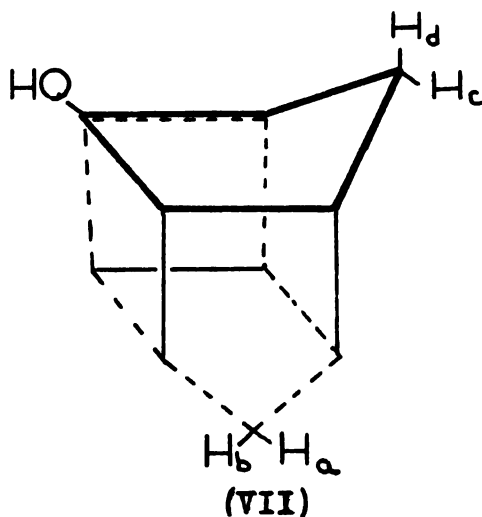
derivatives were fruitless. Likewise IV was unreactive to normal oxidation and reduction procedures. Carbonyl reducing procedures involving the Huang-Minlon modification of the Wolff-Kishner, the Clemmensen, and the Thio-ketal reductions were unsuccessful. With the Clemmensen reduction 80% of the starting material, IV, was recovered. Using the thio ketal reaction, 99% of the starting material IV was recovered. Even drastic conditions utilizing phosphorus pentachloride at high temperatures in a sealed tube failed. Also the Baeyer Villiger and Haller Bauer oxidations did not give any expected products. A quantitative amount of starting material was recovered from the Baeyer Villiger oxidation. Compound IV, under the Haller Bauer conditions did give a nice clean reaction to V.

Elemental analysis showed V to be an isomer of IV. The infrared spectrum compared favorably with the spectra of the product obtained from IV following its reaction with alcoholic potassium hydroxide. The carbonyl band had been replaced by a hydroxyl band. The nmr had lost the singlet at τ 5.4 and did not show any absorptions characteristic of a secondary alcohol. This observation lead to the conclusion that a ring closure had very probably occurred by base-catalyzed homoenolization. Ring closures of this type are not unknown. For example, one of the more familiar cases was the direct formation of the hexachloro birdcage alcohol, VI, as reported by

Winstein.(16) Returning to the models, only IVb and IVc could easily undergo such a homoenolization. IVc though should have been ruled out for not undergoing dehalogenation. Therefore, V could be assigned the structure 2,3,4,4-tetrachloro-pentacyclo[5.3.0.0^{2,6}.0^{3,10}.0^{5,9}]decanol.



If structures V and VI were dechlorinated, then the resulting products would have the relationship of the hydroxyl group to the methylenes shown below.



Compound VIII has been prepared by Winstein; the far methylene protons from the hydroxyl showed an AB type quartet with chemical shift values of τ 8.52 and 8.22 with $J_{AB} = 10.5$ cps, whereas the near methylene H_cH_d signal appeared as a singlet at τ 8.28 superimposed on one member of the H_aH_b quartet. (16) The reasoning extended to this was that H_d was probably deshielded by the hydroxyl.

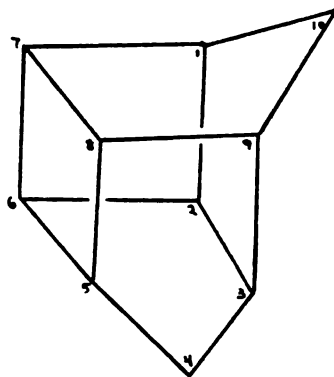
Returning to the models, if IVe actually underwent homoenolization followed by dehalogenation, the resulting compound would have the same hydrocarbon ring structure as compound V, except that the hydroxyl would be in the C-10 position and the predicted splitting of the two methylenes groups would become identical which disagrees with the nmr evidence. Further if in IVe one were to exchange the sin chlorine of the geminal dichloro group with a hydrogen (which would give a further down field shift to that proton than recorded), the predicted final product after ring closure and dehalogenation would again give identical methylene absorptions. Similarly, if in structure IVd the geminal chlorine was replaced with hydrogen to allow homoenolization, the result would be the same as above, contradicting the analogous evidence.

Compound VII was not originally prepared by the dechlorination of V. However it did arise from the lithium metal, *t*-butyl alcohol reduction of IV.

Reduction of IV was originally carried out to obtain its hydrocarbon skeleton. However in the isolated reaction product only two methylene groups appeared in the nmr instead of the expected three, indicating that something had to be amiss. Elemental analysis confirmed this suspicion by reporting two less hydrogens in the product than expected (expected $C_{10}H_{14}O$ and found $C_{10}H_{12}O$). Subsequent work lead to the realization of the possibility of homoeneolozation occurring since lithium metal is a Lewis base. Nmr studies revealed the expected results. In the methylene region of absorption there appeared an AB type quartet with chemical shift values of tau 8.53 and 8.21 with $J_{AB} = 10.5$ cps plus a singlet H_cH_d at tau 8.29 superimposed on one member of the H_aH_b quartet. Further, the bridgehead proton signals which were reported as a broad peak at tau 7.57 (8H) and a complex multiplet at tau 7.87 (1H) in VIII were found in VII as a broad peak at tau 7.59 (6H) and a complex multiplet at tau 7.92 (1H) plus the remaining proton as a singlet at tau 6.89 (1H).

The carbon ring system in V and VII is known. Dilling had prepared the endo and exo hydroxyl derivatives. (17) From here he used phosphorus pentachloride to substitute a chlorine for the hydroxyl, reporting that thionyl chloride was completely unreactive. (18) Dechlorination of the chlorine derivative using the

common lithium metal, t-butyl alcohol in tetrahydrofuran procedure afforded the hydrocarbon IX, pentacyclo[5.3.0.2.6.0^{3,9}.0^{5,8}]decane.

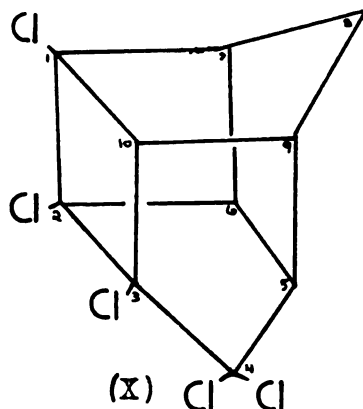


(IX)

Nmr showed a quartet at τ 8.79 and 8.36 with $J = 10.7$ cps, with relative areas indicative of a methylene group containing nonequivalent atoms. The tertiary protons were evident at τ 7.48 and 7.28 with (5.8H to 2.4H) respectively.

