

acidic character of adenosine. This conclusion is confirmed by the fact that a thermometric titration of adenosine 3'(2')-monophosphate with NaOH shows no evidence for proton ionization.

There are at least two possible explanations for the fact that two adjacent hydroxyl groups are a necessary structural feature for acidity in adenosine and its derivatives. First, the combined inductive effect of the vicinal 2'- and 3'-hydroxyl groups could induce the acidity. Second, the anion may be stabilized by a hydrogen bonded ring. Actually, both effects could contribute to the observed acidity. Work is presently in progress to determine the relative importance of these two effects.

The fact that both the 2'- and 3'-hydroxyl groups are necessary for the acidity of adenosine is undoubtedly related to the reactivity of these positions and should aid in the explanation of the differences between the biological roles of adenosine and deoxyadenosine in DNA and RNA. This requirement for acidity in adenosine is also in good agreement with the observations of McLaughlin and Ingram<sup>10</sup> since their research indicates that acylation takes place at both the 2' and 3' positions. Our results also support the proposition that the 2' and 3' positions are associated with the attachment of the amino acid to the soluble-RNA in protein synthesis.<sup>8-10</sup>

In glucose 6-phosphate, the  $\Delta S^\circ$  value is 11-12 eu lower than one would predict for proton ionization from a dinegative ion.<sup>32,33</sup> The fact that the entropy change for glucose 6-phosphate is similar to that for the ionization of a proton from the neutral pentoses and hexoses in this study rather than like that for a dinegative ionization (*e.g.*,  $\text{H}_2\text{P}_2\text{O}_7^{2-}$  ionization<sup>32,33</sup>) indicates that the ionization occurs from a site on the ion which is relatively unaffected by the dinegative charge which is consistent with the previous conclusion that proton ionization occurs from the 1 position in the hexoses. However, the  $\Delta S^\circ$  value obtained for ionization from ribose 5-phosphate is very similar to that which one would expect from a dinegative ion, leading one to suspect that in the case of ribose 5-phosphate the dinegative charge is sufficiently close to influence proton ionization. This may be due to the fact that there is one less carbon atom in ribose 5-phosphate or there may be a configurational difference to account for the result.

**Acknowledgments.** The authors acknowledge several helpful discussions with Dr. H. Smith Broadbent, Dr. Roland K. Robins, and Dr. John H. Mangum.

(32) J. J. Christensen and R. M. Izatt, *J. Phys. Chem.*, **66**, 1030 (1962).

(33) L. D. Hansen, J. A. Partridge, R. M. Izatt, and J. J. Christensen, *Inorg. Chem.*, **5**, 569 (1966).

## Hydrogen Atom Transfer between Free Radicals and Their Diamagnetic Precursors

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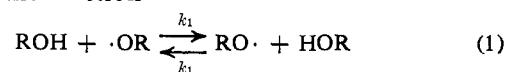
**Abstract:** Magnetic resonance techniques have been used to study the kinetics of hydrogen atom exchange between a series of hydroxylic compounds and their corresponding oxy free radicals. In some cases it was possible to determine the lifetime of a short-lived complex formed during the reaction. The rate constant for exchange was determined in each case. Deuterium was substituted for the hydroxylic proton in two cases and deuterium isotope effects were examined. The temperature dependence of the rate of exchange was examined for each set of compounds.

Rates of chemical processes in systems at equilibrium may often be determined from the dependence of the shapes of magnetic resonance lines on the chemical composition of the systems. The spectra provide a chronicle of the motion of the spins among the various sites which they may occupy. In this paper we describe studies of a set of reactions in which hydrogen atoms move from hydroxylic compounds to the corresponding oxy free radicals. In all cases the spectra yield the over-all rate of hydrogen atom transfer. In certain favorable instances mean lifetimes of short-lived complexes between reactants may be determined from the spectra.

(1) National Institutes of Health Predoctoral Fellow, 1962-1964.

### Theoretical Background

Consider the reaction



where ROH is an even-electron substance.  $\text{RO}\cdot$  is then necessarily an odd-electron substance.  $k_1$  is the rate constant for the reaction in which the hydroxylic hydrogen atom is transferred to a different molecule from the one on which it started.

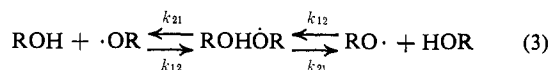
A mixture of ROH and  $\text{RO}\cdot$  exhibits nuclear spin resonance from the nuclei in ROH and electron spin resonance from the unpaired electrons in  $\text{RO}\cdot$ . The spectra are affected by process 1. The nuclear reso-

nances of the nuclei in R will have a contribution to their line breadths

$$\frac{1}{T_2} = k_1[\text{RO}\cdot] \quad (2)$$

under certain conditions. A sufficient condition for the applicability of eq 2 is that the electron spin resonance spectrum of  $\text{RO}\cdot$  in the reaction mixture exhibit hyperfine splitting from the nuclei of R whose nuclear resonance breadths are being used.<sup>2</sup>

Another possible contribution to the line breadth of nuclei in R is a process in which the ROH and  $\text{RO}\cdot$  form a complex and decompose with no transfer of hydrogen atoms. If the complex is symmetrical we may write



The equilibrium concentration of the complex is given by

$$[\text{R}\dot{\text{O}}\text{HOR}] = \frac{k_{12}}{k_{21}}[\text{RO}\cdot][\text{ROH}] \quad (4)$$

The total rate of its decomposition is

$$k_{21}[\text{R}\dot{\text{O}}\text{HOR}] = k_{12}[\text{RO}\cdot][\text{ROH}] \quad (5)$$

Since we have assumed that the complex is symmetrical, only half of its decomposition processes lead to transfer of the hydrogen atom to a new site. The rate constant for such transfers is given by

$$k_1 = k_{12}/2 \quad (6)$$

The preceding description involves two independent rate constants. Both are accessible to measurement since line shapes for two kinds of protons may be observed. The protons in R are subject to the effects which accompany both the formation of the intermediate complex and subsequent transfer of the hydrogen atom. The spectrum of the proton which is transferred is affected only by the formation of the intermediates and by any difference in magnetic environment in its initial and final sites. Such differences could be associated only with spin-spin couplings between the nuclei in R and the hydroxylic proton and are undetectable in the systems which we have investigated.

