degassed and heated at 130° in an ampoule for 200 hr. The reaction mixture was fractionated: fraction I [bp 22–35° (2 mm)], II [bp 35–65° (2 mm)], III [bp 65–120° (2 mm)]. By vpc analysis, it was revealed that the products of this reaction consist of one predominant product (1) appearance temperature 113°) along with several minor products.

Fraction I contained essentially the product 1 with a small amount of dimethyl trisulfide, and the nmr spectrum of the fraction showed a singlet CH_3 peak (τ 8.00) with relative area 2 and a singlet CH_3S peak (τ 7.34) with relative area 1; hence the product 1 was assigned as α-methylmercaptoisobutylonitrile. The independent synthesis of this compound from sodium salt of methanethiol with α-chlorobutylonitrile confirmed the structure.

Registry No.—Dimethyl tetrasulfide, 5756-24-1; Dimethyl trisulfide, 3658-80-8; methyl methacrylate, 80-62-6; acrylonitrile, 107-13-1; cyclohexene, 110-83-8; methyl cyclohexyl monosulfide, 7133-37-1; methyl cyclohexyl disulfide, 10074-84-7; 1-methylcyclohexene, 591-49-1; 1-methylcyclohexyl methyl monosulfide, 10074-85-8; methacrylonitrile, 126-98-7; α-methylmercaptoisobutyronitrile, 10074-86-9; α-methylstyrene, 98-83-9.

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Free-Radical Chlorination Reactions of Iodobenzene Dichloride

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The photoinitiated chlorination of several substituted alkanes with iodobenzene dichloride (IBD) showed product isomer distributions which were remarkably similar to those obtained for halogenation with molecular chlorine. IBD had been previously shown to halogenate 2,3-dimethylbutyl by a mechanism which did not involve chlorine radicals. A more detailed investigation of the mechanism of IBD chlorination, by studying its selectivity, relative reactivity, and primary deuterium isotope effect, has confirmed the proposal that the PhİCl radical is the abstracting species in the radical halogenation reactions of substituted and unsubstituted hydrocarbons. The anomalous results for the halogenation of negatively substituted alkanes are attributed to polar effects on the radical-abstraction reaction.

During the course of the investigation of solvent effects on the photoinitiated chlorination of 2,3-dimethylbutane, Russell reported that when iodobenzene was used as solvent for the reaction the selectivity toward hydrogen abstraction for tertiary to primary hydrogen was 31/1 while for molecular chlorine in carbon tetrachloride a value of 5/1 was observed.[2] It was noted that the yields of alkyl halides obtained were low. To explain these results he proposed that the chain-carrying species in the reaction were PhİCl and Cl· radicals, and that PhİCl must be an extremely selective hydrogen-abstracting radical.

In an attempt to generate PhİCl radicals, Banks, Huyser, and Kleinburg photolized iodobenzene dichloride (IBD) in 2,3-dimethylbutane[3] and noted that the radical selectivity was indeed very high, since they found that no primary halide resulted from the chlorination. They proposed PhİCl as the sole chain-carrying species.

We were interested in this halogenating reagent both for its high selectivity, and as a means of studying polar effects in hydrogen-abstraction reactions using iodobenzene dichloride and substituted iodobenzene dichlorides. Preliminary examination of the products of chlorination of several negatively substituted alkanes with IBD showed isomer distributions which were almost identical with those reported in the literature for halogenation with molecular chlorine. The results of a more detailed examination of these reactions is the purpose of this report.

