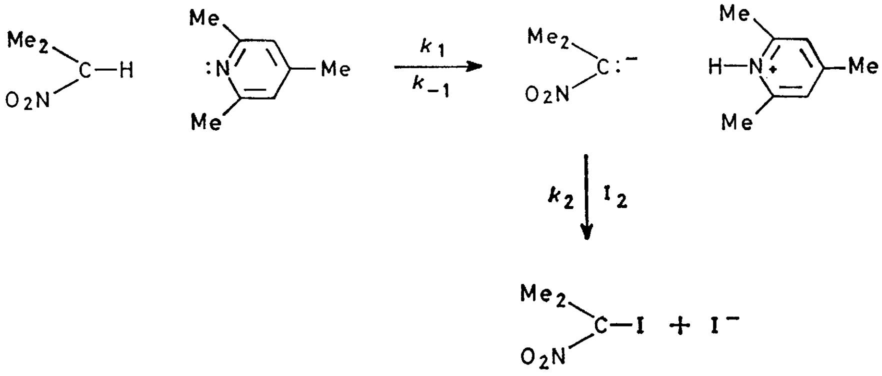
Reactions at High Pressure. Part 6.[1] Anomalous Volumes of Activation, and Kinetic Isotope Effects in the Ionisation of 2-Nitropropane

By **Neil S. Isaacs** * and **Khalid Javaid**, Department of Chemistry, University of Reading, Whiteknights, Reading RG1 2AD

Rates of iodination of 2-nitropropane, catalysed by 2,4,6-trimethylpyridine have been measured in aqueous t-butyl alcohol at 25° at pressures of 1—1 285 bar and similarly for 2-nitro[2-^{2}H]propane. It is found that oxygen affects the measured rates and, if the reaction is carried out under nitrogen, rates are faster and the kinetic isotope effect, k_H/k_D 16, less than previously reported. There is still a large tunnelling contribution and this is found to be pressure dependent, tending towards 7. The volumes of activation for ^{1}H and ^{2}H compounds are different, −31 and −40 cm^3 mol^{-1} respectively; it is believed the former is anomalous. The large negative value of $\Delta V_0^‡$ is consistent with a high degree of proton transfer and almost maximum charge development in the transition state.

IN continuation of our studies on the pressure dependence of kinetic isotope effects (k.i.e.) [1] we now report values of k_H/k_D for the dissociation of 2-nitropropane catalysed by 2,4,6-trimethylpyridine over the range 1—1 285 bar. This is also the first measurement of volumes of activation for a base-catalysed enolisation. The reaction takes place according to Scheme 1 and it is assumed that the conjugate base is very rapidly scavenged by iodine. This system has previously been extensively investigated by Lewis and his co-workers [2-4] and by Bell and Goodall,[5] who have shown that the magnitude of the proton k.i.e. is markedly dependent upon the presence or absence of substituents at positions 2 and 6 in the pyridine base which presumably impose steric effects. Ionisation of 2-nitropropane catalysed by pyridine in t-butyl alcohol–water shows k_H/k_D 9.8 (10.3 in water [5]) whereas when catalysed by 2,6-dimethyl- or 2,4,6-trimethyl-pyridine this value rises to 24 (ref. 5 gives 20). Despite the fact that the methylpyridines are closer in pK to 2-nitropropane than is pyridine, which would tend to increase the isotope effect towards the normal maximum (*ca.* 7), the experimental proton k.i.e.s are so far in excess of this figure that they cannot be explained as a result of differences in zero-point energy. Consequently, this reaction has been cited as an example of a proton transfer which derives considerable rate enhancement from quantum-mechanical tunnelling.[4,6,7] We have previously shown that a ' normal ' isotope effect is essentially independent of pressure, *i.e.* the reactions of the ^{1}H and ^{2}H species show the same volumes of activation but in one case, the reaction of chloranil with Leuco-crystal Violet, the abnormally large isotope effect ascribed to tunnelling is reduced from 11 at atmospheric pressure to *ca.* 7 at 2 kbar.[1] The present investigation was undertaken to ascertain further how general is this effect and whether it is a reliable guide to the incursion of tunnelling during hydrogen transfer.



