culated), presumably because of extreme electrostatic disfavoring of the incipient cumyl cation resonance form that has its positive charge on the *para* carbon. Use of this extreme 0.408 value gave an $\mathcal{R}$ set differing from the one above by having the following order (including some inversions compared to Table I): $F << Cl < Br \sim I < H \sim COO^-$ (0.04) $< S(CH_3)_2^+$ (+0.21) $< COOH$ (+0.27) $< CN < NO_2$. Although the halogen, cyano, and nitro parts seemed possible, we rejected this because we considered it unreasonable for $S(CH_3)_2^+$ to have such a positive $\mathcal{R}$ value, or for COO^- to be so different in its resonance capability from COOH. Also this use of mixed data (experimental where it exists, calculated otherwise) for σ' and σ_p^+ seemed less defensible than use of calculated throughout, and with calculated throughout the results are equivalent to those above ignoring σ_p^+ completely. Finally, the greater abundance and accuracy of pK_A measurements than of kinetic σ_p^+ data make σ_m, σ_p, and σ' more attractive as basis sets.

The use of experimental σ_p^- values in this way that we initially used σ_p^+ values was not attempted, because only 18 experimental values are available, and they represent a wider range of investigators, reactions, and solvents.

Significance of the Results. The correlation coefficients for linear correlation of the 21 natural reaction series *vs.* the field substituent constant $\mathcal{F}$ and the resonance substituent constant $\mathcal{R}$ as independent variables are so high that it appears practicable to drop the use of about 20 other synthetic hybrid σ sets, which are less pure field or resonance measures.

Correlation is not significantly improved by including both σ_p^+ and σ_p^- (in addition to $\mathcal{F}$); therefore, the use of two numbers to characterize the resonance effect, one to represent electron-donating ability and the other to represent electron-attracting ability, is a dubious improvement over characterization of resonance capabilities by a single number ($\mathcal{R}$).

Accepting the assumptions made, one is led to conclude that the order of field constants ($\mathcal{F}$ values) for 13 typical substituents is $COO^- < t\text{-Bu} < Me < H < NH_2 < C_6H_5 < OCH_3 \sim NHAc < COOH < Cl \sim F < NO_2 < N(CH_3)_3^+$ and that the order of resonance constants ($\mathcal{R}$ values) is $NH_2 < OCH_3 < F < NHAc < Cl < CH_3 < t\text{-Bu} < C_6H_5 < H \sim N(CH_3)_3^+ < COO^- \sim COOH \sim NO_2$. Field effects are not equal for *meta* and *para* locations of the same substituent. Resonance effects are significant with *meta* substituents. The average importance of resonance (±5%) is 0% in $\mathcal{F}$ or σ', 22% in σ_m, 53% in σ_p, 56% in σ_p^-, 66% in σ_p^+, 92% in $(\sigma_p - \sigma_m)$, and 100% in $\mathcal{R}$.

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The Influence of Tunneling on the Relation between Tritium and Deuterium Isotope Effects. The Exchange of 2-Nitropropane-2-*t*[1]

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Abstract: Tritium and deuterium isotope effects can be related by an equation derived by Swain and coworkers,[2] without consideration of tunneling. The influence of tunneling on this relationship is explored, with consideration of deviations predicted by some theoretical models. It is shown that conspicuous deviation will occur only under some rather restricted conditions, even when tunneling is quite extensive. Three examples in which tunneling has been believed to be important are subjected to this test. The oxidation of 1-phenyl-2,2,2-trifluoroethanol by alkaline permanganate gives a tritium isotope effect, $k_H/k_T = 57.1$, in close agreement with the value 55.5 calculated with the Swain equation from the previously measured deuterium isotope effect.[3] A very large isotope effect, $k_H/k_T = 82.9$, is calculated from the deuterium isotope effect for the proton transfer from 2-nitropropane to 2,4,6-trimethylpyridine,[4] and the experimental value, $k_H/k_T = 79.1$, is nearly as large. The oxidation of leuco crystal violet by chloranil[5] gives a calculated tritium isotope effect, $k_H/k_T = 27.3$, significantly greater than that found experimentally, $k_H k_T = 20.3$, and the discrepancy is reasonably concordant with that expected from the strong temperature dependence of the deuterium isotope effect. The rate of ionization of 2-nitropropane-2-*t* by 2,4,6-trimethylpyridine measured by exchange is less than that measured by iodination, unless allowance is made for the significantly slow exchange of the pyridinium ion with the aqueous *t*-butyl alcohol solvent.

The problem of tunneling in chemical reactions, although extensively discussed, is generally believed to be significant only in reactions for which the barrier is a restriction on the motion of a hydrogen atom, but it is not generally conceded that tunneling is always

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[1] Taken in part from the Ph.D. Thesis of J. K. Robinson, Rice University, 1966.

[2] C. G. Swain, E. C. Stivers, J. F. Reuwer, Jr., and L. J. Schaad, *J. Am. Chem. Soc.*, **80**, 5885 (1958).

[3] R. Stewart and R. van der Linden, *Discussions Faraday Soc.*, **29**, 211 (1960).

[4] E. S. Lewis and L. H. Funderburk, *J. Am. Chem. Soc.*, **89**, 2322 (1967); L. H. Funderburk and E. S. Lewis, *ibid.*, **86**, 2531 (1964).

[5] J. M. Perry, Ph.D. Thesis, Rice University, 1965.

important in these cases, nor is any estimate of the tunnel correction calculable without knowledge of some details of the potential energy surface in the neighborhood of the saddle point. Even with this information the calculation of the tunnel correction is generally difficult and not rigorously defensible. Nevertheless, since there is a relation between these otherwise experimentally inaccessible features of the potential energy surface and the tunnel correction, it is of substantial interest to try to establish the magnitude of the tunnel correction so as to work this calculation in reverse and calculate the shape of the potential energy surface from it, especially in reactions of complexity sufficient to make calculation of the entire surface out of the question.