The final proof of the structure, then was to get to IX from V. Reactions were carried out with phosphorus pentachloride using Dilling's procedure and also with thionyl chloride. After four days, on work up both reactions were found to be clean and nearly quantitative to give X, 1,2,3,4,4-pentachloro-pentacyclo[5.3.0.0^{2,6}.0^{3,10}.0^{5,9}]decane.

Dehalogenation of X gave the known hydrocarbon IX. Therefore the major photolytic product of endrin can be assigned the structure IVb, 3,3,4,5R-tetrachloro-tetracyclo[5.2.1.0^{2,6}.0^{4,9}]decan-8-one. Its chemical nature



being unreactive to normal oxidation and reduction procedures could justify the reported persistence and toxicity. Its physical properties could help obscure or make difficult its proper identification.

Photolysis of endrin was also conducted at 3600Å (19) and yielded results essentially similar to those obtained at the shorter wavelength (2537Å). This observation is of great importance as it demonstrates that photolytic rearrangements will occur under normal field conditions as the ultraviolet energy reaching the earth's surface has wavelengths above 2863Å. Therefore, application of endrin could lead to IV's subsequent build up in soils, plants, and animals and may even begin to approach toxic levels. Consequently, this as of yet unexplored potential health hazard may exist to man.

EXPERIMENTAL

All melting points are uncorrected and were determined on a Hoover capillary melting point apparatus. Infrared spectra were determined with a Perkin Elmer model 337 grating infrared spectrophotometer, in either carbon tetrachloride solutions or as potassium bromide pellets. Ultraviolet and visible spectra were determined with a Beckman model D.U. and D.B. instruments. Gas chromatography was conducted in a Beckman model GC-4 using a 6' by 1/8" id. quartz tube packed with 5% Dow 11 in 60/80 Chromosorb Q using helium gas as the carrier for electron capture detection and nitrogen gas as the carrier for flame ionization detection. A silanized 2 1/2% SE-30 column was temporarily used in conjunction with the other column. Nuclear magnetic resonance spectra were determined with a Varian A-60 high resolution spectrometer and Jeolco C 60-H instrument using tetramethyl silane as an internal standard. Mass spectrometric spectra were determined with a Consolidated Engineering Model 21-103C machine.

PHOTOLYSIS

Photolysis of endrin was carried out under varying conditions of both concentration of endrin in appropriate solvents and output energy (2537A) of the various medium pressure mercury arc lamps. Endrin was obtained from the commercial Endrin Emulsible Concentrate (20% endrin in 73% petroleum hydrocarbons) by evaporation of the solvent and numerous recrystallizations of the residue from absolute ethanol using activated charcoal until no variation in the melting point of the purified endrin occurred. Gas chromatography of this material at 220° gave a single peak and the nmr spectra showed no interfering impurities. The hexane and cyclohexane solvents used in the photolysis were classified as nanograde-distilled in glass, from the Burdick and Jackson Laboratories. The irradiation for the most part was carried out in a clear fused quartz immersion well using a Hanovia type L, 2537A, 450 watt laboratory photochemical lamp, although a 250 watt lamp was also utilized. It should be noted that no attempt was made to exclude other irradiation wavelengths emitted by the above lamps. A Rayonet Southern New England photochemical reactor (2537A) gave identical results. Varying concentrations of endrin, from 1.200 to 38.09 g., were dissolved in 500 ml. of cyclohexane. Photolysis was carried out at approximately 21° using a magnetically stirred system.

Nitrogen gas was bubbled through the reaction system on various trials, collecting any volatile acids in a standardized sodium hydroxide solution. No change in results was noticeable using nitrogen gas, thus it played no apparent role in the photolysis reaction (0.70 mole of acid per initial mole of endrin was evolved during the reaction).

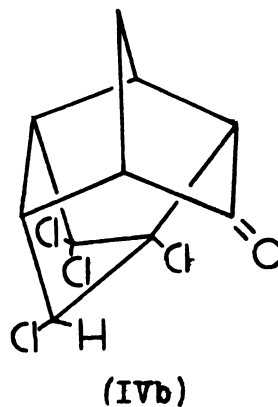
The extent of the reaction was followed by both gas chromatography and infrared spectrometry and showed a minimum of 90% conversion of endrin in eight hours. A coloration change in the reaction medium from a clear solution to dark orange-brown along with the evolution of a pungent odor accompanied the reaction.

Hexane solutions gave essentially the same results as those obtained with cyclohexane except the solubility of endrin in hexane is less.

Precipitation of the white crystalline product, IV, occurred one hour after initiation of light exposure and the reaction was stopped after two hours of reaction time. The product was recovered by filtration. The reaction was then continued until precipitation was no longer apparent. The recovered product was washed with cyclohexane and dried. This photolytic product IV was found to be insoluble in the common organic solvents used in the detection of the organo-chloride pesticides. After thorough grinding to a powder, it could be recrystallized and chromatographed to yield a fine white

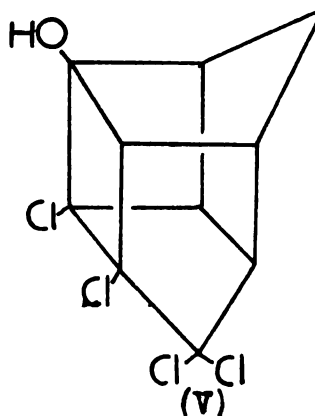
crystalline material, melting at 215-218°. Its infrared spectrum is shown in Figure I. and its nmr spectrum is summarized in Table I. Compound IV was assigned the structure 3,3,4,5R-tetrachloro-tetracyclo [5.2.1.0^{2,6}.0^{4,9}] decan-8-one.

Analysis: Calc'd. for C₁₀H₈Cl₄O: C, 42.00; H, 2.82; Cl, 49.59; and found C, 42.09, 41.93; H, 2.79, 2.88; Cl, 49.64, 49.55.