SCHEME 1

EXPERIMENTAL AND RESULTS

Commercial 2-nitropropane was purified by fractional distillation, collecting the middle fraction, b.p. 119° (lit.,[8] 120°).

2,4,6-Trimethylpyridine was distilled after the addition of boron trifluoride–diethyl ether to entrain less highly substituted pyridines present as impurities. It was then fractionated, and the middle fraction, b.p. 170—172° (lit.,[8] 176—178°) collected under nitrogen. t-Butyl alcohol was shaken with several portions of alkaline potassium permanganate solution until the latter was no longer reduced to green manganate. After washing with water and drying over molecular sieve, t-butyl alcohol was fractionally distilled, b.p. 82.5°, and finally purified by fractional freezing of approximately half the sample; m.p. 25.5°. 2-Nitro[2-^{2}H]propane was prepared according to the method of Cox and Gibson [9] and the deuterium content found to be 99% by n.m.r. For the reaction medium, t-butyl alcohol and water were mixed in the weight ratios 60 : 40 (60% aqueous t-butyl alcohol) or 50 : 50. A stock solution was made up containing iodine (8×10^{-4}M), 2,4,6-trimethylpyridine (0.075M), and perchloric acid as buffer (0.003M) in either of the above solvents. When kept in the dark under nitrogen, the absorbance of this solution was constant over a period of weeks. In a typical reaction, 2-nitropropane (0.22 g, 0.1M) was weighed into a 25-ml volumetric flask and made up to the mark with thermostatted stock solution, maintaining a nitrogen atmosphere. Samples (1.5 ml) were withdrawn at intervals and the iodine determined. Previous workers used spectrophotometry to follow the reactions but this leads to complications since the formation of the more strongly absorbing I_3^- gives rise to an initial increase in absorbance before an eventual decrease. In order to avoid the tedious and possibly unreliable calibration of the complex curve of absorbance against time, we titrated iodine directly against thiosulphate. Since only small volumes of solution were available as samples from the pressure runs, and since also starch indicator does not give a colour with iodine in the presence of t-butyl alcohol, we adopted the following procedure. The sample was placed in a 1-cm spectrophotometer cell and 0.5 ml water added. A 1-mm coated bar magnet was placed in the cell and the titration carried out in the spectrophotometer, magnetically stirred by a rotating magnet located in the cell holder, the titrant being added by means of an autotitrimeter delivering into the cell through fine polyethylene tubing. The end point was taken as the volume needed to reduce the absorbance at 460 nm to zero and could be read to ±1 µl. For reactions at pressure the same mixture of reagents was made up and placed in a Teflon capsule holding *ca.* 13 ml fitted with a free piston at one end. At the other was an outlet which engaged with the top plug of the pressure vessel into which a high-pressure sampling valve was mounted. The reaction vessel was placed into the pressure vessel previously described[1] which was air-thermostatted to ±0.5°. Samples (1.7 ml) were taken at intervals, discarding the first 0.2 ml as being resident in the valve. Iodine in the remaining 1.5 ml was titrated as before. During sample withdrawal, pressure was maintained automatically by means of a Haskell diaphragm pump supplying low-pressure oil to the intensifier at a pressure determined by a preset air supply. Thus, temperature fluctuations during sampling was minimised. Pseudo-zero-order rate coefficients were obtained by least-squares fit of the data (Figure 1) and converted to second-order coefficients (Table 1). Because of the reversibility of the reaction[5] as $[I^-]$ increases, deviations from zero-order were noted above *ca.* 50% reaction so measurements were not continued beyond that point. To obtain volumes of activation, $\Delta V_0^‡$, the slope of the graph of ln k against P as $P \longrightarrow 0$ was obtained by computed least squares fit of the quadratic function (1), whence $\Delta V_0^‡ = -BRT$ (Table 2, Figure 2).