The simplest way to correct for tunneling is to reduce the problem to the one dimension of the reaction coordinate. An early solution of this problem by Wigner[6] described the curvature at the top of the barrier in terms of the imaginary frequency[7] $i\nu^{\ddagger}$ and expressed the correction to multiply the classically calculated rate constant to obtain the true rate constant as eq 1. It should be noted that this separation into classical and real contributions is entirely artificial. Nevertheless we can hope that the tunnel correction can be as useful a concept as the equally unreal one of resonance

$$k = Qk_{\text{class}} \tag{1}$$

energy. Wigner's simplest expression is $Q = 1 + (^1/_{24})(h\nu^{\ddagger}/kT)^2$, also written as $1 + u^2/24$, where $u = h\nu^{\ddagger}/kT$. Bell has approximated the barrier as a truncated parabola, for mathematical convenience, and deduced expressions for Q for various values of u. The solution for $u < 2\pi$ is approximated very well by the expression 2 in which E is the barrier height.[8] Of these,

$$Q = \frac{u/2}{\sin u/2} - \frac{u}{2\pi - u}\exp[-(E/kT)(2\pi - u)/u] \tag{2}$$

only the first term is important for small u or large E/kT. We shall refer to the first term as the high-barrier approximation, and recall Bell's observation that when this is expanded for low u, the first terms are the same as Wigner's. The sharp truncation of Bell's barrier has been suspected of causing some artifacts, and the tunnel corrections for the smoother Eckhart barrier have been calculated. Johnston and Rapp[9] have published a convenient table of Q for different values of u and a parameter which depends in part on the barrier height. They conclude, however, that the one-dimensional barrier approximation is seldom adequate to account for the behavior and present a method of dealing with another dimension.

These varied treatments, none of which is generally applicable or convincingly rigorous, have some features in common. (1) $Q_{\text{H}} > Q_{\text{D}} > Q_{\text{T}} > 1$. (The subscripts refer to the three isotopes of hydrogen in an otherwise identical situation.) (2) Q falls with increasing temperature. (3) Q increases with $\nu_{\text{H}}^{\ddagger}$. Bell has shown that his treatment leads to deviations from the Arrhenius equation and in particular to $A_{\text{H}}^* < A_{\text{D}}^*$, where A^* is the apparent preexponential term of the Arrhenius equation, measured over too small a temperature range to reveal the curvature. Although some of the strong temperature dependence of Q appears to be an artifact of the sharp corners,[9] the experimental observation of $A_{\text{H}}^* < A_{\text{D}}^*$ has not been given any better explanation.[10]

An alternative criterion of tunneling might be found in the comparison of the rates of all three isotopes of hydrogen. When tunneling is neglected, a simple model for hydrogen isotope effects leads to eq 3, which was first derived by Swain, Stivers, Reuwer, and Schaad[2] and will be referred to hereafter as the Swain equation.

$$k_{\text{H}}/k_{\text{T}} = (k_{\text{H}}/k_{\text{D}})^{1.442} \tag{3}$$

Bigeleisen[11] has modified this derivation to include isotope effects on the preexponential factors, which were not neglected by Swain and his coworkers,[2] but are not here included in eq 3. He writes the general eq 4 and concludes that $1.58 \geqslant r \geqslant 1.33$. The upper limit of r is believed to apply to isotope effects which are temperature independent, and can only apply when $k_{\text{H}}/k_{\text{D}} \leq \sqrt{2}$, and the lower value applies to small isotope effects ($k_{\text{H}}/k_{\text{D}} < 2$), where the Wigner tunnel correction is the sole source of the isotope effect. We can normally expect the unmodified Swain equation to be quite good.

$$k_{\text{H}}/k_{\text{T}} = (k_{\text{H}}/k_{\text{D}})^r \tag{4}$$

Swain's treatment specifically ignores tunneling. We can separate the classical and tunneling effects by writing eq 5 and 6, in which the subscript class

$$k_{\text{H}}/k_{\text{D}} = (Q_{\text{H}}/Q_{\text{D}})(k_{\text{H}}/k_{\text{D}})_{\text{class}} \tag{5}$$

$$k_{\text{H}}/k_{\text{T}} = (Q_{\text{H}}/Q_{\text{T}})(k_{\text{H}}/k_{\text{T}})_{\text{class}} \tag{6}$$

refers to a (hypothetical) isotope effect in which tunneling plays no part. We can refer to the relation between the isotope effects now using eq 4, which is now experimentally determined and not necessarily bound by Bigeleisen's limits. It is reasonable to write eq 7

$$(k_{\text{H}}/k_{\text{T}})_{\text{class}} = (k_{\text{H}}/k_{\text{D}})_{\text{class}}{}^{1.442} \tag{7}$$

even if the real reaction has a large tunnel correction, and if we define an s by eq 8, which is not directly measurable, but presumably $\geqslant 1$, we can combine these and get eq 9, from which we can derive eq 10.

$$Q_{\text{H}}/Q_{\text{T}} = (Q_{\text{H}}/Q_{\text{D}})^s \tag{8}$$

$$k_{\text{H}}/k_{\text{T}} = (k_{\text{H}}/k_{\text{D}})_{\text{class}}{}^{1.442}(Q_{\text{H}}/Q_{\text{D}})^s \tag{9}$$

This equation can be solved for the unknowns s and $Q_{\text{H}}/Q_{\text{D}}$ only if we have some other relation between

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(6) E. Wigner, *Z. Physik. Chem.*, **19B**, 203 (1932).

(7) The notation $\nu^{\ddagger}$ used here should not be confused with the notation for any real vibration of the transition state often given this symbol. Here, $\nu^{\ddagger}$ is used instead of the synonymous ν_t of Bell (R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959), so that we can use the subscripts H, D, and T to indicate the isotopes without confusion. For the same reason we omit Bell's subscript on the tunnel correction Q.

(8) This equation appears with slightly different variables in Bell's primary paper (R. P. Bell, *Trans. Faraday Soc.*, **55**, 1 (1959)). In his book (ref 7, p 209, footnote 42) the above notation is used, but the term in the exponent containing the u is upside down. In the original paper, these are the first two terms of an infinite series, but the contributions of subsequent terms are quite negligible for everything in the present paper.

(9) H. S. Johnston and D. Rapp, *J. Am. Chem. Soc.*, **83**, 1 (1961).

(10) It is possible to account for $\sqrt{2} \geqslant A_{\text{H}}/A_{\text{D}} \geqslant 0.5$ with only classical behavior, so that only $A_{\text{H}}/A_{\text{D}} < 0.5$ is taken as evidence of tunneling. However, in quantitative treatment, the value $A_{\text{H}}/A_{\text{D}} = 1$ is usually assumed. The determination of Arrhenius preexponential factors is fraught with the possibility of experimental error. Nevertheless, there are now enough examples of $A_{\text{H}}/A_{\text{D}} < 0.5$, not accompanied by any of $A_{\text{H}}/A_{\text{D}} > 2$, to lend evidence to a claim for a nonrandom cause for the examples of $A_{\text{H}} < A_{\text{D}}$.