In cases to be reported the dominant effect arises from the secular perturbations associated with isotropic hyperfine interactions. Since the theory of line broadening for the cases of interest have already been adequately treated in the literature,<sup>2</sup> we shall simply summarize the results.

Suppose that nuclei of spin  $1/2$  yield a narrow resonance line. When they undergo occasional excursions of short duration into a paramagnetic environment, the lines are broadened with Lorentzian shape. The expression for the broadening is

$$\frac{1}{T_2} = \frac{1}{T} \left[ 1 - \cos \frac{at}{2} \right] \quad (7)$$

where  $1/T_2$  is the contribution to the line breadths (in radians per second) from the chemical process,  $1/T$  is the

(2) (a) H. M. McConnell and S. B. Berger, *J. Chem. Phys.*, **27**, 230 (1957); (b) C. S. Johnson, *ibid.*, **39**, 2111 (1963).

mean frequency of entering the paramagnetic state,  $t$  is the duration of paramagnetic state, and  $a$  is the hyperfine coupling constant. If the durations have an exponential distribution, *i.e.*,  $p(t) = \exp(-t/\tau)$  where  $p(t)$  is the probability of surviving for time  $t$ , the expression for the broadening becomes

$$\frac{1}{T_2} = \frac{1}{T} \left[ \frac{\left[ \frac{a}{2\tau} \right]^2}{1 + \left[ \frac{a}{2\tau} \right]^2} \right] \quad (8)$$

The assumptions, in addition to those already stated, are that  $a$  remains constant in the paramagnetic complex, the probabilities of entering into two paramagnetic states,  $M_s = \pm 1/2$ , are equal, the electron spin lattice relaxation time is long compared with  $t$ , and the off-diagonal contributions of the hyperfine interaction are negligible. As we shall see when we present the experimental data, the assumptions are well fulfilled in our cases.

The rate constants in (4) and the parameters in (7) are related by

$$\begin{aligned} 1/\tau &= k_{21} \\ 1/T &= k_{12}(\text{RO}\cdot) \end{aligned} \quad (9)$$

Equation 8 will now be rewritten to yield the line breadth as a function of rate constants and concentrations.

We distinguish the hydroxyl protons whose resonance is perturbed only by formation of the intermediate,  $\text{ROH}\dot{\text{O}}\text{R}$ , and the protons in R whose spectrum is perturbed both by events in which the intermediate is formed and decomposes to give the original reactants and by the events in which the intermediate is formed and decomposes to exchanged products.

$$\frac{1}{T_{2(\text{OH})}} = k_{12}(\text{RO}\cdot) \left\{ \frac{(a_{\text{OH}})^2}{4(k_{21})^2 + (a_{\text{OH}})^2} \right\} \quad (10)$$

$$\frac{1}{T_{2(\text{R})}} = \frac{k_{12}(\text{RO}\cdot)}{2} \left\{ \frac{(a_{\text{R}})^2}{4(k_{21})^2 + (a_{\text{R}})^2} + 1 \right\} \quad (11)$$

Equation 11 includes the assumption that the probabilities for decomposition of the intermediate into exchanged and nonexchanged products are each 0.5.

The processes involved in eq 10 and 11 may be represented by approximate plots of magnetic field against time. Figure 1 represents the excursion of magnetic field arising from the two types of events.

A source of line broadening which has not yet been considered arises from the reduction of the proton relaxation time by the nucleus-electron dipole-dipole interaction.<sup>3</sup> At 300°K the dipole-dipole contribution amounted to only a small fraction of the line breadth in most cases. We have assumed that the broadening of the tetramethylsilane line gave an approximation of the dipolar broadening and have corrected our data by subtracting its breadth from the total line breadth of the other resonances.

## Experimental Procedures

**A. Samples and Their Preparation.** The hydroxylic compounds whose exchange with the corresponding oxy radicals has been

(3) H. S. Gutowsky and J. C. Tai, *J. Chem. Phys.*, **39**, 208 (1963); N. Bloembergen, E. M. Purcell, and R. V. Pound, *Phys. Rev.*, **73**, 679 (1948).

studied are (I) 2,4,6-tri-*t*-butylphenol, (II) 2,6,2',6'-tetra-*t*-butylindophenol, (III) 2,6,2',6'-tetra-*t*-butylindophenol-*O-d*, (IV) diphenylhydroxylamine, (IVa) 4,4'-dinitrodiphenylhydroxylamine, (V) di-*t*-butylhydroxylamine, (VI) *t*-butyl-2,6-dimethoxyphenylhydroxylamine, and (VII) *t*-butyl-2,6-dimethoxyphenylhydroxylamine-*O-d*.

Tri-*t*-butylphenol was obtained from the Aldrich Chemical Co., recrystallized from absolute alcohol, and finally vacuum sublimed.

Samples were prepared on the vacuum line. The phenoxy radical was formed by oxidation with lead dioxide. Its concentration was determined spectrophotometrically; Cook's extinction coefficients<sup>4</sup> were used.

Tetra-*t*-butylindophenol was obtained from several sources: a gift from Dr. G. Coppinger and samples prepared by R. Krellick and by T. Bauman and E. Zaetsch. No differences in behavior of the various samples was noted. The deuterated compound (III) was prepared by Merck Sharpe and Dohme by repeated recrystallizations from CH<sub>3</sub>OD. Combustion analysis and nmr spectroscopy indicated at least 90 mole % of the hydroxyl hydrogen had been substituted by deuterium.

The tetra-*t*-butylindophenoxy radical was stable enough in air so that it was not necessary to perform all operations on the vacuum line. The solid radical was obtained by oxidation with lead dioxide and subsequent recrystallization from isooctane under nitrogen. The extinction coefficient was determined in solutions which were prepared from weighed samples of the radical. Our value for the molar extinction coefficient of the radical at 454 m $\mu$  is  $(1.8 \pm 0.1) \times 10^4 M^{-1} \text{ cm}^{-1}$ . Subsequent radical concentrations for nmr experiments were determined spectrophotometrically.

Diphenylhydroxylamine, 4,4'-dinitrodiphenylhydroxylamine, and their nitroxide radicals were prepared by the procedure of Wieland and Roth.<sup>5</sup>

Di-*t*-butylhydroxylamine hydrochloride, di-*t*-butyl nitroxide, *t*-butyl-2,6-dimethoxyphenylhydroxylamine and its nitroxide were provided by Dr. A. K. Hoffman.