PREPARATIONS

Preparation of 2,3,4,4-tetrachloro-pentacyclo[5.3.0.0^{2,6}.
0^{3,10}.0^{5,9}]decanol
C₁₀H₈Cl₄O M.W. 286



This compound was prepared under the experimental conditions generally used for the Haller Bauer oxidation. A mixture of 4.00 g. (0.014 moles) of the photo product IV and 1.28 g. (0.033 moles) of sodamide in 150 ml. of nanograde benzene was heated under reflux. After seven hours, the reaction mixture was cooled by immersion in an ice bath and 250 ml. of ice water were slowly added to the rapidly stirred mixture. The organic layer was separated. The aqueous layer was extracted three times with 100 ml. portions of methylene chloride containing a little chloroform, dried over magnesium sulfate, and the solvents were removed under reduced pressure to obtain a white crystalline product. This was dissolved in hot carbon tetrachloride, filtered hot, and cooled in an ice bath to yield 2.60 g. (0.0091 moles) nice white crystals. On removal of the remaining solvent

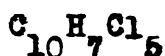
an additional 0.90 g. (0.0032 moles) was recovered to bring the total per cent theoretical yield to 88%. Final purification of the product was afforded by chromatography using neutral alumina and eluting with ten per cent methanol-carbon tetrachloride.

Compound V was also prepared under dehydrohalogenation conditions.(20) A mixture of 2.00 g. (0.0070 moles) photoproduct IV and 1.25 g. (0.022 moles) potassium hydroxide were refluxed in 60 ml. of absolute ethanol. During the seventeen hour reflux time, the reaction solution underwent coloration changes from colorless to yellow to cherry red. The solution was then poured into 200 ml. of ice water, filtered, and extracted three times with 100 ml. portions of ether. The combined ether extracts were saturated with sodium chloride solution, separated, and dried over magnesium sulfate. It was then filtered and the ether was removed by distillation under reduced pressure at room temperature to yield 2.0 g. (0.0070 moles) of crude product. This was recrystallized from 95% ethanol to obtain 1.60 g. (0.0056 moles) product in two crystalline forms; the major portion in the form of needles and the other in the form of clusters. These were purified by chromatography using 55 g. Fisher alumina with carbon tetrachloride-methanol as the elutant, followed by a final recrystallization from ethanol-water to obtain 1.55 g. (0.0054 moles), 75% theoretical yield of the pure

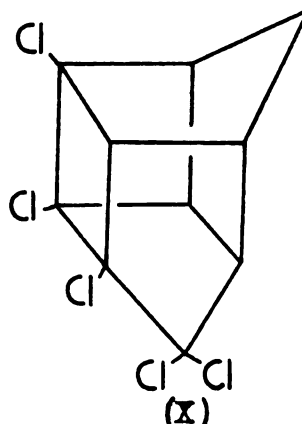
product melting from 204-207°d. The infrared spectrum is shown on figure II, and its nmr spectrum is summarized in Table I.

Analysis: Calc'd. for $C_{10}H_8Cl_4O$: C, 42.00; H, 2.82; Cl, 49.59; and found C, 41.93, 41.96; H, 2.76, 2.84; Cl, 49.65, 49.54.

Preparation of 1,2,3,4,4-pentachloro-pentacyclo[5.3.0.
0^{2,6}.0^{3,10}.0^{5,9}]decane



M.W. 304

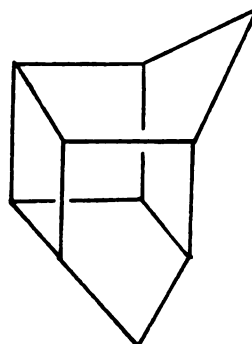


A 0.50 g. (0.0018 moles) quantity of compound V plus 0.70 ml. (0.0022 moles) thionyl chloride were refluxed in 20 ml. of spectrograde carbon tetrachloride. After a refluxing period of one hundred hours, the solvent was removed by distillation under reduced pressure to obtain a yellow oily product, which on being set aside for two weeks crystallized. The crude product precipitated from solutions as an oil on initial recrystallization attempts. However, by setting the dissolved material aside in an ice bath, it did eventually crystallize from solution as a

solid. Gas chromatographic analysis showed a clean reaction had occurred yielding 93% product and 7% of the starting material. The reaction was repeated up to the points of removal of the reaction solvent. At this juncture an infrared spectrum, Figure III, and an nmr spectrum, as summarized in Table I, showed removal of the starting material was complete. The product was then used directly for the next step of the synthesis.

Preparation of pentacyclo [5.3.0.0^{2,6}.0^{3,9}.0^{5,8}]decane

$C_{10}H_{12}$ M.W. 132



(IX)

Compound IX was prepared by the dehalogenation of compound X. To approximately 0.70 g. (0.0023 moles) of essentially pure, as described above, X in 70 ml of anhydrous tetrahydrofuran, was slowly added 0.70 g. (0.100 moles) of finely cut lithium metal under a nitrogen gas atmosphere at 0°. On the addition of 3.4 g. (0.046 moles) of tertiary butyl alcohol to the reaction solution, the solution turned a bluish grey. The reaction mixture was allowed to gradually warm to

room temperature during the thirty six hour reaction period. The mixture was then poured directly into 200 ml. of ice water, saturated with sodium chloride, and extracted with three 85 ml. portions of ether. The combined ether extracts were washed with saturated sodium chloride solution, dried over magnesium sulfate, filtered, and distilled under reduced pressure to obtain a camphor like smelling oily product.

Sublimation of this material at 100° at atmospheric pressure following the suggested procedure of Dilling(17) gave a small yield of a clear liquid. Nmr studies were inconclusive as the sample was not pure. The product was set aside in carbon tetrachloride solution in a closed container for a month, during which time a white sticky material apparently sublimed to the container's top.