(11) J. Bigeleisen, "Tritium in the Physical and Biological Sciences," Vol. 1, International Atomic Energy Agency, Vienna, 1962, p 161.

$$r = \frac{\log (k_H/k_T)}{\log (k_H/k_D)} = 1.442 + \frac{(s - 1.442) \log (Q_H/Q_D)}{\log (k_H/k_D)} \quad (10)$$

them. We shall return to this question later, but first should point out some conditions for deviation from the Swain equation, *i.e.*, $r \neq 1.442$. If we restrict ourselves to reactions with normal classical isotope effects, $k_H/k_D > Q_H/Q_D > 1$, and r will lie between 1.442 and s. No significant deviation from the Swain equation will occur regardless of the magnitude of the tunnel correction unless s is significantly different from 1.442. Secondly, if s is different from 1.442, r will not reflect this importantly unless $\log (Q_H/Q_D)/\log (k_H/k_D)$ is not too much smaller than its upper limit, unity. This can be achieved only if the classical isotope effect, $(k_H/k_D)_{class}$, is quite close to unity, and the tunnel correction is large.[12]

Let us now see if any of the theoretical models will give us a relation between s and Q_H/Q_D suitable for solving eq 10. Let us make the first approximation that we can relate the imaginary frequencies of the three isotopes by the equations $\nu_H{}^{\ddagger} = \sqrt{2}\nu_D{}^{\ddagger} = \sqrt{3}\nu_T{}^{\ddagger}$. This is, of course, seriously in error when the reduced mass of the motion along the reaction coordinate is much greater than the hydrogen mass, but these large reduced masses are not likely to be important for tunneling anyway. With this approximation, we can express the behavior of all three isotopes in terms of the number which we can describe as a barrier parameter $\nu_H{}^{\ddagger}$. Using the Wigner correction, we find $s = {}^4/_3$ at very small u_H and $s = \log 3/\log 2 = 1.58$ at very large u_H, and increasing monotonically from 1.33 to 1.58 as u_H increases. Only the lower values have any significance. Using Bell's correction in the high barrier approximation, s drops sharply as u_H approaches 2π, reaching nearly unity as the tunnel corrections become very large. When finite barriers are considered, using both terms of eq 2, the values of s drop with increasing u_H, but not as much as with the infinite barrier, and with low barriers actually go through a minimum. Figure 1 shows the dependence of s on u_H for the Wigner correction and for the Bell correction with various values of the barrier height. It is also possible to estimate s values for the one-dimensional Eckhart barrier from the Q table of Johnston and Rapp.[9] These behave qualitatively like those for Bell's barrier, being smaller than ${}^4/_3$ for high barriers for significant u_H and larger for any u_H with a small barrier than with a high barrier.[13]

We can conclude however that s can be expected to deviate from 1.442 under some circumstances and that, providing the effect is not swamped by a large classical isotope effect as described above, we can expect to see this change reflected in the value of r. A possible point for further attack is to study the consequences of various refined models on the values of s and r, but it should be pointed out that various calculations so far have shown that one can have significant amounts of tunneling without finding any deviation from the Swain equation.[14] The large areas of ignorance about potential energy surfaces in the neighborhood of the col make it difficult to set reasonable limits for realistic curvatures, so that we do not really know how to make the model calculations. In the face of these difficulties we have chosen to attack the problem experimentally, measuring both isotope effects in some cases for which tunneling has been suggested. The reactions studied are as follows: (1) the alkaline permanganate oxidation of 1-phenyl-2,2,2-trifluoroethanol, in which a large, but barely classically explicable, deuterium isotope effect (k_H/k_D = 16 at 25°) had suggested tunneling;[3] (2) the proton transfer from 2-nitropropane to 2,4,6-trimethylpyridine, where the very large deuterium isotope effect (k_H/k_D = 23 at 25°) was explained in terms of tunneling;[4] (3) the oxidation of 4,4′,4′′-tris(dimethylamino)phenylmethane (leuco crystal violet) by tetrachloro-*p*-benzoquinone (chloranil), in which a study of the temperature dependence of the deuterium isotope effect showed A_H/A_D = 0.04.[5]

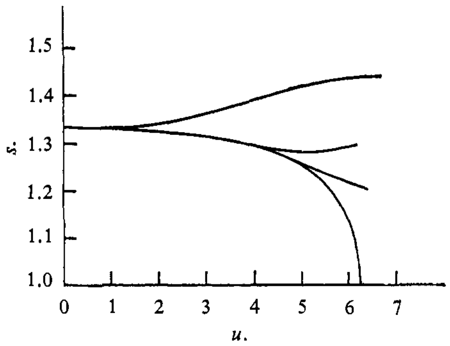

Figure 1. Dependence of s on u. Top curve, simple Wigner correction; lower curves, Bell parabolic barrier for E/kT = 10, 20, and ∞ in descending order.

Results and Discussion

I. The Oxidation of 1-Phenyl-2,2,2-trifluoroethanol by Alkaline Permanganate. This reaction was originally studied by Stewart and van der Linden[3] and was believed to involve hydrogen (probably hydride) transfer from the conjugate base of the alcohol to permanganate ion. The deuterium isotope effect was measured by direct measurements of the rates of the two species, the alcohol and the deuterated alcohol, 1-phenyl-2,2,2-trifluoroethanol-1-*d*. An isotope effect of about 16 at 25° was found, which suggested a tunnel effect contribution but did not demand it. The hydrogen atom removed ends up as a proton and is distributed throughout the solvent water. This suggested the possibility of measurement of the tritium isotope effect directly by measuring the specific activity of the water for various extents of reaction. The extent was controlled by adding insufficient amounts of permanganate; further oxidation by manganate was minimized by a quenching with acid and

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(12) It should be noted that small classical isotope effects can be achieved in linear proton transfers by a highly unsymmetric transition state. It has been pointed out by R. A. More O'Ferrall and J. Kouba (*J. Chem. Soc.*, *B*, 985 (1967)) that these cases are likely to have a very small value of $\nu^{\ddagger}$, hence $\log (Q_H/Q_D)$ will be very small. This situation will not lead to an important deviation from the Swain equation.

(13) The table of ref 9 is not closely enough spaced to allow accurate interpolation when Q is large, nor does it have enough significant figures to establish $\log Q$ (or $\log Q_H/Q_D$) with good precision when Q is near unity. Since they question the applicability of the one-dimensional treatment when tunneling is very important, we have not taken the effort to calculate s with great precision.