$$\ln k = A + BP + CP^2 \qquad (1)$$

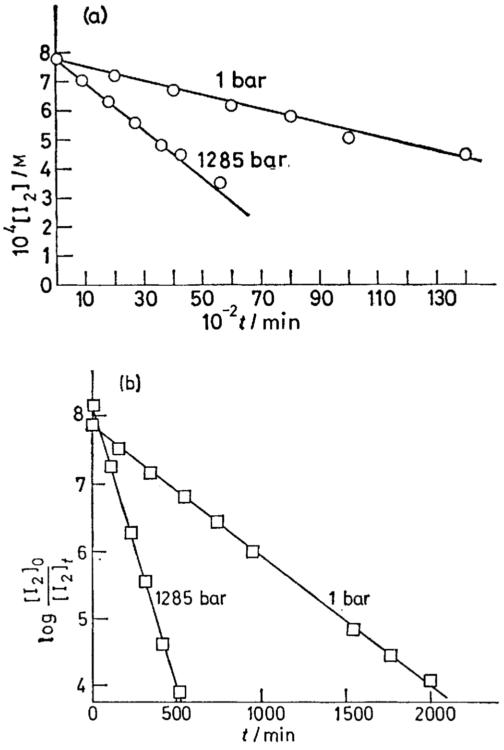


FIGURE 1 Typical rate plots for iodination of (a) 2-nitropropane and (b) 2-nitro[2-^{2}H]propane

TABLE 1

Measured rates and isotope effects for enolisation of 2-nitropropane at 25°

P/bar	10^4k_H/l mol^{-1} min^{-1}	10^4k_D/l mol^{-1} min^{-1}	k_H/k_D
(a) In 60% t-butyl alcohol			
1	2.89	0.176	16.4
300	4.02	0.255	15.7
560	5.42	0.386	14.0
750	6.55	0.501	13.1
850	7.11	0.590	12.1
1 040	8.50	0.701	11.8
1 285	9.67	0.85	11.4
2 000 *			9.3
3 000 *			7.7
(b) In 50% t-butyl alcohol			
1	4.01	0.253	15.9
300	5.58	0.382	14.6
560	7.20	0.540	13.3
750	8.66	0.665	13.0
850	9.62	0.78	12.3
1 040	12.1	1.00	12.0
1 285	13.8	1.28	10.8

* Values extrapolated using equation (1).

TABLE 2

Volumes of activation and coefficients in equation (1)

	A	10^2B	10^7C	$\Delta V_0^‡$/cm^3 mol^{-1}
Me_2CHNO_2 in 60% t-butyl alcohol	−8.159	0.1286	−2.61	−31.4 ±1
Me_2CDNO_2 in 60% t-butyl alcohol	−10.98	0.1652	−2.96	−40.4
Me_2CHNO_2 in 50% t-butyl alcohol	−7.827	0.1149	−1.27	−28.1
Me_2CDNO_2 in 50% t-butyl alcohol	−10.58	0.1419	−1.15	−34.7

No correction was necessary for undeuteriated substrate since this was present in very small amount and would have reacted before the first sample was taken (at least 30 min after mixing). All runs were performed at least in duplicate and were reproducible to at least ±5% (better for the runs at atmospheric pressure). The effect of pressure upon the kinetic isotope effect is shown in Figure 3.

The disappearance of iodine in the absence of collidine, all other components of the reaction mixture being added, proceeded at a negligible rate showing that water catalysis is unimportant. Similarly, OH^- catalysis may be ruled out since the solution was buffered at pH *ca.* 3.

Primary nitro-compounds are known to be considerably more reactive than secondary and it is important that none of the latter are present when the reaction is carried out under zero-order conditions. We found by g.l.c. analysis that 2-nitropropane was very pure, and, in particular, that no detectable 1-nitropropane was present by comparison with an authentic sample. There was, however, a trace of nitroethane amounting to 0.4%. We established the rate of iodination under our conditions to be 15 times that of 2-nitropropane so that the measured rates are probably high, a correction of 6% being required. This, however, should not affect the isotope or pressure effect measurements.