The latter two compounds were recrystallized several times from cyclohexane. The di-*t*-butylhydroxylamine hydrochloride was converted to the hydroxylamine by extraction into the appropriate solvent from alkaline aqueous solutions.

Compound VII was prepared by Merck Sharp and Dohme by repeated recrystallization from CH<sub>3</sub>OD. It was analyzed by infrared spectroscopy and combustion analysis. The deuterium content in the hydroxyl position was greater than 90%.

**B. Solvents.** Carbon tetrachloride, chlorobenzene, and cyclohexane were distilled, dried, and stored over Linde 4A molecular sieves. When it was necessary to exclude oxygen, the solvent were distilled in the vacuum line directly from their storage bottles into the appropriate apparatus.

**C. Nmr Measurements.** The nmr measurements were carried out with a Varian HR-60 spectrometer (operating at 56.4 Mc). Sweep calibrations were made by the conventional side-band counter technique. Line broadenings were obtained by subtracting the natural line width and the broadening of the tetramethylsilane line from the total line width of the appropriate line. The measurement of the broadening of the ring lines of II and III, where overlapping occurred, was accomplished by construction of the appropriate superposition spectra and comparison with the observed ones.

## Results

**A. Phenol-Phenoxy Systems.** The exchange reaction involving these substances exhibit the behavior suggested by eq 10 and 11. Solutions of the pure phenols have well-resolved nmr spectra with lines at  $\tau_{\text{ring}}$  2.80,  $\tau_{\text{OH}}$  5.03,  $\tau_{o-t\text{-butyl}}$  8.54, and  $\tau_{p-t\text{-butyl}}$  8.71 for the tri-*t*-butylphenol. The nmr spectrum of the indophenol consists of three lines from the *t*-butyl protons (intensity ratio 1:1:2) at  $\tau$  8.74, 8.66, and 8.52, the hydroxyl line at  $\tau$  4.68, and the quinonimine and aromatic ring protons at  $\tau$  3.09 and 2.85, respectively. The nonequivalence of the *t*-butyl protons is probably associated with a bent molecular structure.

(4) C. D. Cook and B. E. Norcross, *J. Am. Chem. Soc.*, **81**, 1176 (1959).

(5) H. Wieland and K. Roth, *Ber.*, **53**, 216 (1920).

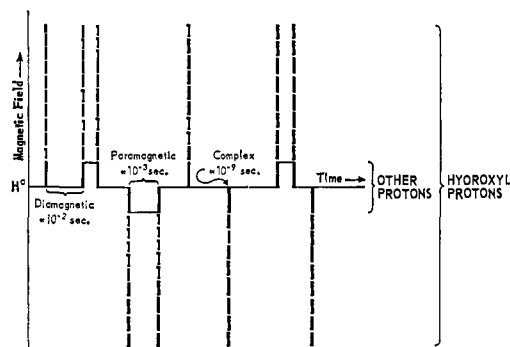


Figure 1. Time variation of the magnetic field at the hydroxyl (dashed lines) and nonhydroxyl protons (solid lines).

The esr spectrum of the phenoxy radical of I exhibits resolved splittings of 0.064 gauss from the *t*-butyl protons in addition to the splitting reported by Atherton.<sup>6</sup>

The esr spectrum of the radical of II shows a splitting from the four ring protons and the nitrogen.<sup>7</sup>

Addition of the phenoxy radicals produces equal broadenings of the ring and *t*-butyl lines and a different broadening of the OH line. At high temperatures (300°K) the latter is the narrowest line in the spectrum.

With decreasing temperature, at a constant concentration of radical, the OH line becomes broader and the ring and *t*-butyl lines narrower. At each temperature the broadenings are proportional to the concentration of radical and independent of the concentration of phenol. These observations are consistent with the exchange reaction outlined in the introduction. The line breadth of the OH protons resonance is determined by both  $k_{12}$  and  $k_{21}$  (eq 10). An increase of  $k_{12}$  leads to broadening, while an increase of  $k_{21}$  leads to narrowing. Since the dependence on  $k_{12}$  is linear and on  $k_{21}$  approximately quadratic, the OH resonance will broaden with decreasing temperature if the activation energies for  $k_{12}$  and  $k_{21}$  are approximately equal. The breadths of the ring and *t*-butyl lines are linear in  $k_{12}$  and are expected to decrease with decreasing temperature. The temperature dependence of the line broadening of II in carbon tetrachloride is given in Figure 2.

The ratio of the hydroxyl and ring line broadenings is limited by the relative number of complexes which decompose into exchanged products. If the probability of decomposition into exchanged products is 0.5, the maximum value of the ratio of broadenings is 2. In some cases, the broadening of the hydroxyl line was more than a factor of 2 greater than that of the ring and *t*-butyl lines. Unfortunately, because of large dipolar broadenings at low temperatures, the errors in our measurements are appreciable. We are, therefore, unable to say how good our estimate of the decomposition probabilities are. The rate constant for hydrogen atom exchange,  $k_1$  (eq 6), is unaffected by this estimate.

Determination of  $k_{12}$  from the broadening of the ring lines is simple because the first term in the brackets of eq 11 is negligible compared with unity. Equation 11 then reduces to the familiar form

$$\frac{1}{T_{2(R)}} = \frac{k_{12}[\text{RO}\cdot]}{2} \quad (12)$$

(6) N. Atherton, E. Land, and G. Porter, *Trans. Faraday Soc.*, **59**, 818 (1963).

(7) C. Coppinger, *Tetrahedron*, **18**, 61 (1962).

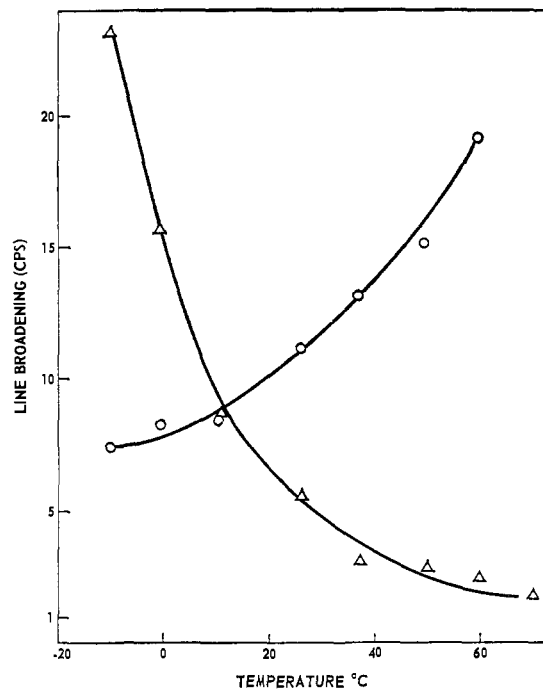


Figure 2. Temperature dependence of the tri-*t*-butylphenol line broadening ( $\text{CCl}_4$ );  $\Delta$ , hydroxyl line;  $\circ$ , ring line.