(14) We thank Dr. R. E. Weston, Jr., for communicating this result to us. Similarly, More O'Ferrall and Kouba[12] did not find Swain equation deviations on introducing substantial tunnel corrections. It is not clear how much these results merely show conditions of substantial classical isotope effects which mask the effect of s on r.

iodide ion. Necessary techniques to avoid mixing problems, isotopic fractionation during water purification, and quenching by small impurities in the solution scintillation counting are described in the Experimental Section. We believe that the principal remaining error is due to oxidation by manganate ion, which is most serious for reactions carried to a large extent of completion. Isotope effects were calculated using eq 11,[15]

$$k_H/k_T = \log(1 - x)/\log(1 - rx) \qquad (11)$$

in which x is the extent of reaction and rx is the fraction of the total available tritium actually present in the water. The results are shown in Table I.

Table I. Tritium Isotope Effects in the Oxidation of 1-Phenyl-2,2,2-trifluoroethanol-1-*t* at 24.9°

Extent of reacn, % (100x)	% of total act.[a] in water (100rx)	k_H/k_T
14.6	0.280 ± 0.017[b]	56.5 ± 3.3[b]
38.4	0.824 ± 0.034	58.3 ± 2.0
58.1	1.46 ± 0.04	58.9 ± 1.5
81.0	2.99 ± 0.04	54.6 ± 0.6

[a] In water. [b] Estimated errors are based upon variations among several identically treated samples. Statistical fluctuations in count rates are less than 1% for even the least active samples, and have therefore not been included.

While we cannot claim to have determined the isotope effect with great precision, the average value $k_H/k_T = 57.1 \pm 2.4$ is a reasonable representation of the data. The value calculated by application of the Swain equation is 55.5.

II. The Ionization of 2-Nitropropane-2-*t* by 2,4,6-Trimethylpyridine. This reaction could not be readily studied by a competitive method similar to that used on the permanganate oxidation, for the problem of separating the mixed solvent, water, and *t*-butyl alcohol from the radioactive starting material and getting a sample of these protons representative of the whole solution without getting any isotopic fractionation appeared impractical. It was likewise impractical to determine the isotope effect in the presence of iodine by observing the increase in specific activity of the unreacted nitropropane, since this method, which is so effective in reactions with small isotope effects, has virtually no precision when the isotope effects are very large. We chose therefore to determine the rate of loss of the tritium compound directly and thus determine k_T for comparison with the previously measured k_H. The very large anticipated isotope effect, together with the small values of k_H and the necessity for extensive reaction when following the starting material concentration, made the time taken for these experiments a serious consideration. We chose to study 2,4,6-trimethylpyridine rather than 2,6-dimethylpyridine, and worked at the highest temperature at which the deuterium isotope effect had been studied to minimize the time of the experiment. Even so, duplicate experiments in two different thermostats on different electric lines were done to minimize the possibility that a run of several months' duration would be ruined by a thermostat or power failure. We were fortunate in that these precautions proved unnecessary.

A further complication is associated with the fact that in most reactions iodine was absent; thus to a first approximation the reaction is merely an exchange, and the specific activity of the nitro compound might be expected to drop to zero in a simple manner. However, after ionization the reprotonation of the anion does not lead quantitatively to the simple nitro compound; instead, the *aci*-nitro compound is formed which undergoes a slow irreversible hydrolysis as well as reconversion to nitropropane. Thus the situation is intermediate between a pure exchange, in which all anions regenerate the starting material and the specific activity drops to zero, and the iodination reaction, in which none of the anion goes back to starting material, and the isotope effect results in a large increase in the specific activity of the unreacted material. This difficulty is avoided by adding to the solution taken for analysis a measured very large amount of unlabeled nitro compound. The specific activity of the isolated pure material then measures only the amount of remaining tritium compound and is very insensitive to the amount of residual original unlabeled compound. Appropriate controls and techniques of the separation, purification, and counting are described in the Experimental Section. This constitutes a sort of reverse isotopic dilution analysis in which the inactive material is used as a carrier and isolation need not be quantitative. The resulting rate constants are presented in Table II.

Table II. Rate of Disappearance of 2-Nitropropane-2-*t* in Aqueous *t*-Butyl Alcohol[a] with 2,4,6-Trimethylpyridine at 31.9°

(Base)[b]	(HCl)[b] × 10^3	$k_T \times 10^7$ l. mol^{-1} sec^{-1}	k_H/k_T[c]
1.055	0	0.972 ± 0.027[d]	155
1.311	0		
1.022	0		
0.989	5	1.29	117
0.975	10	1.48	102
0.479	25	1.77	85.3
1.165	250	1.89	79.9
1.026	10	1.51	100
1.146[e]	10	1.50	101
1.245[f]	. . .	1.95	77.4

[a] This solvent is six volumes of *t*-butyl alcohol made up to ten with water, as in ref 4. [b] These concentrations, in moles per liter, correspond to the amounts added, without considering the reactions. Corrected values of base concentration were used to calculate the rate constant. The nitro compound concentration was *ca.* 0.2 *M*. [c] Based on $k_H = 1.51 \times 10^{-5}$ l. mol^{-1} sec^{-1} from ref 4. [d] There were only ten points taken for these three runs; the rate constant given is derived from them all. [e] This solution contained 0.24 *M* lithium chloride. [f] This solution contained excess iodine. The unlabeled compound reacted virtually completely, and thus gave 1 mol of HI/mol of nitropropane. The collidine concentration was reduced by this amount in the calculation of k_T.

The very large and acidity-dependent isotope effects are not consistent with a simple rate-determining ionization by the base. A reasonable exchange mechanism indeed leads to the conclusion that we should not have expected this. Even the simple mechanism, reactions A, B, and C,[16] which ignores ion pairing and other complications has this feature.

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(15) L. Melander, "Isotope Effects on Reaction Rates," The Ronald Press, New York, N. Y., 1960, p 52.