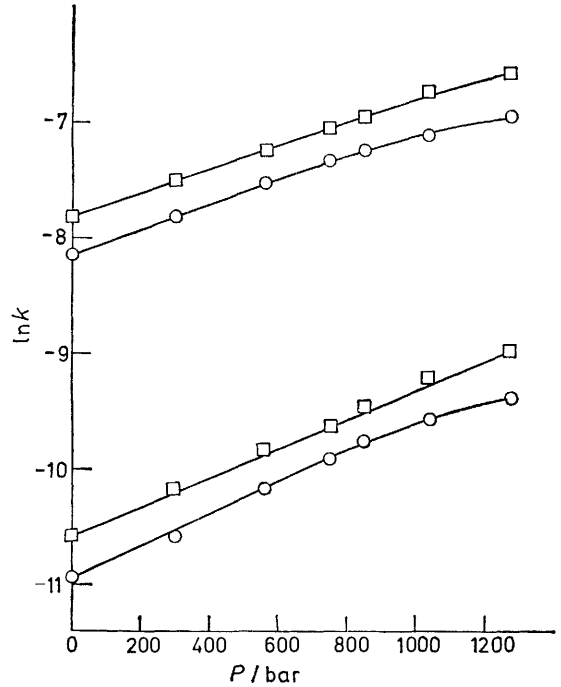


FIGURE 2 Effect of pressure on rates of iodination of 2-nitropropane (upper curves) and 2-nitro[2-^{2}H]propane (lower curve): □, in 60% aqueous t-butyl alcohol; ○, in 50% aqueous t-butyl alcohol

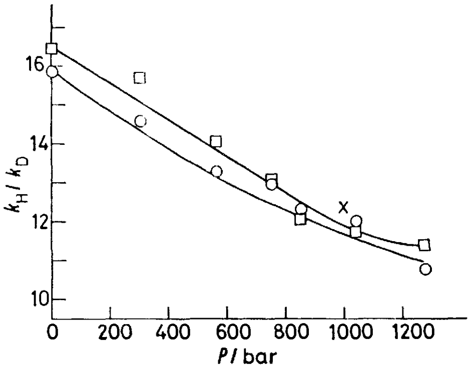
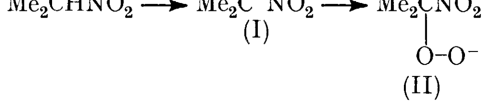


FIGURE 3 Effect of pressure on the kinetic isotope effect for iodination of 2-nitropropane: □, in 60% aqueous t-butyl alcohol; ○, in 50% aqueous t-butyl alcohol; ×, calculated value

DISCUSSION

The effect of oxygen upon the rate of iodination does not seem to have been previously reported, but in the present investigation at least the retarding influence of air on the disappearance of the iodine colour seems consistent and genuine. We find that, by carrying out kinetic measurements under nitrogen, rates of iodination of 2-nitropropane are increased by *ca.* 15% and of 2-nitro[^{2}H]propane by *ca.* 40% since it is a much slower reaction. This results in an isotope effect considerably smaller than that previously reported though still abnormally large. A possible explanation might be the reaction of oxygen with an enolate ion (I) leading to a peroxy-species (II) capable of liberating iodine from iodide. It is notable that the tritium isotope effect for this reaction (in the presence of air) was found to be close to the value predicted from the Swain relationship,[10] $(k_H/k_D)^{1.442} = k_H/k_T$. Thus, for $k_H/k_D = 24.2$, k_H/k_T (calculated) $= 100$. Experimental values near to this and dependent upon buffering acid concentration, have been found.[4] The rates of enolisation of 2-nitro-[^{3}H]propane were measured by tritium loss to solvent rather than by iodination, otherwise this already very slow reaction would have been even more seriously in error.