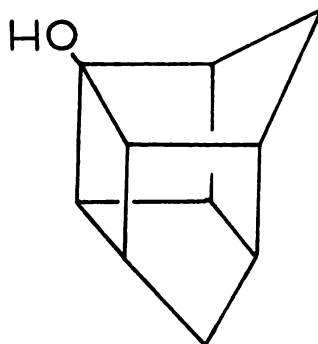
Thin layer chromatography of the sticky material using plates of silica gel F₂₅₄ in methanol and in one to one ratio solution of chloroform and acetonitrile gave identical RF values with that of a known sample of compound IX*, 0.54 and 0.62 respectfully.

The total remaining sample, 0.0012 g. (approximately one per cent theoretical yield) gave an infrared spectrum comparing rather favorably with that of a known sample of compound IX as shown in Figure IV.

* The author would like to extend his appreciation to Dr. Wendell L. Dilling of the Britton Research Laboratory of the Dow Chemical Company for sending a sample of pentacyclo [5.3.0.0^{2,5}.0^{3,9}.0^{4,8}] decane.

Preparation of pentacyclo [5.3.0.0^{2,6}.0^{3,10}.0^{5,9}]decanol

$C_{10}H_{12}O$ M.W. 148



(VII)

To a mixture of 2.00 g. (0.0070 moles) of the photoproduct IV and a minimum of two grams or better than four times the molar ratio per mole chlorine of finely cut lithium metal was stirred under a nitrogen atmosphere in 30 ml. of anhydrous tetrahydrofuran. On the addition of 10 ml. of tertiary butyl alcohol to the mixture, a smooth exothermic reaction was initiated. This was controlled by immersion in an ice bath.

The following day, the unreacted pieces of lithium metal were removed. The reaction mixture was poured into water, extracted with four 60 ml. portions of methylene chloride, dried over magnesium sulfate, and filtered. The solvent was removed by distillation under reduced pressure to obtain 0.750 g. (0.0051 moles) 73% of the theoretical yield.

Product purification involved two chromatographic elutions through Woelm neutral activated grade one alumina and, finally, sublimation at water aspirator pressure to obtain a white crystalline product with a

camphor like smell. The product melted at 184-186°, but the majority of it sublimed prior to melting. Infrared spectra of the pure product is shown on Figure V, and its nmr spectra is summarized in Table I.

Analysis: Calc'd. for $C_{10}H_{12}O$: C, 81.08; H, 8.11; Cl, 0.00; and found C, 82.08; H, 8.32; Cl, 0.00.

ATTEMPTED PREPARATIONS

Attempted Dehalogenation Reaction of Photoproduct IV

Attenburrow's procedure (15) was carried out to examine the possibility of olefin formation from the photolytic product. A 1.72 g. (0.0060 moles) quantity of the photoproduct IV, 1.6 g. of anhydrous sodium acetate, 10 ml. of methylene chloride, 20 ml. of acetic acid, and 5.0 g. (0.077 moles) of zinc dust were stirred at $50 \pm 8^\circ$ for three fourths of an hour. The reaction mixture was filtered hot and the zinc residue was washed with 5 ml. of methylene chloride, 5 ml. of acetic acid, and finally with 5 ml. of methylene chloride.

The volume of the filtrate and washings was reduced to one half of its original volume on the steam bath employing a filtered dry air stream over the surface. Water was added to the concentrated filtrate to the point of developing clouding. Cooling this solution induced crystallization of the product. This was collected by filtration and was vacuum dried to obtain 1.30 g. (0.0045 moles) of a pure white crystalline material. The infrared spectra of this solid showed no olefin formation had occurred and it compared favorably with the spectra of the starting material, even though its melting point was $140-200^\circ$.

Attempted Tosyl Hydrazone Formation of Photoproduct IV

A 1.00 g. (0.0035 moles) quantity of the photoproduct IV and 0.65 g. (0.0035 moles) of tosyl hydrazine were refluxed in 100 ml. of methanol. After a twenty hour reaction period, a small quantity of para toluene sulfonic acid was added as a catalyst. Following an additional thirty four hours of refluxing, one half of the original methanol was removed under reduced pressure to obtain an initial 0.57 g. of a white crystalline material. On cooling the concentrated reaction solution, an additional 0.39 g. of product were obtained. These had a melting point of 213.5-217.5° and 212.0-217.0°, respectively. Mixed melting points of each of the product fractions with starting material were 213.0-217.5°.

Attempted Hydrazone Formation of Photoproduct IV

A 1.00 g. (0.0035 moles) quantity of the photoproduct IV and 0.20 g. (0.0040 moles) of hydrazine hydrate were refluxed in 250 ml. of nanograde benzene. Following a forty eight hour reflux period, the benzene was removed by distillation under reduced pressure to obtain 1.01 g. of a material melting at 212-214°. Gas chromatographic analysis of this material at 190° was

found to be identical with the starting material.

Attempted Wolff-Kischner Reduction of Photoproduct IV

Application of the Huang-Minlon modification of the Wolff-Kischner reduction (21) to the photoproduct IV failed to yield any of the desired products. A 0.500 g. (0.0018 moles) quantity of the photoproduct IV, 0.340 g. (0.0061 moles) of potassium hydroxide, 0.24 ml. of 100% hydrazine hydrate, and 10.0 ml. of ethylene glycol were heated at 120° for an hour. During this initial hour of heating, the solution began to take on a brown coloration. The reaction temperature slowly rose to 182° during the three and one half hours of refluxing. The reaction mixture was cooled, then acidified with 2.5 ml. (0.090 moles) of hydrochloric acid. The acidic solution was extracted three times with methylene chloride and once with hexane. The combined solvents were removed by heating on a steam bath to obtain a dark syrup which dissolved in absolute ethanol and reprecipitated on the addition of petroleum ether.

On neutralization of the water layer, a fine black precipitate formed and was recovered by filtration.

Infrared spectras of both products showed a strong hydroxyl absorption as well as the presence of a carbonyl band. When the photoproduct was found to be unstable

in a basic media due to homoenolization, the merit of the Wolff-Kischner method as a reduction procedure failed.