(16) We omit the reaction $R^- + SH \rightarrow RH + S^-$, because we were unable to find its microscopic reverse as a significant kinetic term in the earlier work.[4]

$$\mathrm{B + TR} \underset{k_{-A}}{\overset{k_A}{\rightleftharpoons}} \mathrm{BT^+ + R^-} \tag{A}$$

$$\mathrm{BT^+ + SH} \xrightarrow{k_B} \mathrm{BH^+ + ST} \tag{B}$$

$$\mathrm{R^- + BH^+} \underset{k_{-C}}{\overset{k_C}{\rightleftharpoons}} \mathrm{RH + B} \tag{C}$$

It can be readily seen that the ionization of TR will lead to exchange only if $k_C(\mathrm{BH^+}) \gg k_{-A}(\mathrm{BT^+})$, and this will be the case only if there is a very large reservoir of $(\mathrm{BH^+})$ or if reaction B takes place much more rapidly than the reverse of A, *i.e.*, $k_B \gg k_{-A}(\mathrm{R^-})$. The exchange reactions of some ammonium salts with solvent are significantly slow, so it is not surprising to find that k_{-A} is important, and the rate measured is too small. In the presence of added $\mathrm{BH^+}$, the observed loss of TR will follow a pseudo-first-order course and the rate constant (k_T), the first-order rate constant divided by the base concentrations, can be shown to be given by eq 12, which leads to eq 13, predicting a linear relationship between $1/k_T$ and $(\mathrm{B})/(\mathrm{BH^+})$, since (RH) is always *ca.* 0.2 *M*. Figure 2 shows this plot, roughly verifying the treatment and giving from the intercept at $(\mathrm{B})/(\mathrm{BH^+}) = 0$ a value of $k_A = 1.92 \pm 0.02 \times 10^{-7}$ l./mol sec, and hence that k_H/k_T for the ionization process is 78.6.

$$k_T = k_A\left[\frac{k_Bk_C(\mathrm{BH^+})}{k_Bk_C(\mathrm{BH^+}) + k_Ak_C(\mathrm{RH})(\mathrm{B})}\right] \tag{12}$$

$$\frac{1}{k_T} = \frac{1}{k_A}\left[1 + \frac{k_{-A}k_{-C}}{k_Bk_C}\frac{(\mathrm{RH})(\mathrm{B})}{(\mathrm{BH^+})}\right] \tag{13}$$

We do not have real confidence in the above simple treatment because it does not distinguish between the presumably unimolecular collapse of the $\mathrm{BT^+R^-}$ ion pair and the bimolecular reaction of this ion pair with $\mathrm{BH^+}$, but we believe that the qualitative role of $\mathrm{BH^+}$ in accelerating the reaction is correct and that the extrapolation to give k_A is adequate. There remains the possibility that the species captured by $\mathrm{BH^+}$ is not the same as that captured by $\mathrm{I_2}$. The last entry in the table shows a run experimentally identical with the first ones except that iodine was added. Except for the very much higher iodine concentration and the long time taken, this run also is identical in conditions with those used earlier to measure[4] k_H and k_D. The rate, $k_T = 1.95 \times 10^{-7}$ l./mol sec, is gratifyingly close to k_A determined above by extrapolation. We may therefore conclude that these numbers represent the rate constant for the ionization of 2-nitropropane-2-*t* by 2,4,6-trimethylpyridine, that neither $\mathrm{BH^+}$ nor $\mathrm{I_2}$ are closely involved, and that the tritium isotope effect, k_H/k_T, = 78 with an error which we can generously estimate at ±5%. The isotope effect is thus not importantly less than the value calculated by the Swain equation, $k_H/k_T = 82.9$. It should be noted that reasonable agreement with the Swain equation is an argument against the attractive hypothesis that the very large deuterium isotope effect is due to some mechanistic complication resulting in an addition of several normal isotope effects. It is unlikely that such a mechanism would give concordant results with a massive label and with tracer levels.

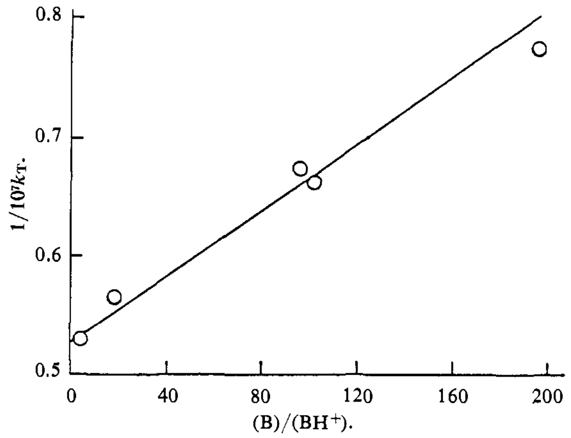

Figure 2. Plot of $1/k_T$ *vs.* $(\mathrm{B})/(\mathrm{BH^+})$ to show extrapolation to $(\mathrm{BH^+}) = \infty$.

III. The Oxidation of 4,4′,4′′-Tris(dimethylamino)-triphenylmethane by Tetrachloro-*p*-benzoquinone. The general oxidation of leuco triphenylmethane dyes, of the form $[p\text{-}(\mathrm{CH_3})_2\mathrm{NC_6H_4}]_2\mathrm{CHAr}$, by tetrachloro-*p*-benzoquinone (chloranil) in methanol solution has been studied.[17] The kinetic isotope effects in the special case of leuco crystal violet ($\mathrm{Ar} = p\text{-}(\mathrm{CH_3})_2\mathrm{NC_6H_4}$) were studied in methanol solution by Grinstein,[18] who found that an adequate fit to the Arrhenius equation required $A_H/A_D = 0.3$, suggesting tunneling by Bell's criterion. In a study designed to add to this information for other cases, Perry[5] found that the course of the reaction was not clear in this medium, but was complicated by the destruction of chloranil by methanol. While this is not a serious correction in the specific case of leuco crystal violet, it is almost certainly a temperature-sensitive correction, so that the small A_H/A_D required reinvestigation. The solvent acetonitrile proved to be polar enough to dissolve the product dye effectively and to be one in which all reagents and products were quite stable. In this solvent the kinetics were clean second order to large extents of completion, they were about half the rougher rates in methanol, and the temperature dependence was studied from 10 to 35°, giving $k_H/k_D = 0.0415 \exp(3359/RT)$, corresponding to the rather large isotope effect of 11.7 at 25°. Thus in this more well-behaved solvent, the evidence for tunneling is even stronger, and the small A_H/A_D, which is statistically correct to better than 40%, is as small as the smallest observed before.[19]

The determination of the rate for the tritium compound followed closely in principle that of the 2-nitropropane reaction. However, because the reaction is far faster, it was necessary to quench the reaction to stop it at the desired time. This was accomplished by rapidly reducing the quinone with aqueous sodium dithionite, and since a large excess of unlabeled leuco crystal violet was then added, the fact that some of the product dye may have been reduced was irrelevant, since no significant tritium would have been incorporated. The most serious problem was in the counting of the recovered leuco crystal violet, since it not only is a very effective quencher of the scintillation process, but the solutions are prone to air oxidation to give the dye which is adsorbed on the walls of the counting vial and thus produces an additional important and variable

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(17) C. D. Ritchie, W. F. Sager, and E. S. Lewis, *J. Am. Chem. Soc.*, **84**, 2349 (1962).