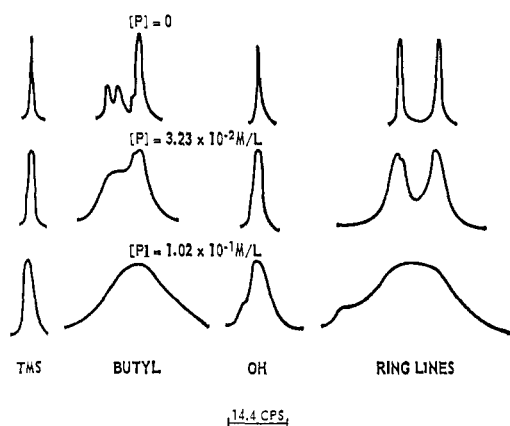


Figure 3. Tetra-*t*-butylindophenol line broadening at different radical concentrations ( $\text{CCl}_4$ ).

Under these conditions eq 10 becomes

$$\frac{1}{T_{2(\text{OH})}} = \frac{2}{T_{2(\text{R})}} \frac{\left(\frac{a_{\text{OH}}}{2}\right)^2}{(k_{21})^2 + \left(\frac{a_{\text{OH}}}{2}\right)^2} \quad (13)$$

Evaluation of  $k_{21}$  from the line broadenings requires an estimate of  $a_{\text{OH}}$ . We expect that  $a_{\text{OH}}$  will be less than the splitting of the hydroxyl radical in ice (102 Mc)<sup>8</sup> and greater than 4.75 Mc. The latter statement follows from the observation that at low temperatures the broadening of the OH resonance is sometimes greater than that of the ring lines. Some evidence bearing on the magnitude of  $a_{\text{OH}}$  is found in the splitting by the NH proton in the tri-*t*-butylaniline radical<sup>5</sup> ( $a_{\text{N-H}} = 33.6$  Mc) and in the  $\text{O}^{17}$  splitting in the tri-*t*-butylphenoxy radical.<sup>9</sup>

(8) H. E. Radford, *Phys. Rev.*, **122**, 114 (1961).

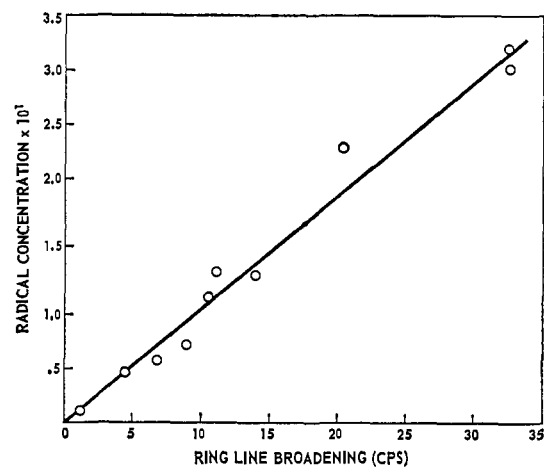


Figure 4. Line broadening of the tri-*t*-butylphenol ring protons vs. tri-*t*-butylphenoxy concentration ( $\text{CCl}_4$  at ca. 27°).

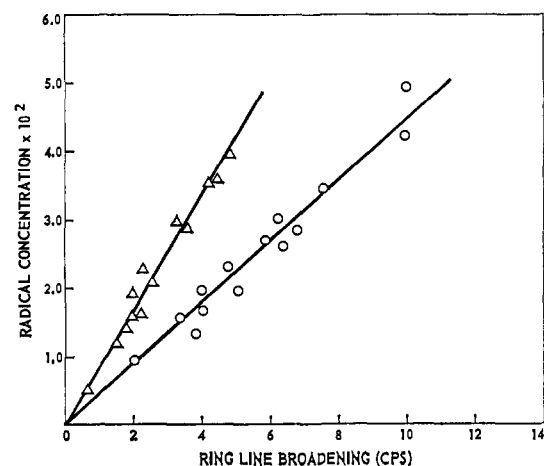


Figure 5. Ring proton line broadening vs. tetra-*t*-butylindophenoxy concentration ( $\text{CCl}_4$  at ca. 27°):  $\circ$ , tetra-*t*-butylindophenol;  $\Delta$ , tetra-*t*-butylindophenol-*O-d*.

In the absence of more direct knowledge we have chosen  $a_{\text{OH}} = 5 \times 10^7$  cps. Many of our conclusions are not very sensitive to the value of  $a_{\text{OH}}$ .

Another assumption in our treatment of the data is that  $a_{\text{OH}}$  is independent of temperature. An error may be introduced into our estimates of the activation parameters for  $k_{21}$  by this assumption.

A typical set of spectra showing the relative line broadenings is given in Figure 3. Dependence of  $1/T_{2(\text{R})}$  on concentration of radical for several experiments are given in Figures 4 and 5. Representative plots of the dependence of  $k_{12}$  and  $k_{21}$  on temperature are given in Figures 6 and 7.

The exchange of the deuterated indophenol (III) with the phenoxy radical yields  $k_{12}$  only.  $k_{21}$  could be obtained from the deuterium resonance but we have not carried these experiments out. Data for the deuterium exchange are included in Figure 5 and the temperature dependence of  $k_{12}$  in Figure 6.

The comparison between the protonated and deuterated indophenols was made by mixing the phenols with two portions of the same radical solution and immediate recording of the spectra. Since the prin-

(9) A. Rieker and K. Scheffler, *Tetrahedron Letters*, **19**, 1337 (1965).

