2-thiouracil, 6-propyl-2-thiouracil, hypoxanthine, 2-methyladenine, xanthine, and orotic acid were photographically recorded on a CEC 21-110B instrument using a gas chromatographic inlet system[24] (6 ft, 1% OV-17). Ion source and carrier gas separator temperatures were 250°; ionizing energy was 70 eV. Exact masses were measured of all ions having relative abundances greater than ~0.5%.

All pyrimidine and purine bases were purchased commercially with the exception of 4-thiouracil (7), which was obtained from the Cancer Chemotherapy National Service Center of the National Institutes of Health. 8-^{14}C-4 containing 67 mol % ^{14}C (equivalent to 40 mCi/mmol) was purchased from International Chemical and Nuclear Corp. Compounds were checked for purity by gas chromatography and mass spectrometry of their trimethylsilyl derivatives.

Formation of Trimethylsilyl Derivatives.—Derivatives were prepared from 0.5–1.5 mg of base at concentrations of 4–10 $\mu g/\mu l$, by one of the three following methods. (A) The base was heated at 100° for 1–2 hr with bis(trimethylsilyl)trifluoroacetamide (BSTFA) (Peninsular ChemResearch, Inc.) and 1% added trimethylchlorosilane in a screw-capped vial. (B) The same procedure as A was followed using bis(trimethylsilyl)acetamide (BSA) (Pierce Chemical Co., distilled before use) in place of BSTFA. (C) The base was allowed to stand at room temperature for 1 hr with occasional shaking in a mixture of BSA and acetonitrile (1:3) with trimethylchlorosilane (1%). d_9-Trimethylsilyl derivatives were prepared by method C, using bis(d_9-trimethylsilyl)acetamide and d_9-trimethylsilylchlorosilane (Merck Sharp and Dohme of Canada, Ltd.).

The method of preparation and column temperature for the LKB gas chromatograph are shown for each compound in Table III. The columns used at a flow rate of 30–40 cc He/min were (A) 9 ft, 1% SE-30; (B) 3 ft, 1% SE-30; (C) 3 ft, 1% OV-17; (D) 6 ft, 1% OV-17; (E) 9 ft, 1% OV-17; (F) 6 ft, 1% SE-30.

The successful gas chromatography of 9-(trimethylsilyl)purine (17) was found to depend strongly on the age and condition of the column. The chromatogram of N^6,9-bis(trimethylsilyl)-1-methyladenine showed a broad, low peak followed closely by a normal peak. Mass spectra of the two peaks showed the same fragment ions but differing relative abundances. Data given in Table I relate to the sharp chromatographic peak, but include some contamination from the second component.

Mass spectra of all compounds were free of peaks above that of the molecular ion, and at improbable mass values below that of the molecular ion. The number of trimethylsilyl groups exchanged during the derivatization reaction was determined from the mass spectra. In some instances, derivatives of purine bases can have structures isomeric with those shown in the text. In most cases silylation is assumed to occur at enolizable carbonyl groups, on amino groups external to the ring, and at N-9, based on infrared[3c,4] and nmr data,[4] and by known reactions of these derivatives in synthetic procedures.[3b,d] In particular, other structures cannot be completely excluded for derivatives of 3-methyladenine (9), 7-methyladenine (12), purine (17), 6-chloropurine (18), and 1-methyladenine (discussed above).

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Registry No.—**1**, 10457-14-4; **2**, 7288-28-0; **3**, 18037-10-0; **4**, 17995-04-9; **5**, 18602-85-2; **6**, 32865-74-0; **7**, 32865-75-1; **8**, 32865-76-2; **9**, 32865-77-3; **10**, 32865-78-4; **11**, 32865-79-5; **12**, 32865-80-8; **13**, 31517-04-1; **14**, 32865-82-0; **15**, 32865-83-11; **16**, 32865-84-2; **17**, 32865-85-3; **18**, 32865-86-4; **19**, 32865-87-5; 5-methylcytosine-$(SiMe_3)_2$, 32865-88-6; hypoxanthine-$(SiMe_3)_2$, 17962-89-9; 1-methyladenine-$(SiMe_3)_2$, 32958-85-3; 2-methyladenine-$(SiMe_3)_2$, 32865-90-0; 7-methylguanine-$(SiMe_3)_2$, 32958-86-4; 7-methylxanthine-$(SiMe_3)_2$, 32865-91-1; 5-hydroxyuracil-$(SiMe_3)_3$, 32865-92-2; 6-hydroxyuracil-$(SiMe_3)_3$, 31111-39-4; xanthine-$(SiMe_3)_3$, 18551-03-6; orotic acid-$(SiMe_3)_3$, 32865-94-4; uric acid-$(SiMe_3)_4$, 18547-59-6; 5-methyl-2-thiouracil-$(SiMe_3)_2$, 32865-96-6; 6-methyl-2-thiouracil-$(SiMe_3)_2$, 32865-97-7; 6-propyl-2-thiouracil-$(SiMe_3)_2$, 32958-88-6.