Discussion and Results

Products of Photoinitiated Halogenation.—Examination of the products of photochlorination of cyclohexane with IBD (40°, in carbon tetrachloride) showed high yields of cyclohexyl chloride, and a material balance for the reaction products was in agreement with that obtained by Huyser[3] (see Table I). In addition to the cyclohexyl chloride reported by Huyser, small amounts of chlorobenzene and cyclohexyl iodide were obtained as well as small amounts of products resulting from the photolysis and thermolysis of IBD itself.[4]

TABLE I

PRODUCTS OF PHOTOINITIATED REACTIONS

Cyclohexane with IBD
(1:10 Mole Ratio, 40°, CCl_4 Solvent)

IBD	$C_6H_{11}Cl$	C_6H_5I	HCl	Other products[a]
1.04	...	...	1.09	...
1.05	1.09	1.07	...	<0.05
0.960	0.860	0.879	...	<0.05
0.989	0.963	0.943	...	<0.05

1-Chlorobutane with IBD
(1:10 Mole Ratio, 40°, CCl_4 Solvent)

IBD	HCl	$C_4H_8Cl_2$ (all isomers)	C_6H_5I	C_6H_5Cl	Photorearrangement product	Other products[a]
1.22	1.04	...	...	...	...	...
1.15	1.05	...	...	...	...	...
1.20	...	0.567	0.765	0.038	0.362	<0.1
1.16	...	0.523	0.777	0.034	0.341	<0.1
1.20	...	0.548	0.782	0.039	0.340	<0.1
1.19	...	0.553	0.749	0.039	0.331	<0.1

[a] Yields of unidentified products were estimated by comparing their integrated areas of glpc chromatograms with those of the chlorinated 1-chlorobutanes.

(1) Presented in part at the 49th National Meeting of the Chemical Institute of Canada, Saskatoon, 1966.

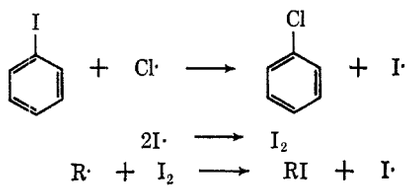
(2) G. A. Russell, *J. Am. Chem. Soc.*, **80**, 4987 (1958).

(3) D. F. Banks, E. S. Huyser, and J. Kleinburg, *J. Org. Chem.*, **29**, 3692 (1964).

(4) Unpublished work from this laboratory.

The IBD photochlorination of 1-chlorobutane (Table I) showed lower yields of chlorinated substrate, higher percentages of chlorobenzene, and products believed to be iodinated 1-chlorobutane, and gave a substantially higher yield of products resulting from the photo and thermal rearrangements of IBD.[4]

The conversion of iodobenzene to chlorobenzene can be explained by a radical-displacement reaction by chlorine atoms on iodobenzene, the iodobenzene having been produced in the reaction of IBD with substrate. This displacement is similar, by analogy,

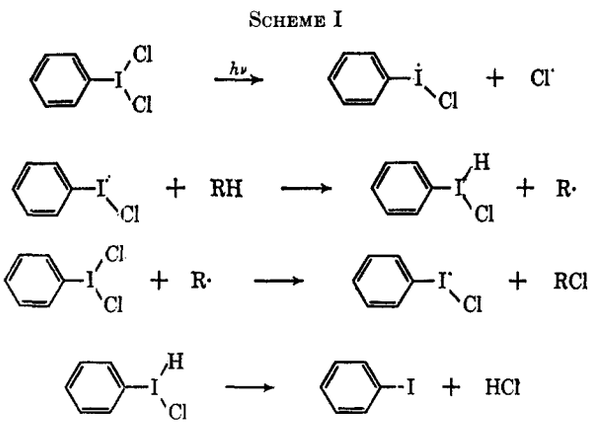


to that studied by Miller and Walling[5] for the displacement of bromine atoms by chlorine radicals on bromobenzene. Since no iodine was detected at the completion of the reaction either visually or by iodometric titration, the iodine produced by displacement must have been scavenged by hydrocarbon radicals produced by abstraction reactions. Scavenging by iodine would not only tend to lower the yield of chlorinated hydrocarbons but also make uncertain the relative yields of primarily produced radicals. The occurrence of the displacement reaction seemed to be greater in the chlorinations of the less reactive negatively substituted hydrocarbons.

Although the possibility of selective scavenging by iodine was not likely, the reactivity of the abstracting species could be better investigated by use of relative reactivities calculated from the disappearance of reactants, instead of the appearance of products. Since both methods of studying the reactivity of this reagent were applicable, comparative studies by the two methods were made.

