Effect of Dimethyl Sulfoxide Solvent in the Thermolysis of Alkyl Nitrates Elucidated by the Temperature Dependence of a Kinetic Isotope Effect

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The cyclic, bent TS^{*} of gas-phase thermolytic decomposition of benzyl nitrate has been compared to the analogous thermal elimination of amine oxides in diglyme solution. The use of Me₂SO solvent in amine oxide thermolysis has been shown to alter the TS^{*} to one which accommodates linear H transfer. Me₂SO solvent in the case of benzyl nitrate is now found to afford a nearly quantitative conversion to benzaldehyde. Other alkyl nitrates show a similarly facile reaction to produce good yields of the carbonyl product. However, through measurement of the temperature dependence of $k_{\rm H}/k_{\rm D}$ with benzyl- α -d nitrate it is found that the TS^{*} for decomposition is little altered by comparison with the gas-phase thermolysis reaction. The differences in behavior of the amine oxide and alkyl nitrate reactions in Me₂SO and the possible origins of these differences are discussed briefly.

The gas-phase elimination of nitrite ion from benzyl nitrate (1) has been claimed¹ to involve a cyclic TS^{*} of nonlinear H transfer on the basis of a temperature-independent isotope effect $(k_{\rm H}/k_{\rm D} = A_{\rm H}/A_{\rm D} = 1.42)$. This TS^{*} was suggested to be quite analogous to that characterized² for the thermolysis of amine oxides in an inert solvent, as shown for comparison purposes in Chart I. The temperature-independent isotope effect determined for the amine oxide thermolysis $(k_{\rm H}/k_{\rm D} = A_{\rm H}/A_{\rm D} = 2.21)^2$ is, however, noticeably larger than that for the nitrate thermolysis. Among the questions which arise in this connection is the one which asks how the magnitude of a temperature-independent isotope effect is related to features of the TS^{*} geometry.

It must be emphasized that the nitrate thermolysis was conducted in the absence of solvent, while it has already been shown that certain solvents can influence both the magnitude and nature of the isotope effect in an amine oxide thermolysis when they are capable of a bonding interaction with the **2b** oxyanion function.³ This is certainly the case where the solvent used was dimethyl sulfoxide (Me₂SO). Through its ability to coordinate the amine oxyanion to the sulfoxide center in 3, Me₂SO thus destroys the pseudopericyclic nature⁴ of **2b** and subsequently transforms it into a seven-membered cyclic TS^{*} of product-like structure **3a**.



We proposed, therefore, to assess the effect of a solvent in the nitrate thermolysis reaction in order to understand its influence (if any) on the isotope effect. It is well-known⁵ that ionizing solvents of protic nature cause solvolytic cleavage of the C-O bond in nitrates and give rise to an entirely different product composition than the thermolytic





reaction under study. The course of reaction in the presence of aprotic, high dielectric solvents has not (to the best of our knowledge) been previously described. By using Me_2SO as the solvent, we could hope to gain a full comparison with the TS^* change we have observed to occur in the amine oxide reaction.

Results and Discussion

The gas-phase reaction of 1 has previously been shown¹ to be a unimolecular process forming the product of HNO_2 elimination, namely, the aldehyde. The gas-phase thermolyses of simple nitrates,⁶ e.g., ethyl nitrate, have been shown to travel another road, with the reaction showing signs of a radical chain-cleavage mechanism which forms little or no aldehyde. When alkyl nitrates such as *n*-octyl nitrate or α -phenethyl nitrate are decomposed at temperatures of 140–180 °C in relatively dry (distilled over CaH₂) Me₂SO solution, a vigorous evolution of nitrogen oxides is observed but *no reduction products* of Me₂SO such as methyl sulfide are formed. The product readily isolated in the *n*-octyl case in >80% recovered yield was identified as the octanal corresponding to the stoichiometry expressed in eq 1. The product isolated from α -phenethyl

$$CH_3(CH_2)_6CH_2ONO_2 \xrightarrow{\Delta} CH_3(CH_2)_6CHO + HNO_2$$
(1)

nitrate in similar recovered yields proved to be acetophenone (see eq 2). The analogous reaction of benzyl

$$C_{6}H_{5}CH(CH_{3})ONO_{2} \xrightarrow{\Delta} C_{6}H_{5}C(CH_{3}) = 0 + HNO_{2}$$
(2)

nitrate gave benzaldehyde in near quantitative yield.