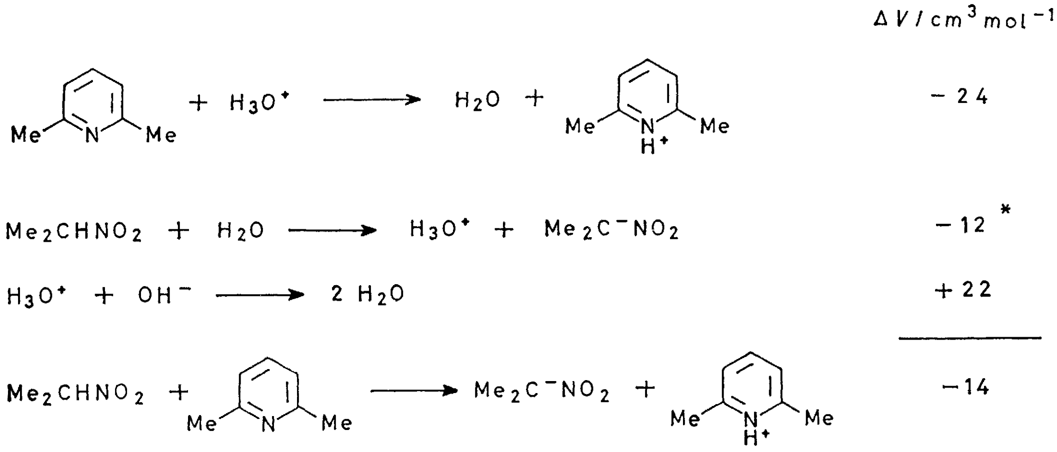
$$\mathrm{Me_2CHNO_2} \xrightarrow{\mathrm{B:}} \underset{\text{(I)}}{\mathrm{Me_2C^{-}NO_2}} \xrightarrow{\mathrm{O_2}} \underset{\text{(II)}}{\underset{\mathrm{O{-}O^{-}}}{\mathrm{Me_2CNO_2}}}$$

Again, enolisation rates of methyl 4-nitrovalerate have been measured both by iodination and by racemisation.[11] If oxygen were to interfere in this reaction (and assuming the formation of any sort of peroxy-species represents only a minor pathway) the two rates might be different, iodination being slower than racemisation. The values found differ in this sense by *ca.* 5% but, since this represents the precision of the measurement no conclusions can be drawn as it is uncertain as to whether nitrovalerate would react with oxygen in a similar manner to nitropropane even though their enolisation rates are close.

The measured rates are all pressure-dependent to a remarkable degree and volumes of activation strongly negative. No volumes of activation have hitherto been measured for base-catalysed enolisation but we may estimate how reasonable are our values from the following information. If k_{-1} is negligible, *i.e.* enolisation is not reversible since $k_2[\mathrm{I_2}] \gg k_{-1}[\mathrm{HA}]$ and also assuming $k_1 \ll k_2$ the entire contribution to the volume of activation occurs in the proton transfer reaction. The maximum value of $\Delta V_0^{\ddagger}$ would be the volume of reaction for the proton transfer which may be estimated from the cycle in Scheme 2. The value -14 cm^3 mol^{-1} for proton transfer would be that expected for aqueous solution in the absence of tunnelling. For comparison, the deuteriated compound should be used and a solvent correction applied. The negative volumes of reaction result from electrostriction of solvent, ΔV_e which may be expressed by the Drude–Nernst equation (2) where q is the charge

$$\Delta V_e = \frac{q^2}{2r} \cdot \frac{1}{\varepsilon^2} \frac{\partial \varepsilon}{\partial P} = \frac{q^2 \psi}{2r} \qquad (2)$$