Mechanism of Halogenation.—The mechanism, proposed by Huyser[3] to explain the high selectivity observed in the 2,3-dimethylbutane chlorinations, proceeded entirely by abstraction of hydrogen by PhICl (Scheme I). An alternative mechanism which would be compatible with the products formed, but not with the selectivity reported by Huyser, is one proceeding through a sequence of reactions where chlorine radicals

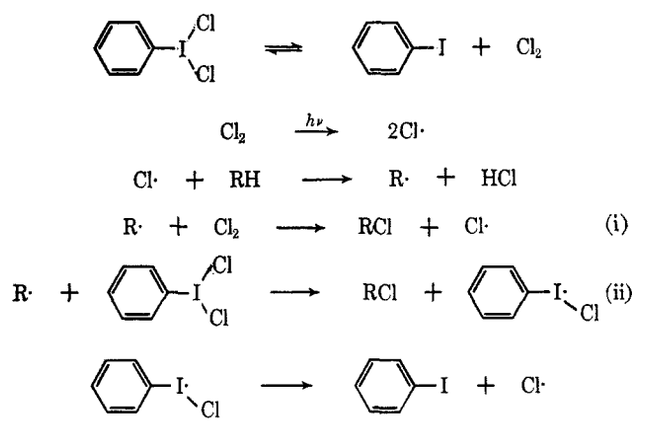
SCHEME I



(5) B. Miller and C. Walling, *J. Am. Chem. Soc.*, **79**, 4187 (1957).

are the abstracting species, and chain transfer is from IBD (eq ii, Scheme II) or from molecular chlorine (eq i, Scheme II). A combination of the first and second mechanism would agree with the proposals of Russell.[2] The second mechanism however seemed to agree with the anomalous results obtained in our chlorinations of substituted alkanes.

SCHEME II



The observation of the formation of small amounts of chlorobenzene inferred, if the Walling and Miller mechanism was in operation, that some quantity of chlorine atoms was present during the halogenation reaction. The reaction of the chlorine atom in the displacement does not necessitate however, that these radicals entered into the chain halogenation of the hydrocarbon substrate.

Halogenation of Substituted Alkanes.—The halogenation of negatively substituted alkanes is a standard method of investigating the selectivity and response to polar effects of the radical carrying out the abstraction process. Generally, for chlorination, electron withdrawal deactivates the molecule for C–H abstraction. The effect on a particular C–H bond decreases as the C–H bond involved is more removed from the electron-withdrawing substituent. On the other hand, the C–H bond strengths are lowered by electron withdrawal thus increasing their reactivity. The two effects oppose each other and the combination of these effects determine the reactivity of the particular C–H bond toward a specific abstracting species. The magnitude and relative importance of these effects are determined by the electrophilicity of the abstracting radical.[6-11]

Radical halogenations with chlorine show low selectivity in competitive hydrogen abstraction reactions.[2,9,12] In halogenation reactions of negatively substituted alkanes, however, a large deactivating effect is observed on C–H bonds adjacent to the electron-withdrawing group.[9] Halogenation with *t*-butyl hypochlorite gives a distribution of products

(6) For a summary of this subject through 1955, see C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, pp 363–365.

(7) C. Walling and B. B. Jacknow, *J. Am. Chem. Soc.*, **82**, 6113 (1960).

(8) H. Kloosterziel, *Rec. Trav. Chim.*, **82**, 508 (1963).

(9) C. Walling and M. F. Mayahi, *J. Am. Chem. Soc.*, **81**, 1485 (1959).

(10) W. Thaler, *ibid.*, **85**, 2607 (1963).

(11) P. S. Fredericks and J. M. Tedder, *J. Chem. Soc.*, 144 (1960); 3520 (1961).