To determine whether the Me₂SO had entered the TS^{*} of this nitrate thermolysis in the same way that it had participated in the amine oxide thermolysis, we undertook measurement of the temperature dependence^{2,3,7} of $k_{\rm H}/k_{\rm D}$

⁽¹⁾ Kwart, H.; George, T. J.; Horgan, A. G.; Lin, Y. T. J. Org. Chem. 1981, 46, 1970.

⁽²⁾ Kwart, H.; George, T. J.; Louw, R.; Ultee, W. J. Am. Chem. Soc. 1978, 100, 3927.

⁽³⁾ Kwart, H.; Brechbiel, M. W. J. Am. Chem. Soc. 1981, 103, 4650.
(4) Ross, J. A.; Seiders, R. P.; Lemal, D. M. J. Am. Chem. Soc. 1976, 98, 4325.

⁽⁵⁾ Baker, J. W.; Heggs, T. G. J. Chem. Soc. 1955, 516.

⁽⁶⁾ Levy, J. B. J. Am. Chem. Soc. 1954, 76, 3254, 3790.

Table I. Primary Kinetic Deuterium Isotope Effect in Thermolysis of Benzyl- α -d Nitrate in Dimethyl Sulfoxide Solution as a Function of Temperature^d

	temp, °C	time at temp, ^a min	$m_{\rm L}/m_{\rm H}^{b}$	$k_{\rm H}/k_{\rm D}^{c}$	
_	100	600	0.6733 ± 0.0002	1.304 ± 0.002	
	120	360	0.6743 ± 0.0003	1.302 ± 0.001	
	140	180	0.6728 ± 0.0001	1.305 ± 0.003	
	160	30	0.6731 ± 0.0003	1.305 ± 0.002	
	180	10	0.6722 ± 0.0002	1.307 ± 0.001	

^a More than the time required for complete decomposition of the substrate as evidenced by complete cessation of gas evolution. ^b The ratio of mass 287/mass 286. For $C_6H_5CHNNHC_6H_3(NO_2)_2$, $m_L/m_H = 6.158 \pm 0.002$; for $C_6H_5CDNNHC_6H_3(NO_2)_2$, $m_L/m_H = 0.0514 \pm 0.0003$. There were 15 000 mass spectral ratio determinations per sample. ^c The equation below expresses the value of the isotope effect corrected for the presence of other isotopic elements in the molecular composition and the small contributions of extraneous fragment peaks.

$$\begin{aligned} k_{\rm H}/k_{\rm D} &= 1/\left[\left(1 - \frac{1}{1 + m_{\rm L}/m_{\rm H}} \right) - \left(\frac{0.0514}{1 + 0.0514} \right) / \\ \left(\frac{1}{1 + m_{\rm L}/m_{\rm H}} \right) - \left(\frac{1}{1 + 6.158} \right) \right] \\ \\ ^{d} \text{ Average } k_{\rm H}/k_{\rm D} &= 1.305 \pm 0.002; \text{ standard deivation} = \\ 1.82 \times 10^{-3}; \text{ Variance} &= 2.46 \times 10^{-6}. \end{aligned}$$

for this reaction. A pressure bottle fitted with a solventresistant, elastomeric diaphragm was charged with 50 mL of dried Me₂SO and brought to a stipulated reaction temperataure in a thermostat. When thermal equilibrium was established, the nitrate was injected through the stopple under vigorous agitation of the contents. The evolved gases could escape freely through a stainless needle in the stopple which vented the flask during injection of the nitrate reactant.

The data in Table I were obtained by thermolysis of benzyl- α -d nitrate in Me₂SO solution over an 80 °C temperature interval and analysis of the deuterium contents of the benzaldehyde 2,4-dinitrophenyldrazone derivative by means of the high-precision mass spectrometric technique developed for very accurate mass ratio measurements.⁸ The temperature-independent isotope^{2,3,7} effect $(k_{\rm H}/k_{\rm D} = A_{\rm H}/A_{\rm D} = 1.30)$ computed from these data, though slightly smaller than the gas-phase value previously measured,¹ is still larger than the maximum value of the frequency factor ratio $(A_{\rm H}/A_{\rm D} = 1.2)$ determined through model calculations for linear H-transfer transition states.⁹ We may infer, therefore, that in Me_2SO , as in the unimolecular gas-phase process previously studied,¹ the decomposition of benzyl nitrate has a five-membered, pseudopericyclic⁴ TS^{*} resembling that shown in 2a.