Attempted Clemmensen Reduction of Photoproduct IV

When the photoproduct IV was found to be stable in acidic solutions, it was first reacted under the Clemmensen reduction procedure using the mild conditions with methanol as the reaction solvent. (22) When the recovered material was found to be starting material, more rigorous reaction conditions were used. (23) Zinc amalgam was freshly prepared by adding 0.5 ml. of concentrated hydrochloric acid (37%) to 6.7 g. of granular zinc and then quickly adding 4 ml. of water followed by 0.50 g. of mercuric chloride. After stirring the slurry for five minutes, the mixture was decanted and added to the reaction flask containing 2.05 g. (0.0070 moles) of the photoproduct IV, 25 ml. of concentrated hydrochloric acid, 15 ml. of water, and 60 ml. of glacial acetic acid. After the first hour of reflux, 15 ml. of concentrated hydrochloric acid was added followed by the addition of 5 ml. acid after the third hour.

The reaction was stopped after a total of twenty four hours under reflux, diluted with 200 ml. of cold water, filtered, neutralized to pH 6, saturated with

sodium chloride, extracted four times with methylene chloride and chloroform. The combined extracts were dried over magnesium sulfate, filtered, and the solvents were removed by distillation under reduced pressure. On the addition of acetone a precipitate formed which remained insoluble on the addition of 95% ethanol and methylene chloride. This material was submitted to column chromatography and was eluted through 70 g. Woelm activation grade one alumina. This gave no real separation of the four products shown to be present by gas chromatographic analysis at 220°. Chloroform and methylene chloride were used as the elutants. Infrared analysis of the chromatographic fractions indicated that some carbonyl reduction had occurred but in very low yield. Further, the major carbon hydrogen stretching frequencies were above 3000K indicating possible decomposition. Since the object was the conversion of the photoproduct IV into a known structure, the practicality of using this experimental route became undesirable and further work with the Clemmensen reduction was discontinued.

Attempted Thio Ketal Reduction of Photoproduct IV

The smooth, reliable thio ketal, rainy nickel reduction for difficulty reducible ketones was next

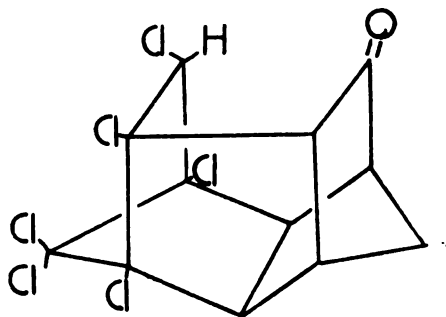
considered. To a 1.4 ml. (0.0167 moles) quantity of freshly distilled ethane dithiol, 1.00 g. (0.0035 moles) of the photoproduct IV, 10 ml. of methylene chloride was slowly added until the solution became homogeneous, after which 1.4 ml. of freshly distilled boron trifluoride etherate was stirred into the reaction mixture at room temperature. During the reaction period of an hour and half, the solution underwent coloration changes from colorless to a very light clear tan orange. The reaction solution was extracted with four 20 ml. portions of ether and once with 25 ml. of methylene chloride. The combined extracts were washed with 5% sodium hydroxide solution, twice with water, and finally with a saturated sodium chloride solution. Removal of the solvents yielded 0.99 g. of material whose infrared spectrum was identical to the spectrum of the starting material.

Attempted Baeyer Villiger Oxidation of Photoproduct IV

To a stirred solution of 0.500 g. (0.0018 moles) of the photoproduct IV and 11 ml. of methylene chloride (dried over magnesium sulfate) cooled to 0°, was added 0.40 g. of 40% peracetic acid in acetic acid followed by two ml. of glacial acetic acid. After five minutes, the reaction flask was removed from the ice bath and set aside for a week at room temperature.

The reaction mixture was then neutralized to pH 8 with a saturated solution of sodium bicarbonate; and 10 ml. of methylene chloride was added to the neutralized solution. The organic layer was separated and washed with 30 ml. water. The aqueous portion was extracted twice with 30 ml. portions of ether. The combined organic portions were dried over magnesium sulfate, filtered, and the solvent was removed under reduced pressure to obtain 0.50 g. (0.0018 moles) of a white crystalline material melting from 213.0-216.5°. A mixed melting point of this material with photoproduct IV melted at 211.5-216.7°.

Photolysis of Compound II, 1,9,10,10,11, exo-12-hexachloropentacyclo [7.2.1.0^{2,6}.0^{4,8}.0^{7,11}]dodecan-3-one



(II)

Compound II was readily prepared using Soloway's procedure (4) to determine whether II might be a possible route in the formation of IV from I. A 1.45 g. (0.0038

moles) quantity of II was ground to a fine powder in order to be dissolved in an equivalent amount of cyclohexane that was used in the photolysis of I. However compound II's solubility in cyclohexane was considerably less than compound I and it only partially dissolved (perhaps 85%) in 1250 ml. of the solvent. After twenty six hours of irradiation at 2537Å, the clear colorless reaction solution was concentrated under reduced pressure (bp. solvent 25°) to 50 ml. total volume.

Gas chromatographic analysis of the remaining solution strongly suggests that compound II is not a significant intermediate in the photosynthesis of compound IV from compound I.