(18) R. H. Grinstein, Ph.D. Thesis, Rice University, 1961.

(19) R. P. Bell, J. A. Fendley, and J. R. Hulett, *Proc. Roy. Soc.* (London), **A235**, 453 (1956).

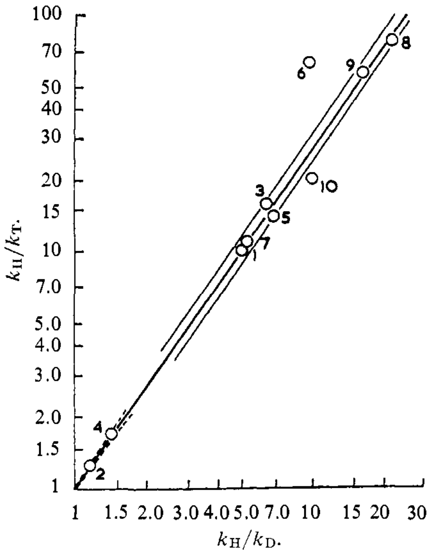

Figure 3. Relation between deuterium and tritium isotope effects, logarithmic scales. Lines are for the equation $k_H/k_T = \alpha(k_H/k_D)^r$. Solid lines, $r = 1.442$; $\alpha = 1.157$, 1.000, and 0.907 from top to bottom; dotted lines, $\alpha = 1$, $r = 1.58$ and 1.33. Point identification in text.

color quench. While we were able to overcome these difficulties to a major extent, this is probably the source of the remaining error. Three runs at 35.5° gave $k_T = 10.2 \pm 1.1 \times 10^{-3}$, $9.22 \pm 0.99 \times 10^{-3}$, and $9.27 \pm 0.45 \times 10^{-3}$ l./mol sec; of these the first used an earlier model counter with less precise quenching correction. The average value, $k_T = 9.56 \pm 0.6 \times 10^{-3}$ l./mol sec, combined with Perry's value,[5] $k_H = 19.5 \pm 0.7 \times 10^{-2}$ l./mol sec, gives $k_H/k_T = 20.4 \pm 1.3$. From the deuterium isotope of 9.90 at this temperature,[5] the Swain equation gives k_H/k_T (calcd) = 27.3, and the deviation is significant.

Figure 3 shows a plot of $\log(k_H/k_T)$ *vs.* $\log(k_H/k_D)$ for several reactions. The center line is a plot of eq 3 and the upper and lower parallel lines are the limits estimated by Swain for preexponential factor effects. The dotted lines near the origin show Bigeleisen's limits,[11] which apply to small isotope effects. The individual points are numbered as follows: (1) proton transfer from α-phenylisocaprophenone to acetate ion;[2] (2) hydride transfer from triphenylsilane to water;[20] (3) ethoxide ion promoted eliminations from 1-bromo-2-phenylpropane, for which $A_H/A_D = 0.396$;[21] (4) hydride transfer from pyridinediphenylborane to water with $A_H/A_D = 1.41$;[22] (5) proton transfer from water to pyridinediphenylborane, with $A_H/A_D = 0.94$;[22] (6) proton transfer from acetone to hydroxide ion;[23] (7) methoxide-promoted elimination from 2,2-diphenylethyl benzenesulfonate, with $A_H/A_D = 1.1$;[24] (8) proton transfer from 2-nitropropane to 2,4,6-trimethylpyridine, with $A_H/A_D = 0.146$; (9) oxidation of 1-phenyl-2,2,2-trifluoroethanol by alkaline permanganate, with $A_H/A_D = 0.25$; (10) oxidation of leuco crystal violet by chloranil, with $A_H/A_D = 0.04$.

Of these points, Swain and his coworkers had access only to the first two, and the first comment is that the equation holds up very well indeed with more data. We shall discuss only four of these points. The deviation of point 2 is probably within experimental error. Point 4 on the figure has $r = 1.58$, the extreme upper limit allowed by Bigeleisen.[11] He suggested that this could be attained only if all the isotope effects were in the Arrhenius preexponential factor, in gratifying agreement with the original observation that these isotope effects were entirely temperature independent. Point 6 is well outside the limits allowed and the deviation was originally attributed to a tunneling contribution,[23] but these data, which yield $r = 1.81$, would require $s > 1.8$; the earlier considerations give $s < 1.4$, at least for all reactions of important activation energy. We are therefore led to suspect an experimental or computational source for this result, rather than that proposed by the author. Finally, point 10 deviates in the direction expected for tunneling, giving $r = 1.31$, and it is certainly plausible to relate the small A_H/A_D to the small r. Nevertheless the other cases with possibilities of tunneling (3, 7, and 8) do not deviate importantly, and we must conclude that Swain equation deviations is to be expected only when tunneling is extreme.

Table III restates these deviations, showing rough estimates of the tunnel correction on the isotope effects and the values of r calculated from eq 10, using a connection between $\nu_H{}^{\mp}$, Q_H, Q_D, and s based upon the Bell high barrier expression, except for the case noted in which the Bell two-term expression was used. It is assumed throughout that $\nu_H{}^{\mp} = \sqrt{2}\,\nu_D{}^{\mp}$; if this is wrong the ratio is certainly closer to unity than this, and we therefore underestimate the extent of tunneling, since there can be some weakly reflected in the isotope effect and hence not readily detected. We use the variable $\nu_H{}^{\mp}$ to describe the barrier shape rather than Bell's a and E, since there is a temptation to overinterpret a. The relation between them is $\nu_H{}^{\mp} = E^{1/2}/\pi a(2m_H)^{1/2}$, where m_H is the proton mass. The agreement between calculated and observed is unimpressive, but it confirms the statement that tunneling can be extensive without much deviation from the Swain equation. Our inability to account for $r > 1.44$ is obviously due to the neglect of the preexponential terms, and if one assumes that the extreme variation in preexponential factor allowed

Table III. Estimates of Extent of Tunneling and the Swain Exponent, r

Reacn	$\nu_H{}^{\mp}$, cm^{-1}	k_H/k_D	Q_H/Q_D	r_{calcd}	r_{obsd}
3	900[a]	6.4	1.68[a]	1.40[a]	1.47
5	350[a]	6.7	1.07[a]	1.44[a]	1.38
8	1060[b]	21.4	2.4[b]	1.39[b]	1.42
	1020[a]	21.4	2.16[a]	1.39[a]	1.42
9	960[a,c]	16.2	1.88[a,c]	1.41[a,c]	1.45
10	1080[a]	9.9	2.85[a]	1.35[a]	1.31
	1150[d]	9.9	3.0[d]	1.36[d]	1.31

[a] Estimated from A_H/A_D following Bell,[7] using the one-term expression. [b] In this case Q_H/Q_D was estimated first as the ratio between the observed isotope effect and that expected for an unhindered base of the same strength.[4] [c] The data on the temperature dependence are limited and perhaps of uncertain precision. [d] The two-term Bell expression, eq 2, was used. The H compound rate was represented experimentally by $k_H = 10^{5.07} \cdot e^{-8152/RT}$.