(12) H. B. Hass, E. T. McBee, and P. Weber, *Ind. Eng. Chem.*, **28**, 333 (1936).

which reflects the greater selectivity of *t*-butoxy radicals when compared to chlorine,[13] since the polar properties of the two radicals are about equal.[7] Comparison of the isomer distributions obtained from the chlorination of several negatively substituted alkanes with molecular chlorine, *t*-butyl hypochlorite, and IBD are shown in Tables II and III. Since the isomer distributions in IBD chlorinations are similar to those obtained with molecular chlorine but very different from those obtained with the more selective *t*-butyl hypochlorite, several interpretations of the results are possible. The possibilities are that the IBD chlorinations proceed by a chlorine atom chain, Scheme II; that PhICl is the chain-carrying radical and that this radical has the same selectivity and response to polar effects as did the chlorine radical; or that PhICl is indeed a selective radical, but that it is strongly susceptible to deactivation by the polar substituents. A further possibility exists that the extremely stable PhICl radical is so deactivated by polar substituents that, although with hydrocarbon substrates the reaction proceeds primarily by PhICl abstraction, with polar substrates the radical decomposes to iodobenzene and a chlorine atom, and that chlorine atom abstraction is then the predominant chain-carrying reaction in these halogenations (see the section on relative reactivities for a discussion of this possible combination of mechanisms).

TABLE II

COMPARISON OF THE ISOMER DISTRIBUTIONS FOR THE HALOGENATION OF 1-CHLOROBUTANE WITH SEVERAL CHLORINATING REAGENTS[a] (40°, PHOTOINITIATION, CCl_4 SOLVENT)

Reagent (temp, °C)	Solvent	Isomer distribution, % 1,1 Cl—CH_2—	1,2 —CH_2—	1,3 —CH_2—	1,4 —CH_3
Cl_2 (34)[b]	Neat	6.8	23.5	51.4	18.8
$PhICl_2$ (40)	Neat	5.0	21.3	61.6	12.2
	CCl_4	5.2	24.0	55.9	15.4
	50% PhI–CCl_4	Trace	20.2	65.8	14.2
$PhICl_2$ (0)	CCl_4	6.2	22.4	50.9	20.9
t-C_4H_9OCl (40)[c]	CCl_4	21.1	19.4	43.9	15.5

[a] Values are averages of the results of three or more independent experiments. [b] Taken from ref 9. [c] Taken from ref 7.

TABLE III

COMPARISON OF THE ISOMER DISTRIBUTIONS FOR THE HALOGENATION OF 1-CHLOROPROPANE AND *n*-BUTYRONITRILE[a] (40°, PHOTOINITIATION, CCl_4 SOLVENT)

Reagent	Isomer distribution, % 1,1 Cl—CH_2—	1,2 —CH_2—	1,3 —CH_3
$PhICl_2$	17.6	47.9	34.8
Cl_2	11.8	57.6	30.7
t-C_4H_9OCl[b]	47.7	41.4	10.9

Reagent	1,1 N≡C—	1,2 —CH_2—	1,3 —CH_2—	1,4 —CH_3
$PhICl_2$ (neat)	...	0	57.0	43.0
Cl_2[c]	...	0	69	31
t-C_4H_9OCl[b]	...	22.4	43.7	33.9

[a] Values are averages of the results of three or more independent experiments. [b] Taken from ref 7. [c] Taken from A. Bruylants, M. Tits, C. Dieu, and R. Gauthier, *Bull. Soc. Chim. Belges*, **61**, 266 (1952).

(13) C. Walling and B. B. Jacknow, *J. Am. Chem. Soc.*, **82**, 6108 (1960).

Halogenation of 1-chlorobutane, if it proceeded by Scheme II, would involve the equilibrium between iodobenzene, molecular chlorine, and IBD. Lower temperatures and high concentrations of iodobenzene would favor the formation of IBD; if the reaction proceeded by a mixed chain (Schemes I and II), a change in either of the two reaction variables should effect the distribution of products observed in the chlorination. Experiments at 0° and with added iodobenzene failed to change significantly the distribution of products observed (see Table II).