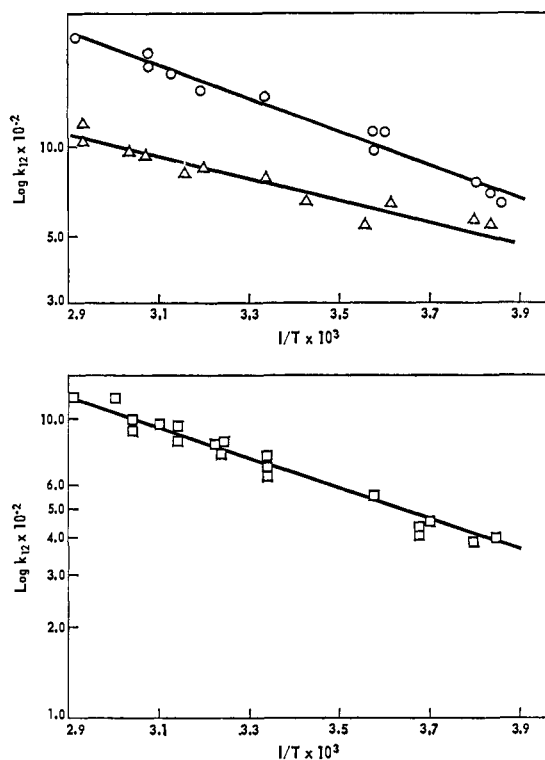


Figure 6.  $\text{Log } k_{12}$  vs.  $1/T$  ( $\text{CCl}_4$ ):  $\circ$ , tetra-*t*-butylindophenol;  $\Delta$ , tetra-*t*-butylindophenol-*O-d*;  $\square$ , tri-*t*-butylphenol.

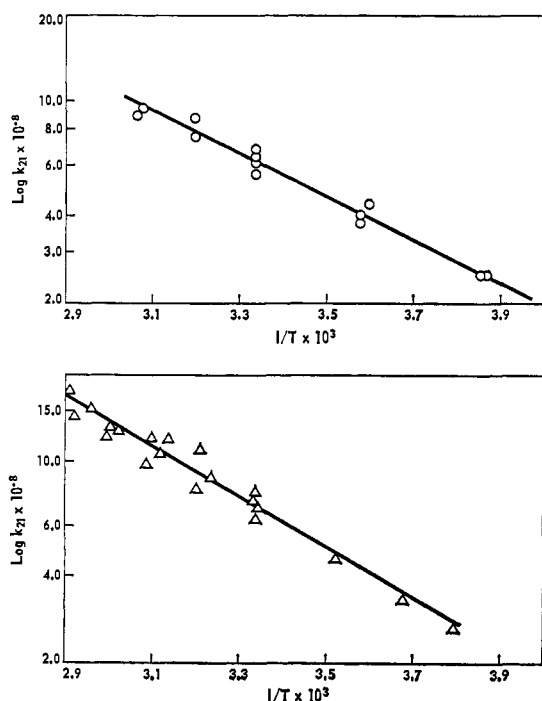


Figure 7.  $\text{Log } k_{21}$  vs.  $1/T$  ( $\text{CCl}_4$ ):  $\circ$ , tetra-*t*-butylindophenol;  $\Delta$ , tri-*t*-butylphenol.

cial uncertainty in determination of the absolute values of  $k_{12}$  is the radical concentration, the ratio  $k_{12(\text{H})}/k_{12(\text{D})}$  determined by the above procedure is probably more reliable than the individual rate constants. At 300°K for the indophenol system in carbon tetrachloride  $k_{\text{OH}}/k_{\text{OD}} = 1.77$ .

From the temperature dependence of the rate constants we have determined the activation parameters for

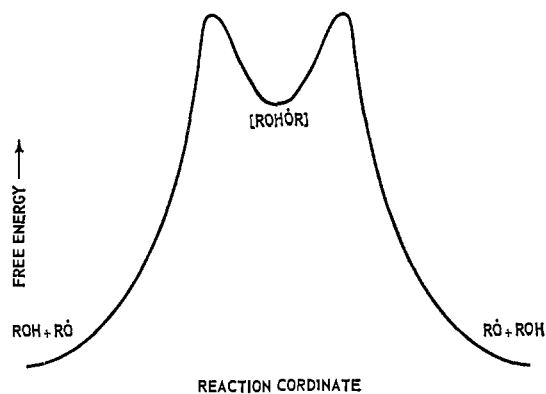


Figure 8. Reaction coordinate for hydrogen atom exchange in phenolic systems.

the formation of the complex from the reactants. These data are found in Table I along with values of the equilibrium constant at 300°K. The dependence of the free energy on the reaction coordinate is shown in Figure 8. The slowness of the reactions as well as the low equilibrium constant for formation of the intermediates are accounted for by the large negative entropies of activation necessary for formation of the intermediate. These are accounted for by the steric effects of the *t*-butyl groups.

**B. Hydroxylamine-Nitroxide Systems.** Only a lower limit for the rate constant for the exchange between IV and its nitroxide could be obtained. Because of a disproportionation reaction,<sup>10</sup> the hydroxylamine is always contaminated with sufficient radicals to produce a large broadening of the nmr lines. The reaction is rapid enough to be observed by broadening of the esr lines of the radicals. Because of difficulties in determinations of concentrations, quantitative measurements were not made. At 300°K in  $\text{CCl}_4$   $k_{12} > 10^7 \text{ M}^{-1} \text{ sec}^{-1}$ . In a qualitative observation it was found that the exchange between 4,4'-dinitrodiphenylhydroxylamine and its nitroxide is slower than that of diphenyl compound by at least two orders of magnitude.

Exchange rates between hydroxylamines V and VI and their respective nitroxides in carbon tetrachloride or chlorobenzene are in a convenient range for measurements by nmr. Because of broadening of the OH lines, probably by spin-spin interaction with the nitrogen nucleus which in turn relaxes through its quadrupole moment, it was not possible to measure  $k_{21}$ .

Although the proton hyperfine splitting in the esr of the nitroxide of V is only partially resolved, eq 11 remains applicable. This is shown by the observation that the line breadth is independent of hydroxylamine concentration. The nmr spectrum of V consists of a single line at  $\tau$  8.77. Plots of the dependence of broadening on radical concentration in carbon tetrachloride and chlorobenzene solutions are given in Figure 9. The temperature dependence of the line broadening is given in Figure 10.