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(20) L. Kaplan and K. E. Wilzbach, *J. Am. Chem. Soc.*, 77, 1297 (1955).

(21) V. J. Shiner, Jr., and B. Martin, *Pure Appl. Chem.*, **8**, 371 (1964).

(22) E. S. Lewis and R. H. Grinstein, *J. Am. Chem. Soc.*, **84**, 1158 (1962).

(23) J. R. Jones, *Trans. Faraday Soc.*, **505**, 95 (1965).

(24) A. V. Willi, *J. Phys. Chem.*, 70, 2705 (1966).

by Swain is in fact often achieved, then none of these cases deviated importantly. We prefer to believe that deviations as large as that of case 10 probably do indicate tunneling, but that we cannot get good measures of the extent of tunneling from these. It is worthy of comment that the two entirely independent measures of the quantum correction to the isotope effect are in reasonable agreement: in reaction 8, the one from the A_H/A_D (marked a) and one derived exclusively from the discrepancy of the deuterium isotope effect from that expected from its base strength (marked b). It should therefore be noted, as was suggested before,[4] that the marked deviation from the Brønsted relationship of k_H/k_D itself can be taken as evidence of tunneling, even when the isotope effects are themselves entirely within the "normal" range.[25]

Finally, if we accept the interpretation that the leuco dye oxidation goes with important tunneling, we must ask why this case is particularly favorable. We believe that in general a hydride transfer reaction will have a narrower barrier than a proton transfer, primarily because an electron-deficient atom can approach without the electron repulsion characteristic of nucleophilic substitution. This accounts for the variable stereochemistry of bimolecular electrophilic substitution and led to the proposal of a triangular transition state[26] for electrophilic attack on a bond to hydrogen. This picture clearly then involves a relatively small motion between start and finish and hence a narrow barrier. The narrow barrier is not necessarily tied to the triangular transition state, however, for Swain, Wiles, and Bader have shown that this is highly plausible even if the transition state is linear.[27] We suggest that large isotope effects in hydride transfers will be very likely associated with tunneling. The reactions represented in Figure 3 contain four examples of hydride transfers, reactions 2, 4, 9 and 10. Reactions 9 and 10 both have large isotope effects and show some evidence of tunneling, perhaps not very convincing for reaction 9. Reactions 2 and 4 are both simultaneous proton and hydride transfers, yielding diatomic hydrogen gas, and in both reactions the large primary isotope effect of the protonic hydrogen shows that the motion along the reaction coordinate is very sensitive to the mass of the proton. It seems reasonable to conclude then that changing from H to D to T in the hydride position does not change the reduced mass of the imaginary vibration by even nearly as much as the ratio 1:2:3. Thus the tunneling, if present, will not increase the isotope effect significantly.

Experimental Section

I. Oxidation of 1-Phenyl-2,2,2-trifluoroethanol. 1-Phenyl-2,2,2-trifluoroethanol-1-*t*. Trifluoroacetophenone (39.2 g) was added to a stirred ether solution of 1.5 g of lithium aluminium hydride containing 25 mCi of the tritide. Stirring was continued for 4 hr, then an excess (1.5 g) of lithium aluminium hydride was added and stirring was continued for 2 hr more. Then 10% sulfuric acid was added until the solids dissolved, the ether layer was separated and washed several times with water, and the alcohol was distilled twice (bp 82° (13 mm)), yielding a product containing impurities of less than 0.1% by gas chromatography. The infrared and nmr spectra were consistent with the alcohol structure, but with 1 g in 15 ml of scintillation solution, containing ethanol (30%), 2,5-diphenyloxazole (PPO), 1,4-bis-2-(5-phenyloxazoyl)benzene (POPOP), and toluene, no counts (not even background) were recorded. Similarly, no counts were recorded in a scintillator solution made from 2,5-bis-2-(5-*t*-butylbenzoxazoyl)thiophene (BBOT) in toluene. However, counting was reasonably high when a dilute water solution of the alcohol was counted in the first medium, so that the inactivity merely represents a very effective quench.

Samples of this alcohol apparently underwent slow air oxidation, converting the tritium to a water-exchangeable form. Samples were therefore washed with dilute alkali and redistilled frequently to avoid this source of error.

Reaction of 1-Phenyl-2,2,2-trifluoroethanol-1-*t* with Alkaline Permanganate. A fresh solution of potassium permanganate was made up and placed in a flask in the thermostat. A sample of this was assayed iodimetrically. Another flask in the same thermostat contained a weighed amount of the tritiated alcohol in 0.2 *N* sodium hydroxide. After temperature equilibrium was attained, 5 ml of each solution was measured into each side of an erlenmeyer flask with a creased bottom to separate it into two compartments. The reaction was started by vigorously shaking the flask and allowed to continue for 15–30 sec, by which time the color had changed to the pure green of the manganate ion, then about four drops of concentrated sulfuric acid and an excess of dry potassium iodide was added to stop the reaction. It was shown that this very rapid mixing and rapid quench were essential to reproducible results. The resulting mixture was extracted four times with petroleum ether without loss of any of the water, which was accomplished by freezing the water before pouring off the petroleum ether. Residual petroleum ether was finally removed from the frozen aqueous phase by pumping.

The water was then treated with excess reagent grade copper powder, to remove iodine, and the water was then quantitatively sublimed at a pressure of 20–50 μ. Often iodine removal was not quantitative, so that the copper treatment and sublimation procedure were repeated. After visible traces of iodine were gone, a sample was counted, and the remainder was again treated with copper and sublimed. All results reported are based on count rates unaltered by further purification. The water was counted as a weighed sample of 0.100 ± 0.003 g in 15 ml of a solution of three parts of ethanol, seven of toluene, containing 4 g of PPO and 0.100 g of POPOP per liter. No results are based on less than 10^4 total counts, most on at least ten times this number.