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Photochemical Oxidations. V. Concerted *vs.* Radical Stepwise Addition of Oxygen to the Carbon–Hydrogen Bond of Hydrocarbons

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The stereochemistry of the initial stage of the photooxidation of hydrocarbons was studied. During this stage, the reaction products originate directly from the excitation of a contact charge transfer complex between oxygen and the hydrocarbons. The liquid-phase oxidation of (+)-3-methylhexane produces a racemic tertiary alcohol, and the *cis*- and *trans*-decalins give mixtures of cis and trans tertiary decalols. Thus, a radical, stepwise mechanism for the formation of the intermediate alkyl hydroperoxides is postulated rather than a concerted oxygen insertion into the carbon–hydrogen bond.

The primary process occurring during the photooxidation of saturated hydrocarbons has now been shown to be the excitation of a contact charge transfer complex between oxygen and hydrocarbons.[1–4] Product accumulation studies on the photooxidation of hydrocarbons have demonstrated that alkylhydroperoxides are the primary products and the secondary products are alcohols and ketones.[1] Relative reactivity studies of primary, secondary, and tertiary C–H bonds of several hydrocarbons proved that the C–H bond rather than the C–C bond was the donor site in the contact charge transfer complex.[5]

Equations 1–3 summarize the initial steps in the

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$$R{-}H + O_2 \rightleftharpoons R{-}H\cdots O_2 \overset{h\nu}{\rightleftharpoons} R\cdot H^+\cdots O_2^- \quad (1)$$

$$R\cdot H^+\cdots O_2^- \longrightarrow R\cdot + HO_2\cdot \quad (2)$$

$$R\cdot + HO_2\cdot \longrightarrow RO_2H \quad (3)$$

recently formulated photooxidation mechanism for saturated hydrocarbons.[1] Alternately, a concerted insertion of the O_2 into the C–H bond could be envisioned, *i.e.*, according with or similar to eq 4 and 5.

$$R{-}H\cdots O_2 \overset{h\nu}{\longrightarrow} [R{-}H\cdots O_2]^* \quad (4)$$

$$[R{-}H\cdots O_2]^* \longrightarrow RO_2H \quad (5)$$

The results of studies designed to determine which set of reactions is actually involved are discussed here. Two separate experiments were performed for this purpose: the photooxidation of (+)-3-methylhexane and the corresponding reaction of the *cis*- and *trans*-decalins.

Results and Discussion

It has been well documented that, when free alkyl radicals are formed at the single asymmetric center of an optically active compound, racemic products are produced.[6,7] This lack of stereospecificity is interpreted in terms of a planar arrangement of the atoms attached to the radical center or a set of nonplanar radicals in rapid equilibrium with each other. Presumably a concerted insertion of oxygen into the C–H bond would lead to retention of stereochemistry. These concepts form the basis for evaluating the results of the experiments described here. Using this idea, Wiberg and Foster[8] interpreted the chromic acid oxidation of (+)-3-methylheptane to (+)-3-methyl-3-heptanol in terms of a stereospecific mechanism.

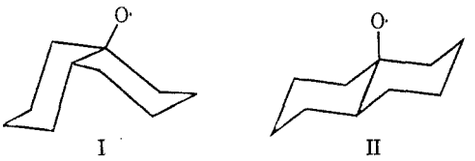
There are two stages in the photoxidation of hydrocarbons: the first where the reactions occurring in solution result directly from excitation of the charge transfer complex, and the second more rapid stage where the excitation process is augmented by a radical chain process. Since it is only the steps directly resulting from the excitation process that we are interested in, it is necessary to restrict the oxidation to the first stage, which means working with low conversions, *ca.* <0.01%, and a concomitant difficult isolation problem.