on the ion and r its radius and ε is the dielectric constant of the medium. The values of $\psi = 1/\varepsilon^2 . \partial\varepsilon/\partial P$ are not known for t-butyl alcohol–water mixtures but to accommodate the activation volumes obtained would have to be 17 (60% aqueous t-butyl alcohol) or 15 × 10^{-7} bar^{-1} (50% aqueous t-butyl alcohol). These values seem quite reasonable when compared with those for water, ethanol, and acetone for which $\psi = 6.01, 37.6$, and 69.1,[12] respectively and in any case are in the expected order, the more negative volume of activation associated with the less polar solvent. Both for ^{1}H and ^{2}H compounds, the curvature of the plot (*i.e.* $C = \mathrm{d}^2\ln k/\mathrm{d}P^2$) is greater for 60% t-butyl alcohol than for 50% although the significance of this is not clear. What is significant, however, is that $\Delta V_0^{\ddagger}$ (^{1}H) < $\Delta V_0^{\ddagger}$ (^{2}H). Since it is generally supposed[14] that isotopic substitution has no effect on geometries, volumes, or charge distributions of the transition state, we must regard the former at least as being anomalous, due to a change in the tunnelling contribution with pressure. As in the case of Leuco-crystal Violet and chloranil, the isotope effect appears to fall towards a constant value of k_H/k_D *ca.* 7, the maximum 'normal' value at the experimental temperature. By extrapolation the isotope effect would appear to level off at *ca.* 3 kbar although we were unable to make measurements above 1 285 bar since the preparation time would have exceeded a half-life while at lower temperatures greater errors would have been introduced into the slowest reactions.



SCHEME 2 * Value estimated from dissociations of other acids which are usually in the range 10—14 cm³ mol⁻¹ for a wide range of structural types.[13]

The proton is a particle of such low mass that tunnelling effects might be generally expected during transfer reactions. That this is not the case probably is a result of the motion of the proton being co-ordinated with translational and rotational motion of solvent molecules which thereby increase the effective mass of the particle. Tunnelling seems to be important in transfers within highly sterically hindered systems as in the present case, only 2,6-disubstituted pyridines give highly abnormal isotope effects. It would appear that the application of pressure by forcing solvent molecules into the reaction sphere diminishes the importance of tunnelling by increasing the interations between solvent and proton. The present investigation adds to the experimental evidence that pressure studies may be used as a criterion for quantum-mechanical tunnelling.

[9/071 *Received*, 16*th January*, 1979]

REFERENCES

[1] Part 5, N. S. Isaacs, K. Javaid, and E. Rannala, *J.C.S. Perkin II*, 1978, 709.

[2] E. S. Lewis and J. D. Allen, *J. Amer. Chem. Soc.*, 1964, **86**, 2022.

[3] E. S. Lewis and L. H. Funderburk, *J. Amer. Chem. Soc.*, 1967, **89**, 2322.

[4] E. S. Lewis and J. K. Robinson, *J. Amer. Chem. Soc.*, 1968, **90**, 4337.

[5] R. P. Bell and D. M. Goodall, *Proc. Roy. Soc.*, 1966, **A294**, 273.

[6] R. P. Bell, 'The Proton in Chemistry,' Chapman and Hall, London, 1973.

[7] E. Caldin and V. Gold, eds., 'Proton-transfer Reactions,' Chapman and Hall, London, 1975; ch. 10, E. S. Lewis, 'Tunnelling in Hydrogen Transfer Reactions.'

[8] 'Handbook of Chemistry and Physics,' 53rd edn., Chemical Rubber Co., Cleveland, 1973.

[9] B. G. Cox and A. Gibson, *J.C.S. Perkin II*, 1977, 1812.

[10] C. G. Swain, E. C. Stivers, J. F. Reuwer, and L. J. Schaad, *J. Amer. Chem. Soc.*, 1958, **80**, 5885.

[11] H. Wilson, J. D. Caldwell, and E. S. Lewis, *J. Org. Chem.*, 1973, **38**, 564.

[12] S. D. Hamann, *Modern Aspects Electrochem.*, 1974, **9**, 47.

[13] T. Asano and W. J. LeNoble, *Chem. Rev.*, 1978, **78**, 407.

[14] L. Melander, 'Isotope Effects on Reaction Rates,' Ronald Press, New York, 1960.