The water purification scheme was checked by using water with 7220 cpm per 0.1 g for carrying out the reaction with unlabeled alcohol. After purification, 100 mg of water recorded 7219 cpm, well within the statistical error.

It was shown that the fast quench was necessary, for when a solution of manganate made by reducing permanganate with unlabeled alcohol was mixed with labeled alcohol for 3 min, 2.5% of the activity of the alcohol was introduced into the water. It was also shown that no activity from the radioactive alcohol ended in the water if it was introduced after the quench. Finally it was shown that a slow oxidation of the alcohol occurred after the quench, presumably by iodine, to the extent of 0.25% in 24 hr. The time of work-up was such that this error was negligible.

The procedure for complete oxidation of the alcohol was the same except that an excess of permanganate was added and the solution was allowed to stand for 1 day.

II. Ionization of 2-Nitropropane-2-*t*. 2-Nitropropane-2-*t*. This was prepared by Mr. L. H. Funderburk by exchange of 2-nitropropane with water containing tritium and sodium hydroxide. Ether extraction, distillation (bp 120–122° (760 mm)), and finally preparative scale gas chromatography on a column of Carbowax 20M on Chromosorb W gave a sample without important impurity. This column also led to no exchange, since the activity was unaltered by further passes.

The 2,4,6-trimethylpyridine was purified as described previously,[4] and the solvent was made up as before.

Reaction of 2-Nitropropane-2-*t*. A solution of a weighed sample of about 7 g of 2,4,6-trimethylpyridine and about 1 g of 2-nitropropane-2-*t* in 50 ml of solution was placed in an amber flask in a thermostat at 31.9 ± 0.1°. Aliquots of 5 ml each were removed at 2–6 week intervals.

Activity Determination. The above aliquot was added to about 5 g, accurately weighed, of inactive 2-nitropropane, the samples were then neutralized with hydrochloric acid, and after thorough

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[25] Such a case has been brought to our attention by Professor E. Grovenstein, whom we thank for this information prior to publication: E. Grovenstein, Jr., and F. C. Schmalsteig, *J. Am. Chem. Soc.*, **89**, 5084 (1967).

[26] M. F. Hawthorne and E. S. Lewis, *ibid.*, **80**, 4296 (1958).

[27] C. G. Swain, R. A. Wiles, and R. F. W. Bader, *ibid.*, **83**, 1945 (1961).

mixing, the solution was extracted with petroleum ether (bp 30–60°). The petroleum ether was mostly removed on a rotary evaporator, and the residue was subjected to purification by gas chromatography as described above. The pure samples were assayed by solution scintillation counting, with consideration taken of the serious quenching characteristics of 2-nitropropane. A plot of count rate *vs.* mass of sample showed a maximum at about 20 mg (in a 10-ml sample). All results reported were measured at a concentration of about 0.04 mg in 20 ml of a solution of PPO (4 g/l.) and POPOP (100 mg/l.) in toluene, and at this low concentration the count rate was proportional to concentration. The amount of activity in the initial aliquot is then found from the final observed count rate, the mass taken, and the amount by which it was diluted. In some cases a second aliquot was taken for gas chromatographic analysis, which confirmed that the base was not being destroyed, and that the nitro compound was. A peak of the same retention time as acetone appeared. The destruction of nitro compound was taken into consideration in calculating the dilution factor when this information was available, but the dilution was so great that this correction is only of the order of 1%. The gas chromatographic method also showed that in the run containing added iodine, the nitro compound disappeared quite early, confirming qualitatively the large isotope effect.

III. Oxidation of Leuco Crystal Violet. 4,4',4''-Tris(dimethylamino)triphenylmethane-*t* (leuco crystal violet, 4,4',4''-methylidynetris(N,N-dimethylaniline)) was prepared by Mr. R. H. Grinstein, by reduction of crystal violet chloride (biological stain grade, 99% pure) with lithium aluminium tritide (and then hydride) in tetrahydrofuran solution (and suspension). After reduction was complete the solution was diluted with a large volume of ethyl ether and washed repeatedly with water. Evaporation of the ether left the crude leuco dye which was purified by recrystallization from ethanol, mp 177–178°, 66%.

The inactive leuco dye was prepared by the method of Cigen.[28]

Tetrachloro-*p*-benzoquinone (chloranil) was commercial material recrystallized from ethyl acetate. It melted at 290° in a sealed tube.

Acetonitrile was from several sources, Eastman "anhydrous" grade, Matheson Coleman and Bell ordinary grade, and the latter firm's practical grade distilled from phosphorus pentoxide were indistinguishable, but the unpurified practical grade material develops an intense color with chloranil. The rates are insensitive to the presence of small amounts of water or acetic acid, although water is to be avoided since it reacts with chloranil.

Rate of Oxidation of Tritiated Leuco Crystal Violet. A solution (10 ml, containing 0.0400 g of leuco crystal violet-*t* in 50 ml of acetonitrile) was added with mixing to a solution (10 ml, containing 1 g/l. of chloranil in acetonitrile) and held in the thermostat. Several identical such solutions were made up, and they were quenched at about 2-hr intervals by addition of sodium dithionite (1 g in 50 ml of water). Inactive leuco dye (*ca.* 1.5 g of accurately weighed) dissolved in chloroform was then added. The solution was then stirred, and the solvent removed on a rotary evaporator. The leuco dye was then recovered from the residue by recrystallization from absolute ethanol.

The efficacy of quenching was checked potentiometrically. A solution of chloranil and leuco crystal violet containing a platinum electrode and a reference electrode was treated with excess dithionite solution. The potential fell to a constant value essentially at the mixing rate.

It was shown that when inactive reagents were used, but the dithionite was dissolved in tritiated water, no detectable activity was introduced into the leuco dye.

Activity Measurements on Leuco Crystal Violet-*t*. This substance quenches the scintillation process quite effectively, and a plot of count rate *vs.* mass of leuco dye added showed a maximum. Unlike the nitropropane, it was not possible to reduce the concentration to a point where quenching was negligible. Counting was done at a concentration about half of the one giving maximum count rate, and efforts to reproduce the quenching were made. In all but the first run, we had access to a solution scintillation counter with automatic efficiency determination, and this facilitated these measurements. A serious further problem is that in addition to the quenching by the leuco dye, there is a facile autoxidation to the dye, crystal violet, which absorbs the scintillation flashes. Correction is possible but of low precision, and we believe that even with automatic correction, efficiency variation is the principle source of error.

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