The saturated hydrocarbon, (+)-3-methylhexane, which could be synthesized by known methods,[9,10] was selected as the optically active starting material. Although a number of products could be expected from the photooxidation of this compound, the tertiary C–H bond is the most reactive,[5] and, as a consequence, a sufficiently high yield for isolation of its corresponding tertiary alcohol was expected. The tertiary alcohol, 3-methyl-3-hexanol, was isolated by glpc. The alcohol exhibited no detectable optical activity when either the sodium D lines (589.0 and 589.6 nm) or the Hg line (546.1 nm) was used. The difficulty with the analysis of this result is that the specific rotation of the pure, optically active alcohol is unknown. However, if the alcohol has a specific rotation greater than 3.0°, the optical activity would have been observed at the concentration used. It is safe to assume that the optical rotation of the alcohol is larger than 3.0°. The basis for this is that the chromophore of the alcohol is nearer the monitoring wavelengths than that of the hydrocarbons, which has a specific rotation of 9.43°. As a consequence of the lack of rotation of the tertiary alcohol, the stepwise mechanism for the initial steps of the photooxidation is favored. However, because of the assumption made concerning the optical rotation of the alcohol, supplementary evidence on this conclusion was sought *via* the photooxidation of *cis*- and *trans*-decalin.

The stereochemistry of 9-decalyl free radicals has been studied by Bartlett, *et al.*[11] The radicals were generated by the thermal decomposition of *cis*- and *trans*-9-carbo-*tert*-butylperoxydecalins in cyclohexane. In the presence of 1 atm of oxygen, the radicals react to form hydroperoxides at the 9 position of decalin. These hydroperoxides were reduced to alcohols and the compositions were determined. Starting from the *cis*-9-carbo-*tert*-butylperoxydecalin, the alcohols formed were 89% trans and 11% cis. The data was interpreted in terms of the reaction having an intermediate 9-decalyl free radical. On the other hand, Hamilton, *et al.*,[12] demonstrated a large amount of retention of stereochemistry during the ozonation of *cis*- and *trans*-decalins. *trans*-Decalin gave 80% *trans*- and 20% *cis*-decalols while *cis*-decalin gave 85% *cis*- and 15% *trans*-9-decalols.

In the photooxidation described here, *trans*-decalin produced a mixture of 81% *trans*- and 19% *cis*-9-decalols after lithium aluminum hydride reduction. Under identical conditions, *cis*-decalin produced a mixture of 66% *trans*- and 34% *cis*-9-decalols. Clearly, considerable isomerization had taken place; however, it was incomplete. This implies the presence of a cage effect or a more rapid spin interconversion relative to interconversion of *cis*-9-decalyl radical to trans (or to a planar radical) for the photooxidation reaction, which allows only partial isomerization of the reacting carbon of the intermediates.

Tertiary alkoxy radicals are known to partially decompose by cleavage of an adjoining C–C bond. In other words, the tertiary decalols are some of the products coming from the proposed intermediates I and II. In this study of the *cis*- and *trans*-decalins,



I II

the assumption is made that I and II decompose with C–C bond cleavage at similar rates and, therefore, would not interfere with the percentage of alcohols formed at the tertiary C–H centers.

The two sets of results, that of the photooxidation of (+)-3-methylhexane and the decalins, prove that considerable stereochemical equilibration at the C–H site takes place during the photooxidation of hydrocarbons. Thus the concerted insertion of O_2 into a

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C–H bond can be ruled out, and the dissociative, stepwise mechanism in a solvent cage can be invoked to explain the existing data.

In retrospect the radical, stepwise mechanism is the most logical. Molecular oxygen is a ground-state triplet, and its two highest occupied degenerate antibonding π^* orbitals contain one electron each. In the charge-transfer process an electron from the donor hydrocarbon C–H is transferred to one of the occupied orbitals of molecular oxygen and is paired with the electron already present in the orbital. The remaining two electrons, one on the hydrocarbon and the other in the still untouched degenerate π^* orbital of oxygen, must then be unpaired. Before the hydroperoxide can be formed, the hydrogen ion must be transferred to the now negatively charged oxygen, and the remaining two electrons must become paired in order to form the covalent C–O bond in the hydroperoxide (step b of reaction 6). The unpaired spins of the species re-

$$R{\cdot}H^{+}\cdots O_2^{-} \xrightarrow{a} R{\cdot}\uparrow + \uparrow{\cdot}O_2H \xrightarrow{b}$$

$$R{\cdot}\uparrow + \downarrow{\cdot}O_2H \xrightarrow{c} RO_2H \quad (6)$$

sulting from step a of reaction 6 allows time for equilibration to occur.

Experimental Section

Apparatus.—The light source for the irradiations was a 550-W Hanovia lamp (673A36) placed inside a quartz immersion well. A Beckman GC-5 gas chromatograph equipped with a flame ionization detector and a 20% Carbowax 20M–Chromosorb W column was used. Optical rotations were determined on a Rudolph Model 80 polarimeter.