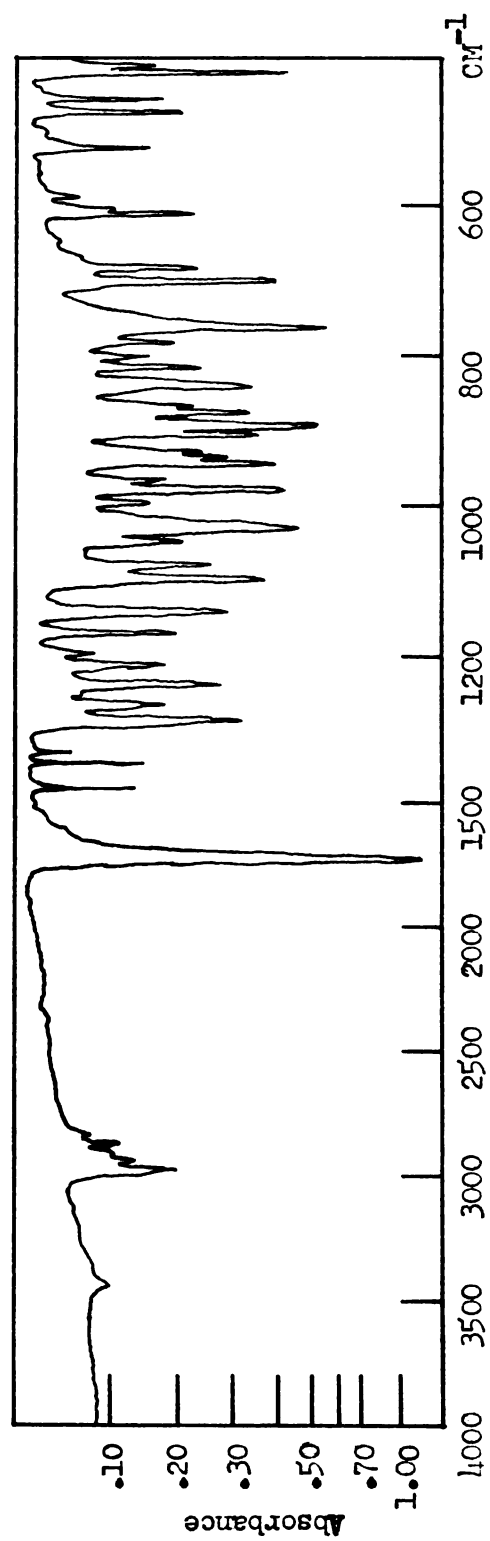


Figure I. The Infrared Spectrum of 3,3,4,5R-Tetrachloro-Tetracyclo[5.2.1.0^{2,6}.0^{4,9}]Decan-8-one in KBr

]

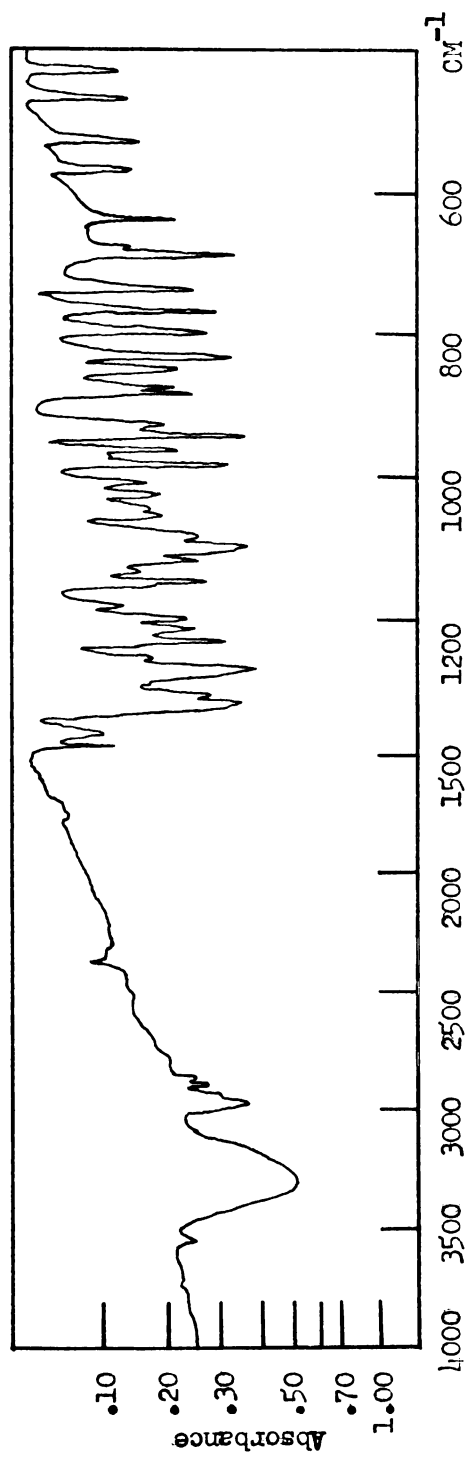


Figure II. The Infrared Spectrum of 2,3,4,4-Tetrachloro-Pentacyclo [5.3.0.0^{2,6}.0^{3,10}.
O^{2,9}]Decanol in KBr

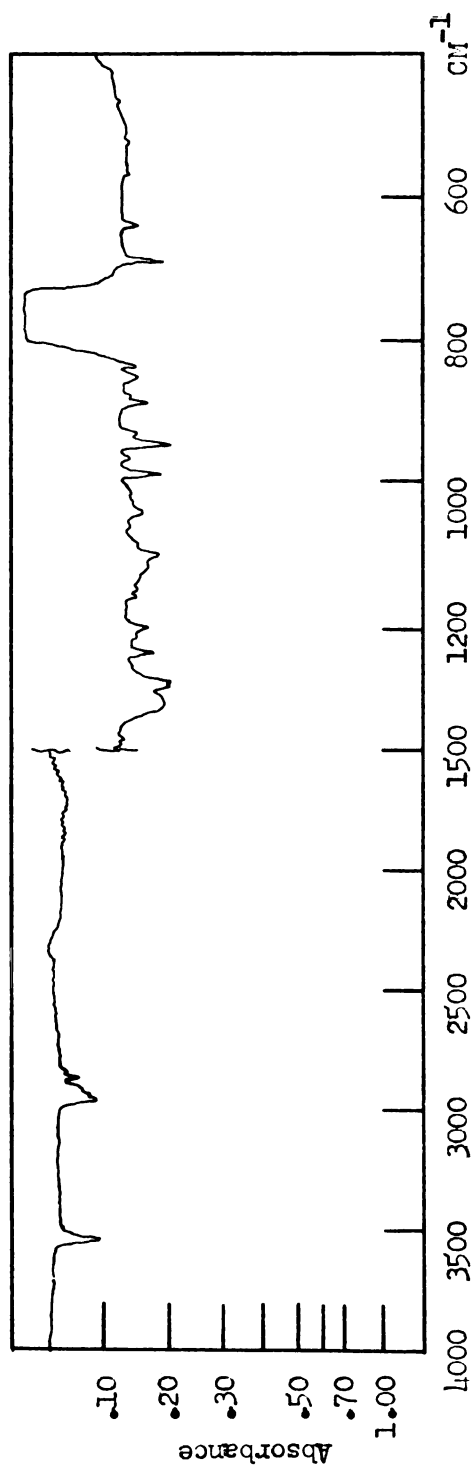


Figure IIa. The Infrared Spectrum of 2,3,4,4-Tetrachloro-Pentacyclo[5.3.0.0^{2,6}.0^{3,10}.0^{8,9}]Decanol in Carbontetrachloride