The esr spectrum of the nitroxide radical of VI consists of three groups of 13 lines. The major splitting of 13.22 gauss is assigned to  $\text{N}^{14}$  and the smaller splittings to ring and methoxy protons. The nmr line of the methoxy protons (3.7 ppm) was used in the rate de-

(10) K. H. Meyer and W. Reppe, *Ber.*, **54**, 327 (1921).

**Table I.** Thermodynamic Parameters for Phenolic Exchange Reactions<sup>a</sup>

| Compound                                     | $\Delta F^\circ$ | $\Delta H_{12}^*$ | $\Delta H_{21}^{*b}$ | $\Delta H^{ob}$ | $\Delta S_{12}^*$ , eu | $\Delta S^\circ$ , eu | $K$ , $M^{-1}$                 |
|--|------------------|-------------------|----------------------|-----------------|------------------------|-----------------------|--------------------------------|
| Tri- <i>t</i> -butylphenol                   | $8.4 \pm 0.2$    | $1.2 \pm 0.6$     | $3.6 \pm 0.4$        | $-2.3 \pm 1.0$  | $-43.4 \pm 1.6$        | $-35.0 \pm 3.0$       | $(9.3 \pm 3.6) \times 10^{-7}$ |
| Tetra- <i>t</i> -butylindophenol             | $7.8 \pm 0.2$    | $2.1 \pm 0.3$     | $2.8 \pm 0.2$        | $-0.65 \pm 0.2$ | $-37.5 \pm 1.0$        | $-28.4 \pm 1.0$       | $(1.7 \pm 0.3) \times 10^{-6}$ |
| Tetra- <i>t</i> -butylindophenol-O- <i>d</i> | ...              | $1.4 \pm 0.2$     | ...                  | ...             | $-36.7 \pm 0.5$        | ...                   | ...                            |

<sup>a</sup>  $CCl_4$  solvent. <sup>b</sup> In kcal/mole.

terminations, since their broadening followed eq 11. The broadening of the *t*-butyl nmr line in this case did not obey eq 11. The broadening is smaller than that of the methoxy line and depends on the concentration of

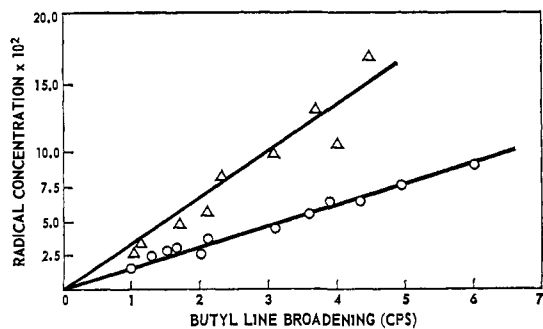


Figure 9. Line broadening of the di-*t*-butylhydroxylamine *t*-butyl protons vs. di-*t*-butyl nitroxide concentration (ca. 27°): Δ, in chlorobenzene; ○, in carbon tetrachloride.

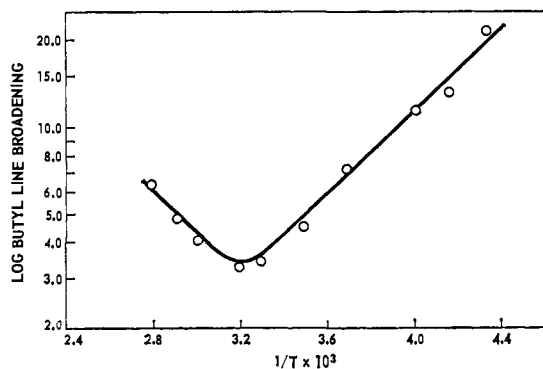
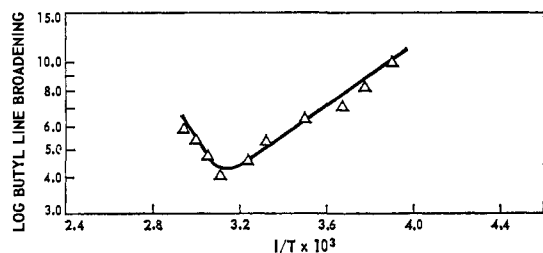


Figure 10. Log butyl line broadening vs.  $1/T$ : Δ, di-*t*-butylhydroxylamine in  $CCl_4$ ; ○, di-*t*-butylhydroxylamine in chlorobenzene.

VI. These observations indicate that the *t*-butyl proton hyperfine coupling constant in the nitroxide of VI is considerably less than that of the methoxy protons.

The dependence of the line broadening of compounds VI and VIII on radical concentration is shown in

Figures 11 and 12. Temperature dependences are shown in Figures 13 and 14.

The rates for the exchanges involving compounds V, VI, and VII were strongly dependent on solvent. Thus, the rate of exchange at 300°K between VI and its radical is five times faster in carbon tetrachloride than

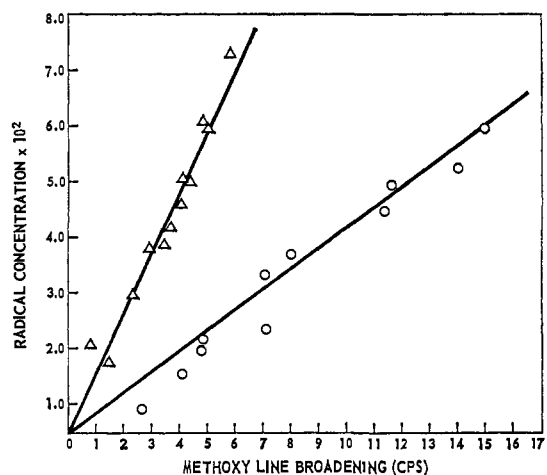


Figure 11. Line broadening of the *t*-butyl-2,6-dimethoxyphenylhydroxylamine methoxy protons vs. *t*-butyl-2,6-dimethoxyphenyl nitroxide concentration (ca. 27°): Δ, in chlorobenzene; ○, in  $CCl_4$ .