Selectivity of IBD in Hydrogen Abstraction.—The photohalogenation of *n*-butane and 2,3-dimethylbutane with IBD confirmed the results of Huyser[3] that PhICl is a very selective hydrogen-abstracting radical. Under our conditions (40°, in carbon tetrachloride) primary halogenation was observed in the case of 2,3-dimethylbutane chlorination, thus enabling us to measure the primary to tertiary ratios. A comparison of the selectivity, per H, for halogenation of these two substrates between chlorine, *t*-butyl hypochlorite, and IBD is shown in Table IV. Since the selectivity observed in hydrogen-abstraction reactions is directly related to the stability of the abstracting radical and the strength of the C–H bond being broken, the magnitude of the primary dueterium isotope effect is correlated to the radical selectivity. Relative reactivities, calculated from the disappearance of reactants, of norbornane to cyclohexane and to perdeuteriocyclohexane yield a value of k_H/k_D for IBD halogenation of 1.9. A comparison of several halogenating reagents with IBD shows the selectivity values for tertiary to secondary hydrogen abstraction to parallel the k_H/k_D ratios, *i.e.*, the higher the selectivity the higher is the primary deuterium isotope effect (see Table V). These high k_H/k_D ratios constitute further evidence for the high selectivity of PhICl radicals and substantiates the assumption that the selectivity is reflected in the final product distribution.

TABLE IV

COMPARISON OF THE SELECTIVITY OF SEVERAL CHLORINATING REAGENTS FOR PRIMARY, SECONDARY, AND TERTIARY HYDROGEN ATOMS (PHOTOINITIATION, CCl_4 SOLVENT, 10:1 SUBSTRATE TO REAGENT RATIO)

Chlorinating agent (temp, °C)	Selectivity —CH_3	>CH_2	>CH
Cl_2 (27)[a]	1	3.9	5.1
t-C_4H_9OCl (40)[b]	1	8	44
$PhICl_2$ (40)[c]	1	21	368

[a] P. C. Anson, P. S. Fredericks, and J. M. Tedder, *J. Chem. Soc.*, 918 (1959). [b] Taken from ref 13. [c] Values reported are averages of three or more independent experiments.

TABLE V

COMPARISON OF SELECTIVITY AND THE DEUTERIUM ISOTOPE EFFECT FOR SEVERAL HALOGENATING AGENTS

Reagent	*t*/*S* (temp, °C)	k_H/k_D[a] (temp, °C)
Cl_2	1.5 (68)[b]	1.4 (80)[c]
$PhICl_2$	17.5 (40)	1.9 (40)
Br_2	36 (25)[d]	2.4 (80)[c]

[a] Values of k_H/k_D for hydrogen abstraction from cyclohexane and deuterated cyclohexane. [b] Taken from ref 9. [c] W. H. Urry, cited by K. B. Wiberg, *Chem. Rev.*, **55**, 713 (1955). [d] G. A. Russell and H. C. Brown, *J. Am. Chem. Soc.*, **77**, 4025 (1955).

Relative Reactivities in Halogenation.—Relative reactivities for halogenation with IBD calculated from the disappearance of reactants were compared with those obtained by photochlorination with molecular chlorine under similar conditions (Tables VI and VII).

TABLE VI

RELATIVE REACTIVITIES OF HYDROCARBONS TOWARD IBD,[a] MOLECULAR CHLORINE, AND *t*-BUTYL HYPOCHLORITE

Substrate (temp, °C)	Relative reactivity per molecule: $PhICl_2$	t-C_4H_9OCl[b] (temp, °C)	Cl_2[c] (temp, °C)
Cyclohexane	1.00	1.00	1.00
2,3-Dimethylbutane (40)	1.73 ± 0.06		0.86 (68)
Cyclopentane (40)	0.28 ± 0.01		0.75 (68)
Norbornane (40)	0.61 ± 0.03		0.75 (68)
1-Chlorobutane (40)	Too small to measure	0.248 (40)	0.192 (68)

[a] Reported results are averages of three or more independent experiments. [b] Taken from ref 7. [c] Taken from ref 9.