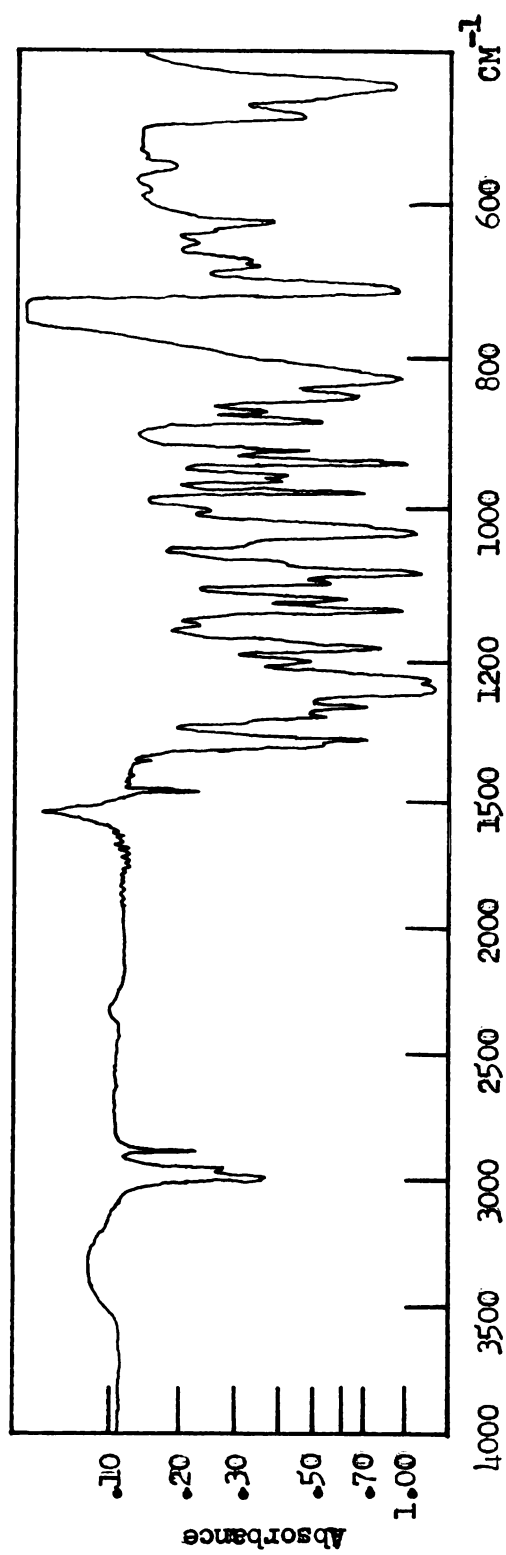


Figure III. The Infrared Spectrum of 1,2,3,4,4-Pentachloro-Pentacyclo[5.3.0.0.0^{2,6}.0^{3,10}.0^{5,9}]Decane Concentrate in Carbon tetrachloride

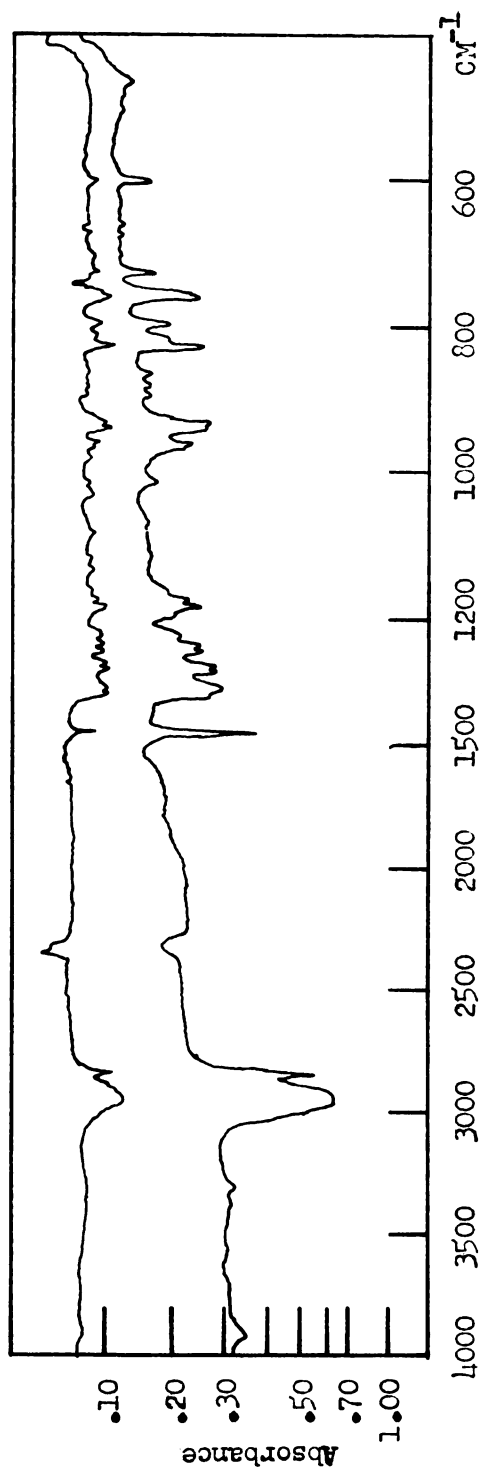


Figure IV. The Infrared Spectrum of Pentacyclo[5.3.0.0^{2,6}.0^{3,9}.0^{5,8}]Decane Superimposed on a Known Authentic Sample in KBr