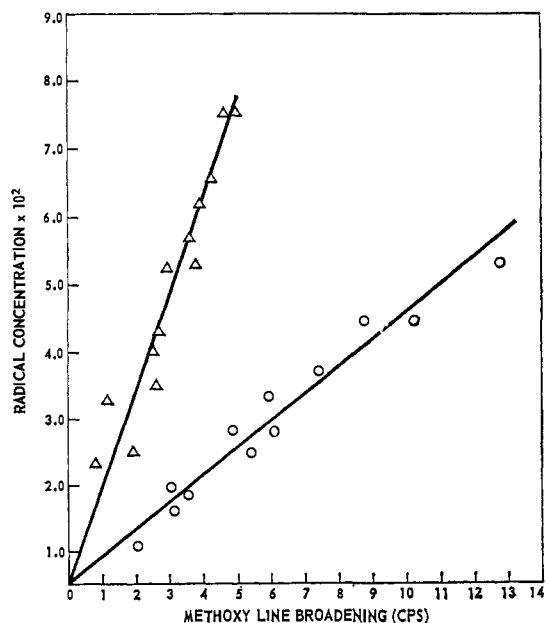


Figure 12. Line broadening of the *t*-butyl-2,6-dimethoxyphenylhydroxylamine-O-*d* methoxy protons vs. *t*-butyl-2,6-dimethoxyphenyl nitroxide concentration (ca. 27°): Δ, in chlorobenzene; ○, in  $CCl_4$ .

Table II. Rate Constants for the Various Exchange Reactions at 27°

| System   | Solvent                                 | $k_{12}, M^{-1} \text{sec}^{-1}$ | $k_{21}, \text{sec}^{-1}$   |
|--|---|----------------------------------|-----------------------------|
| Tri- <i>t</i> -butylphenol                                   | CCl <sub>4</sub>                        | $(6.6 \pm 1.0) \times 10^2$      | $(6.7 \pm 1.2) \times 10^8$ |
| Tetra- <i>t</i> -butylindophenol                             | CCl <sub>4</sub>                        | $(1.4 \pm 0.3) \times 10^8$      | $(8.3 \pm 0.4) \times 10^8$ |
| Tetra- <i>t</i> -butylindophenol-O- <i>d</i>                 | CCl <sub>4</sub>                        | $(7.8 \pm 0.6) \times 10^2$      | ...                         |
| Tetra- <i>t</i> -butylindophenol                             | Cyclohexane                             | $(2.2 \pm 0.6) \times 10^8$      | $(1.1 \pm 0.2) \times 10^9$ |
| Diphenylhydroxylamine  | CCl <sub>4</sub>                        | $>10^7$                          | ...                         |
| Di- <i>t</i> -butylhydroxylamine                             | CCl <sub>4</sub>                        | $(3.2 \pm 0.4) \times 10^2$      | ...                         |
| Di- <i>t</i> -butylhydroxylamine                             | Chlorobenzene                           | $(2.4 \pm 0.6) \times 10^2$      | ...                         |
| <i>t</i> -Butyl-2,6-dimethoxyphenylhydroxylamine             | CCl <sub>4</sub>                        | $(2.0 \pm 0.4) \times 10^3$      | ...                         |
|  | Chlorobenzene                           | $(5.2 \pm 0.4) \times 10^2$      | ...                         |
|  | Acetone, chloroform, methylene chloride | $<20$                            | ...                         |
| <i>t</i> -Butyl-2,6-dimethoxyphenylhydroxylamine-O- <i>d</i> | CCl <sub>4</sub>                        | $(1.3 \pm 0.2) \times 10^3$      | ...                         |

in chlorobenzene. The exchanges in methylene chloride, chloroform, and acetone were too slow for measurement ( $k < 20 M^{-1} \text{sec}^{-1}$ ).

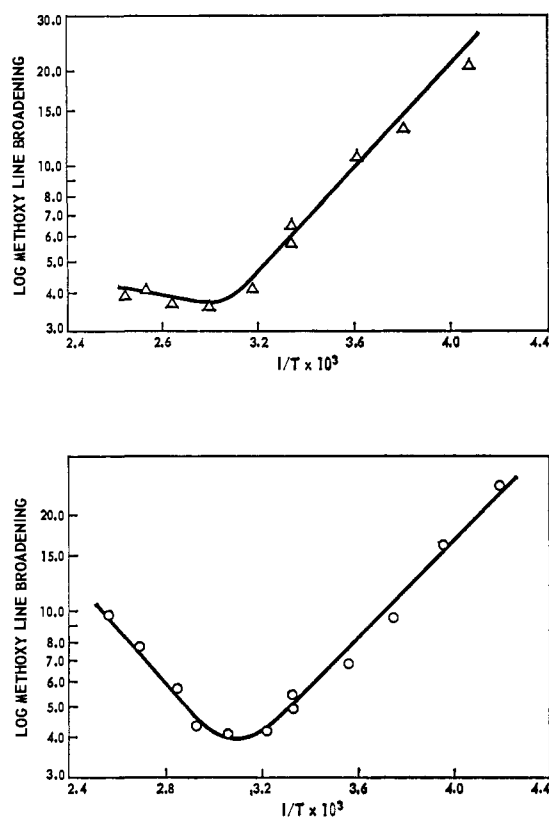


Figure 13. Log methoxy line broadening vs.  $1/T$ : ○, *t*-butyl-2,6-dimethoxyphenylhydroxylamine in chlorobenzene; Δ, *t*-butyl-2,6-dimethoxyphenylhydroxylamine-O-*d* in chlorobenzene.

It can be seen from Figures 11 and 12 that at 300°K, substitution of deuterium for protium in the hydroxyl position has no measurable effect on the rate. At temperatures above 320°K  $k_{\text{OH}}/k_{\text{OD}} > 1$ , and the ratio increases with increasing temperature.

### Discussion

In both phenol-phenoxy systems which have been investigated, intermediates with lifetime of the order of  $10^{-9}$  sec are involved in the hydrogen atom transfer.

The activation parameters correspond, not to the over-all hydrogen transfer, but to the formation and decomposition of the intermediate. The small kinetic isotope effects require, in the language of transition state theory, that the transferring hydrogen is either unsymmetrically bound or has acquired high frequency bending modes in the transition state. The intermediate whose existence our experiments demonstrates is, of course, a *bona fide* chemical species with lifetime much longer than ordinary vibrational periods.