TABLE VII

REACTIVE REACTIVITIES OF IBD AND MOLECULAR CHLORINE TOWARD SUBSTITUTED HYDROCARBONS

Substrate	Relative reactivity per molecule[a,b]: $PhICl_2$	Cl_2
1-Chloropropane	1.00	1.00
1-Chlorobutane	1.08 ± 0.03 (2)	1.26 ± 0.06 (2)
n-Butyronitrile	0.47 ± 0.05 (3)	0.60 ± 0.09 (4)
1,1-Dichlorobutane	0.55 ± 0.05 (3)	0.84 ± 0.05 (3)

[a] Numbers in parentheses indicate the number of independent experiments carried out. [b] Errors indicate average deviations from the mean values reported.

The results with IBD were markedly different from those obtained with molecular chlorine when the competing substrates were both unsubstituted hydrocarbons, were a substituted and an unsubstituted hydrocarbon, and where the reactants were both substituted hydrocarbons.

The difference between IBD and molecular chlorine in relative reactivity measurements between two negatively substituted hydrocarbons appears to eliminate the possibility that the PhICl radicals are too unreactive to react with these polar substrates. If this were the case and PhICl decomposed to iodobenzene and a chlorine radical the reactivity ratios for IBD halogenation would have to be the same as those obtained for molecular chlorine.

Conclusions

In Scheme II, the chlorine atom chain is clearly not the primary sequence of reactions both for the chlorination of alkanes or negatively substituted alkanes, as demonstrated by the observed selectivity of the IBD halogenations, by the results from the study of the deuterium isotope effect, and by the relative-reactivity experiments. The selectivity and k_H/k_D results unambiguously establish the high sensitivity of the PhICl radical to the bond strength of the C–H undergoing displacement. The anomalous results obtained for the halogenation of negatively substituted alkanes are best explained, therefore, by Scheme I, where PhICl, the very selective chain-carrying radical, is one which is subject to strong deactivation by polar substituents. Some support was lent to this argument when a comparison was made for the relative reactivity of 1-chlorobutane–cyclohexane with several chlorinating reagents. The k(chlorobutane)/k(cyclohexane) for halogenation with molecular chlorine is 0.192 (68°).[9] *t*-Butyl hypochlorite, a more selective reagent, but one having a very similar response to polar effects, shows a k(chlorobutane)/k(cyclohexane) ratio of 0.25 (40°).[7] The results observed for the reaction of the highly selective IBD halogenations showed 1-chlorobutane to be so strongly deactivated by its chloro substituent that the 1-chlorobutane was experimentally unreactive in competitive halogenations with cyclohexane (see Table VI).

Experimental Section

Materials.—IBD was prepared following the method of Lucas and Kennedy.[14] The dichloride was recrystallized from chloroform and air dried before use and its purity (98–100%) was determined by iodometric titration.

Cyclohexane-d_{12} was obtained from Stohler Isotope Chemicals, and was shown by its MS-9 mass spectrum to >99.6% deuterated.

Hydrocarbons cyclohexane, cyclopentane, *n*-butane, and 2,3-dimethylbutane were Phillips research grade and were used without further purification. All other substrates were commercially available materials; their purity after distillation was checked by glpc, and their physical constants (boiling point and refrative index) were compared with those reported in the literature.

Chlorinations with IBD.—Reactions were carried out in sealed Pyrex ampoules which had been degassed by the freeze–thaw method. The sealed ampoules were allowed to reach equilibrium in a thermostated Pyrex water bath (40.0 ± 0.2°) in the absence of light. The reaction mixtures were irradiated using several 200-w incandescent light bulbs; the tubes were continuously shaken during the photolysis period. The reaction was completed when the solid IBD had all gone into solution and the reaction mixture was colorless, usually from 0.5 to 3 hr. The ampoules were opened and the reaction mixtures were subjected to analysis by glpc. All values reported are averages of three or more independent experiments. Peak areas were measured using a Model 201-B Disc integrator or by the method of peak height and half-height peak widths. The reaction mixtures were analyzed in triplicate and deviation from the average values was always less than 4% of the reported values. Typical chlorination mixtures were 0.2–0.3 *M* in IBD and 2.0–3.0 *M* in substrates.