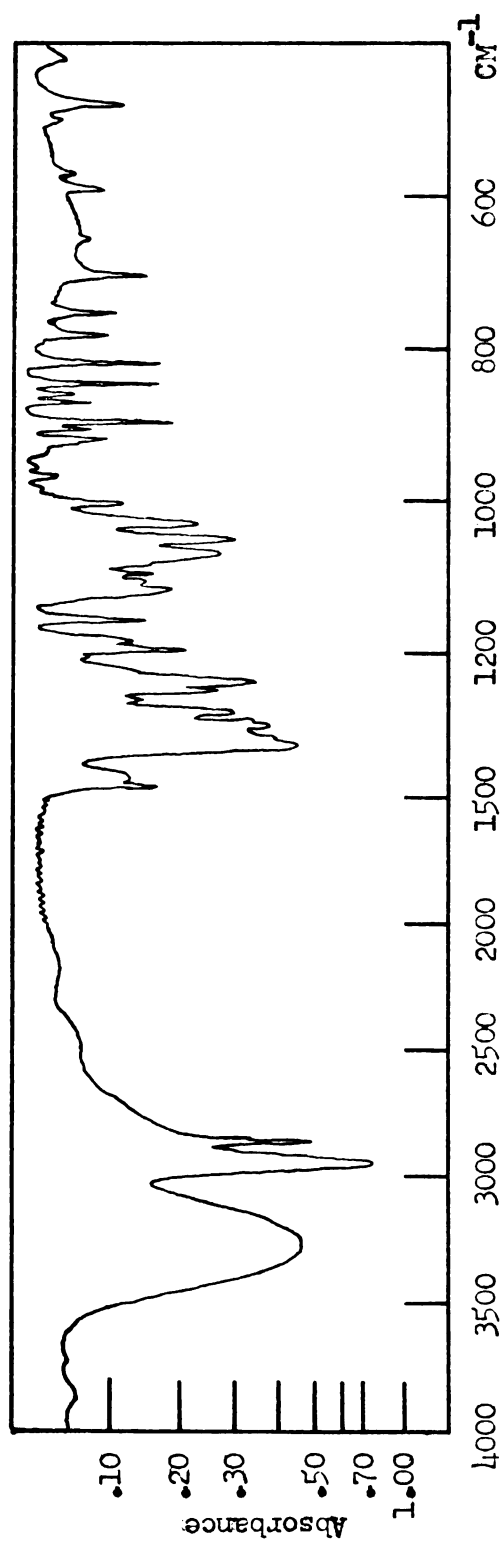


Figure V. The Infrared Spectrum of Penta cyclo[5.3.0.0^{2,6}.0^{3,10}.0^{5,9}]Decanol in KBr

Compound Number	Solvent	Chemical Shift Tau Values (Area Integration)	
		Methylene Protons	Methine Protons
I	CCl ₄	9.07 8.14 q (2H) J = 6.2cps	7.10 m (2H) 6.81 s (4H)
II	CH ₂ Cl ₂	8.47 8.19 q (2H)	7.05 m (1H) 6.5-6.9 m (4H) 4.97 s (1H)
IV	CCl ₄	8.16 s (2H)	7.15 m (1H) 6.7-6.9 m (4H) 5.4 s (1H)
IV	CH ₂ Cl ₂	8.44 8.16 q (2H) Δν = 7.4cps J = 7.2cps	7.26 m (1H) 6.7-6.9 m (4H) 5.44 s (1H)
IV	DMF D ₂ O	8.35 7.85 q (2H) Δν = 16.6cps J = 7.0cps	(observed) 6.5-6.7 m (4H) 5.4 s (1H)
V	CH ₂ Cl ₂	8.21 bs (2H)	7.43 bs (2H) 7.09 m (4H) 6.84 6.81 (2H)
VII	CDCl ₃	8.53 8.21 q (2H) 8.29 s (2H) J = 10.5cps	7.92 m (1H) 7.59 m (6H) 6.89 s (1H)
IX (18)*	CDCl ₃	8.79 8.36 q (4H) J = 10.7cps	7.48 m (5.8H) 7.28 m (2.4H)
X	CCl ₄	8.0 m (2H)	6.7-7.0 m (5H)

* These values ascertained from Wil. Dilling

Table I. Nuclear Magnetic Resonance Data

BIBLIOGRAPHY

1. L.E. Mitchell in "Organic Pesticides in the Environment", R.F. Gould, Ed., American Chemical Society Publications, Washington D.C., 1966, pp 1-21.
2. R.C. Cookson and E. Grundwell, Chem. Ind. (London), 1004 (1958).
3. R.C. Cookson and E. Grundwell, Chem. Ind. (London), 703 (1959).
4. S.B. Soloway, J. Am. Chem. Soc., 82, 5377 (1960).
5. C.W. Bird, R.C. Cookson, and E. Grundwell, J. Chem. Soc., 4809 (1961).
6. D.D. Phillips, G. Pollard, and S.B. Soloway, J. Agr. Food Chem., 10, 217 (1962).
7. L. DeVries and S. Winstein, J. Am. Chem. Soc., 82, 5363 (1960).
8. P. Bruck, S. Winstein, and D. Thomson, Chem. Ind. (London), 590 (1960).
9. B.I. Sparr, et. al. in "Organic Pesticides in the Environment", op. cit., pp 146-162.
10. I. West, ibid., p 44.
11. C.S. Myers, Penna. Dept. of Health Research Report #45, (1958).
12. C.H. VanMiddelen in "Organic Pesticides in the Environment", op. cit., pp 228-249.
13. J. Roburn, Chem. Eng. News, 1555 (1963).
14. J.D. Rosen and D.J. Sutherland, Bull. Environ. Contamin. Toxicol., 1, 133 (1966).
15. J. Attenburrow, J. Chem. Soc., 4547 (1961).
16. P. Carter, R. Howe, and S. Winstein, J. Am. Chem. Soc., 87, 914 (1965).

17. W.L. Dilling and C.E. Reineke, Tetrahedron Lett., 27, 2547 (1967).
18. W.L. Dilling et. al., Tetrahedron, 23, 1211 (1967).
19. private communication, M.J. Zabik.
20. O. Grummitt, A. Buck, and A. Jenkins, J. Am. Chem. Soc., 67, 155 (1945).
21. D. Todd in "Organic Reactions", Vol. IV, John Wiley and Sons Inc., New York, p 378.
22. J.H. Brewster, J. Am. Chem. Soc., 76, 6364 (1954).
23. E.L. Martin in "Organic Reactions", Vol. I, op. cit., p 155.

MICHIGAN STATE UNIVERSITY LIBRARIES



3 1293 03061 3982