Preparation and Purification of Materials.—The criterion of purity used for the hydrocarbons was that the sample, when flushed with nitrogen and placed in a 1-cm quartz spectrophotometric cell, be virtually transparent to 200 nm. Aldrich 97% pure *trans*- and 99% pure *cis*-decalins were insufficiently pure for the purposes of these experiments. The *trans*-decalin was stirred overnight with fuming sulfuric acid at 50°, extracted with cold, concentrated sulfuric acid until both layers were clear, extracted with water, dried, and distilled at reduced pressure. It was found that *cis*-decalin reacted with fuming sulfuric acid. However, the cis compound, that survived treatment with fuming sulfuric acid, was passed over a column of activated alumina which made it sufficiently pure for use.

Eastman (−)-2-methyl-1-butanol (328 g) was treated with 542 g of phosphorus tribromide to form 381 g of (+)-2-methyl-1-bromobutane.[9] The nmr spectrum of the bromide was characteristic of its structure showing a downfield doublet at τ 6.9, while the infrared spectrum agreed with that in the literature.[13] The specific rotation of the bromide, $[\alpha]^{25}D$, was +3.18° (lit.[9] $[\alpha]^{25}D$ +4.04°. The crude bromide (213 g) was coupled with 461 g of ethyl bromide and 100 g of sodium.[10] The crude reaction mixture was fractionally distilled to give 48 g of (+)-3-methylhexane, bp 92–93°. The crude hydrocarbon (48 g) was then refluxed for 1 hr with sodium and absolute ethanol, in order to destroy any bromine compounds still present. The reaction mixture was then distilled, extracted with cold, concentrated sulfuric acid several times, washed with water, dried, and redistilled. Preparative glpc gave 17 g of (+)-3-methylhexane, bp 92–93° (lit.[10] 91°). The specific rotation of the hydrocarbon, $[\alpha]^{25}D$, was +7.50° (lit.[14] $[\alpha]^{19.5}D$ +9.43°). The nmr spectrum of the compound was characteristic of a saturated hydrocarbon, showing only upfield absorption in the alkyl region. The glpc retention time of the compound was slightly longer than that of 3-methylpentane. The mass spectrum of the compound showed an intense peak at *m/e* 100. Standard samples for the 9-decalols were prepared from independently synthesized materials.[15,16]

Irradiation Procedures.—The immersion well containing the lamp was placed in a water bath kept at 10° (±0.1°). The water in the bath was monitored to ensure that it was still transparent to uv light. The hydrocarbons were placed in a 1-cm quartz absorption cell and a fine stream of oxygen was introduced *via* a finely-drawn capillary connected to a microvalve.

Identification of Products.—The product of interest from the irradiation of (+)-3-methylhexane was 3-methyl-3-hexanol. This was identified in the reaction mixtures after reduction by triphenylphosphine[1] by a comparison of the retention times and spiking procedures with those of an authentic sample of 3-methyl-3-hexanol (Aldrich). It was then isolated from the reaction mixtures by preparative glpc. The isolated product was then diluted to 1.5 ml with carbon tetrachloride and its concentration (3.3 mg/ml) was determined by a glpc comparison with a standard solution of the alcohol. The solution had no optical rotation using sodium light (589.0 and 589.6 nm) or mercury light (546.1 nm). In order to ensure that racemization had not taken place during the preparative glpc isolation of the alcohol, a sample of (−)-2-methyl-1-butanol was injected and collected from the gas chromatograph. No loss of optical activity occurred during this procedure.

Two samples of *cis*- and two of the *trans*-decalin were irradiated separately for 20 min. The irradiated samples were then diluted with ether treated with triphenylphosphine and refluxed with lithium aluminum hydride for 1 hr. After cooling the solutions, a small amount of a saturated solution of sodium sulfate was added, the resulting suspension was filtered, and the ether was distilled until 1–2 ml remained. This treatment prevented ketonic products from interfering with the gas chromatographic analysis. For this analysis three different columns were employed, namely 20% Carbowax 20M, 20% 1,2,3-tris(2-cyanoethoxy)propane, and 20% tetracyanoethylated pentaerythritol on Chromosorb W. The 9-decalols were identified by retention time comparison with known samples on all three columns. Since Carbowax offered the best resolution, it was used to determine the percentage of *cis*- and *trans*-9-decalols in in the reaction mixtures. The percentages reported are the averages for two runs, each for *cis*- and *trans*-decalin. The agreement for each set of two runs was within 3%.

Registry No.—*trans*-Decalin, 493-02-7; *cis*-decalin, 493-01-6; (+)-3-methylhexane, 6131-24-4.

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