In the material balance experiments, all product peaks were measured relative to an internal standard Freon 112. Molar amounts were calculated from calibration plots of area ratios *vs.* mole ratios for Freon 112 *vs.* the authentic samples. Hydrochloric acid was determined by iodometric titration with standard sodium thiosulphate.[15]

1-Chlorobutane chlorination mixtures were analyzed using a 10 ft × 1/8 in. neopentyl glycol succinate (NPGS) column having firebrick as the solid support. The reaction product peaks were identified as the assigned products by direct comparison of their retention times with those of authentic commercially available samples (see Tables I and II). Chlorobenzene was isolated from the reaction mixture by glpc and was further identified by its infrared spectrum.

1-Chloropropane chlorination products were analyzed on the 10 ft × 1/8 in. NPGS column. Two of the three chlorination product peaks were identified by their identical retention times on three different glpc columns with commercially available compounds. The 1,1-$C_3H_6Cl_2$ isomer was assigned by elimination. A check on the assignments of the isomer peaks was made by repeating the halogenation experiments of Walling using *t*-butyl hypochlorite,[7] and comparing their assignments with ours.

***n*-Butyronitrile** reaction mixtures were analyzed by glpc using a 10 ft × 1/8 in. Carbowax 20 M column having Chromosorb W as the solid support. The products of chlorination were identified by comparison of the known distribution of products resulting

(14) H. J. Lucas and E. R. Kennedy, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p 482.

(15) G. H. Cady, *Inorg. Syn.*, **5**, 156 (1957).

from the *t*-butyl hypochlorite halogenation of *n*-butyronitrile.[7] As a check on the assignments, the retention time of the commercially available 4-chlorobutyronitrile was compared with the assignment made from the *t*-butyl hypochlorite reaction.

Chlorination of *n*-Butane and 2,3-Dimethylbutane.—The primary/secondary/tertiary selectivity ratios were calculated from a comparison of product distributions in the usual manner.

***n*-Butane** chlorination products were analyzed on a 10 ft × 1/8 in. UCON 50 HB2000 polar on firebrick column. The structure of the 1-chlorobutane was assigned to its corresponding peak on the chromatogram by comparison of its retention time by glpc with that of an authentic sample. The remaining chlorination product peak was assigned the structure of the secondary halide.

2,3-Dimethylbutane chlorination products were analyzed by glpc on the 10 ft × 1/8 in. NPGS column. Two minor, low-boiling products and two higher boiling products were observed. The low-boiling products (1–2%) were believed to be 2,3-dimethyl-2-butene and 2,3-dimethyl-1-butene, resulting from dehydrohalogenation of the tertiary halide during analysis. The 2,3-dimethyl-2-butene structure was assigned to its corresponding peak by the comparison of its retention time with that of an authentic sample. The two higher boiling alkyl halides, >98% of the chlorinated products obtained, were assigned the structures 2-chloro-2,3-dimethylbutane and 1-chloro-2,3-dimethylbutane. The tertiary chloride was prepared by the method described by Shiner[16] and its retention time by glpc was found to be the same as that for the major isomer assigned that structure. The assignments were further verified by comparison with those obtained from a repetition of the halogenation with *t*-butyl hypochlorite.[13]

Chlorination of 1-Chloropropane with Molecular Chlorine.—A standard solution of chlorine (0.2 *M*) in carbon tetrachloride containing 1-chloropropane (2.0 *M*) was irradiated in sealed, degassed, Pyrex ampoules. The reaction and analysis were carried out in the manner previously described.