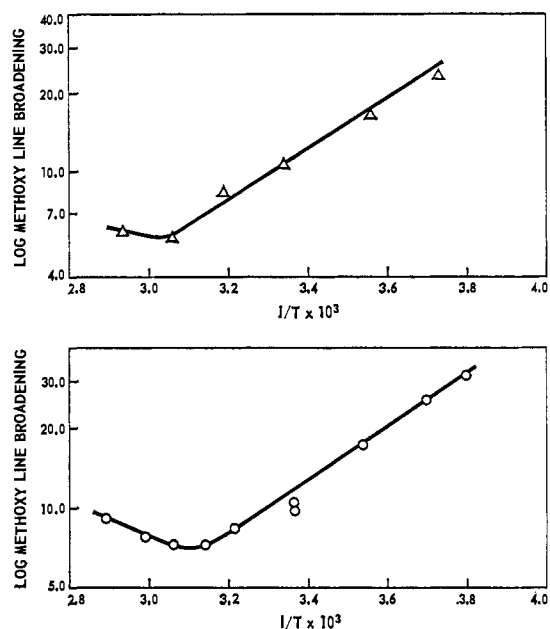


Figure 14. Log methoxy line broadening vs.  $1/T$ : ○, *t*-butyl-2,6-dimethoxyphenylhydroxylamine in CCl<sub>4</sub>; Δ, *t*-butyl-2,6-dimethoxyphenylhydroxylamine-O-*d* in CCl<sub>4</sub>.

Our data yield  $k_{12(\text{OH})}/k_{12(\text{OD})}$  and  $E^*_{\text{OH}} - E^*_{\text{OD}}$  for exchange between the indophenol and indophenoxy radical. These results are not compatible with a normal interpretation of kinetic isotope effects. However, although we believe that the ratio of the rate constants at room temperature is reliable, we feel that the activation energies are subject to errors of at least 1 kcal. This error arose because of the decomposition of the radical during the prolonged periods required for

measurements over a wide range of temperatures. In view of these errors no speculation based on the difference would appear to be warranted. We note that our data provide  $\Delta H^\circ$ ,  $\Delta S^\circ$ ,  $\Delta F^\circ$ , and  $K$  for formation of the complex. These values are listed in Table I. The thermodynamic quantities are compatible with a loose complex between highly hindered species. A summary of the various rate constants is given in Table II.

The most striking feature of the hydroxylamine-nitroxide exchanges is the temperature dependence of the rate. It is possible to account for this anomalous temperature dependence by a model in which the exchange reaction can proceed by two or more paths with different temperature dependences.

At high temperatures where the rate increases with increasing temperature  $k_{\text{OH}}/k_{\text{OD}}$  is greater than 1 and increases with increasing temperature. In the region of anomalous temperature dependence  $k_{\text{OH}}/k_{\text{OD}} = 1$ . If a two-path model is adopted, the predominant high-

temperature path would be one which has a normal isotope effect and the low temperature one with no isotope effect.

### Conclusion

Our conclusions appear to be meager relative to the amount of experimental information which has been obtained. The work illustrates the possibility of finding short-lived intermediates by magnetic resonance methods. It demonstrates how complex an apparently simple reaction, the transfer of a hydrogen atom, can be. With further work the conclusions may approach the richness of the experimental information.

**Acknowledgments.** We wish to thank Drs. A. K. Hoffman and G. Coppinger who kindly supplied some of the samples used in our experiments. This research has been supported by the National Science Foundation under GP 2676 and by the National Institutes of Health under GM 13205.

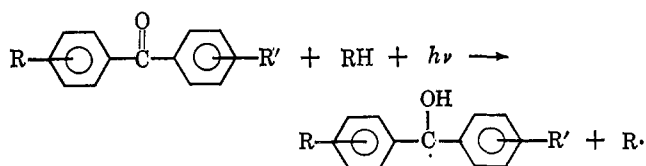
## Reactivity of Excited States. Intramolecular Hydrogen Atom Abstraction in Substituted Butyrophenones<sup>1a</sup>

E. J. Baum, J. K. S. Wan, and J. N. Pitts, Jr.<sup>1b</sup>

*Contribution from the Department of Chemistry, University of California, Riverside, California. Received December 9, 1965*

**Abstract:** The quantum efficiency of photocycloelimination of ethylene ("type II process"),  $\phi_{\text{II}}$ , from butyrophenone and several *para*-substituted derivatives is highly sensitive to the electron-donating character of the substituent and to the nature of the lowest triplet state. Thus at 3130 Å, 25°, and in several solvents,  $\phi_{\text{II}}$  drops from 0.42 and 0.39 in butyrophenone and *p*-methylbutyrophenone, respectively, to 0.00 in the *p*-NH<sub>2</sub>, *p*-OH, and *p*-C<sub>6</sub>H<sub>5</sub> derivatives. Energy-transfer and spectroscopic studies indicate that the photoreaction proceeds from the lowest triplet state of these ketones and that this state is (n,π\*) for reactive and (π,π\*) for unreactive ketones. *p*-Bromo- and *o*-hydroxybutyrophenone do not undergo photocycloelimination. The former eliminates bromine atoms with a quantum yield of 0.25. The latter photoenolizes in a reaction similar to that observed for *o*-hydroxy- and *o*-methylbenzophenone. The photocycloelimination reaction is temperature dependent with an activation energy of about 2 kcal/mole for butyrophenone.

Recent studies concerning the photochemical reactivity of aryl ketones and their ring-substituted derivatives toward *intermolecular* hydrogen atom abstraction, giving ketyl radicals and ultimately pinacol formation, have greatly expanded our knowledge of the



effect of substituents on the reactivity and low-lying excited-state structure of these compounds.<sup>2-8</sup>

(1) (a) Presented in part at the Symposium on "Structure and Photochemistry of Excited States," 149th National Meeting of the American Chemical Society, Detroit, Mich., April 1964, p7S; and the IVth International Congress on Photobiology, Oxford, July 1964; (b) author to whom inquiries concerning this paper should be sent.

(2) J. N. Pitts, Jr., L. D. Hess, E. J. Baum, E. A. Schuck, J. K. S. Wan, P. A. Leermakers, and G. Vesley, *Photochem. Photobiol.*, **4**, 305 (1965).

It is now recognized that the introduction of substituent groups into the aromatic rings of benzophenone, for instance, can drastically alter the *intermolecular* hydrogen atom abstracting ability of the carbonyl group. Two substituent effects have been established, one related to *ortho* substitution and one related to *para* substitution. The *ortho* effect involves formation of a transient six-membered ring followed by transfer of a hydrogen atom from the *ortho* group to the oxygen atom of the carbonyl chromophore, to form what Yang has classified as a photoenol.<sup>7-9</sup> This process is reversible and no net photochemistry results.

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