Competitive Chlorination of Hydrocarbons with IBD.—Individual experiments consisted of weighing IBD into small Pyrex ampoules, adding aliquots of standard carbon tetrachloride solutions of the two substrates and an internal standard, vacuum degassing and sealing the tubes, and carrying out the photolysis in the manner described. Reaction mixtures were typically 0.08 *M* in each substrate and 0.12 *M* in IBD. Internal standards used were either (0.05 *M*) Freon 112 or Freon 113. Relative reactivities were calculated *via* the method reported previously by this laboratory.[17]

Competitive halogenations between cyclohexane and norboranane and between perdeuteriocyclohexane and norbornane allowed us to calculate the value of k_H/k_D reported in Table V.

Registry No.—Iodobenzene dichloride, 932-72-9; 1-chlorobutane, 109-69-3; 1-chloropropane, 540-54-5; *n*-butyronitrile, 109-74-0; *n*-butane, 106-97-8; 2,3-dimethylbutane, 79-29-8; cyclohexane, 110-82-7; cyclopentane, 287-92-3; norbornane, 279-23-2; 1,1-dichlorobutane, 541-33-3.

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(16) V. J. Shiner, *J. Am. Chem. Soc.*, **76**, 1603 (1954).

(17) D. D. Tanner and E. Protz, *Can. J. Chem.*, **44**, 1555 (1966).

(18) University of Alberta Postdoctoral Fellow, 1966–1967.

Microbial Transformation of a Series of Androgens with *Aspergillus tamarii*

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Incubation of androsterone (**5**) with *Aspergillus tamarii* gave 11α and 11β hydroxylation of **5**. Isoandrosterone was converted into 11β-hydroxyisoandrosterone. Incubation of 1,4-androstadiene-3,17-dione (**12**) gave 11α and 11β hydroxylation of **12**, 1,4-androstadien-17β-ol-3-one (**13**), and 1,4-androstadiene-11β,17β-diol-3-one (**14**). Compound **13** was shown to be the precursor of **14**. Adrenosterone and 4-androstene-3,11,17-trione gave the respective 17β-hydroxy derivatives. Incubation of 5β-androstane-3,17-dione gave 5β-androstan-7β-ol-3,17-dione, whereas 5α-androstane-3,17-dione (**24**) gave 5α-androstan-6β-ol-3,17-dione and 11β-hydroxy-5α-dihydrotestololactone (**27**). Androstanolone gave 5α-androstane-11β,17β-diol-3-one (**30**), **24**, and **27**. Compound **30** was shown not to be a precursor of **27**. Analogously with the progesterone to testololactone conversion, 5α-pregnane-3,20-dione was converted into 5α-dihydrotestololactone (**32**) and **27**. A C-11 hydroxyl substituent has been shown to inhibit transformations by *A. tamarii* which do occur with the unsubstituted androgens. A discussion of microbial hydroxylation substrate specificity is presented.

The sequential removal of the side chain from C_{21} steroids by microorganisms to yield D-ring lactones was first reported by Peterson, *et al.*,[1] and by Fried and co-workers.[2] Since then numerous organisms have been found[3–8] which will remove an acetyl, α-ketol, or dihydroxyacetone side chain from pregnene steroids to yield testololactone or its derivatives.

More than one mechanism has been shown[9,10] to be operative in the microbial removal of the acetyl side chain of progesterone (**1**) as shown in Scheme I. However, insertion of the ethereal oxygen between C-13 and C-17 of **3** is in accordance with the chemical mechanism of per acid attack on the C-17 ketone to produce the lactone as shown in Scheme I.[2,11]

In an earlier study[12] incubation of progesterone (**1**) with *Aspergillus tamarii* Kita gave testololactone (**4**) as the major metabolite. A second product from incubation of this substrate was 11β-hydroxytestosterone, which appeared to be formed from hydroxylation of testosterone (**2**). Although **2** is an intermediate in the conversion of progesterone to testololactone, the 11β-hydroxy analog of **2** is not metabolized further by this fungus. This inability of *A. tamarii* to metabolize

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