Conducting the reaction in Me₂SO clearly does not involve any significant alteration in mechansim. That is to say, the TS^{*} is not altered through the coordinative participation of a Me₂SO molecule, which was ascertained³ to be the case in amine oxide thermolysis as is illustrated in 3. The incorporation of the Me_2SO in this altered, linear, H-transfer TS* is evidently due to the high, available electron density on the (unhydrated) oxyanion function. This attacks the electron-deficient sulfur in the Me₂SO and thereby transmits to the sulfoxide oxygen the anionic charge capability necessary for the cyclic H abstraction. The seven-membered cyclic arrangement, which accommodates the coaxial (O.-H.-C) H-transfer geometry shown in 3a, is uniquely consistent with the temperature-dependent isotope effect^{3,7} $[k_{\rm H}/k_{\rm D} = 1.14 \exp(-695/RT)]$, where $[\Delta E_{\rm a}]_{\rm D}^{\rm H} \leq 1.15 \text{ kcal/mol and } A_{\rm H}/A_{\rm D} < 1.15 \text{ kcal/mol and } A_{\rm H}/A_{\rm D} < 1.15 \text{ kcal/mol and } A_{\rm H}/A_{\rm D} < 1.15 \text{ kcal/mol and } A_{\rm H}/A_{\rm D} < 1.15 \text{ kcal/mol and } A_{\rm H}/A_{\rm D} < 1.15 \text{ kcal/mol and } A_{\rm H}/A_{\rm D} < 1.15 \text{ kcal/mol and } A_{\rm H}/A_{\rm D} < 1.15 \text{ kcal/mol and } A_{\rm H}/A_{\rm D} < 1.15 \text{ kcal/mol and } A_{\rm H}/A_{\rm D} < 1.15 \text{ kcal/mol and } A_{\rm H}/A_{\rm D} < 1.15 \text{ kcal/mol and } A_{\rm H}/A_{\rm D} < 1.15 \text{ kcal/mol and } A_{\rm H}/A_{\rm D} < 1.15 \text{ kca$ 1.2,⁹ found for amine oxide thermolysis in Me₂SO.

The failure to realize any bonding participation of the Me₂SO in the reaction of benzyl nitrate is to be correlated with the fact that (unlike the amine oxyanion center) the nucleophilic characteristic of the nitrate oxyanion center in undertaking attack on the Me₂SO sulfur is extremely low, though its basicity is apparently sufficient to effect proton transfer in the pseudopericyclic⁴ (sigmatropic) mechanism shown in 2a. The catalysis of this cyclic mechanism of nitrite ellimination by strong alkoxide bases¹⁰⁻¹² is, moreover, effected through a process which greatly increases the basicity of the nitrate group and provides stronger equipment (in 4) for bringing about an intramolecular, sigmatropic H transfer. This is depicted for the case of the hindered base tert-butoxide anion as shown in eq 3.



However, the Me₂SO obviously has a significant influence on the rate of the cyclic elimination, and this is most plainly manifest in the reduced value of $A_{\rm H}/A_{\rm D}$ compared to the value in the gas-phase reaction. One is inclined to attribute this to a classical solvent effect.¹³ The unimolecular cyclic elimination process, occurring in a hole within the highly structured Me₂SO solvent, is made more probable by restrictions in bond free rotations and, in all likelihood, by a shortened distance of angular O---H transfer accompanying the solvent striction influence.

Synthetic Applications

The high yields obtained in the decomposition of alkyl nitrates in Me₂SO suggest that this might prove to be a useful synthetic route for introducing a carbonyl group through conversion of an alcoholic function. The problem, however, lies in the necessity of making the alkyl nitrate from the alcohol in a simple way. The present procedure^{1,10} requires intermediate conversion to the alkyl halide, followed by reaction with silver nitrate. This is far too cumbersome and expensive and thus recommends against any general synthetic application of the method. Other widely recognized procedures for preparing nitrate esters from alkanols such as the use of HNO_3 -H₂SO₄ frequently involve conditions of acid concentrations which are incompatible with the presence of acid-sensitive functional groupings, for example, double- and triple-bond structures in unsaturated alkanols. However, we are presently exploring alternative methods of preparing nitrates, via the reaction of alcohols with the inexpensive and readily available reagent nitryl chloride, which do not appear to possess these limitations.

⁽⁷⁾ See for a full discussion: (a) Kwart, H.; Latimore, M. C. J. Am. Chem. Soc. 1971, 93, 3770. (b) Kwart, H.; Nickle, J. H. Ibid. 1973, 95, 3994; 1976, 98, 2881. (c) Kwart, H.; Sarner, S. F.; Slutsky, J. Ibid. 1973,

⁽⁸⁾ See for further discussion: (a) Kwart, H.; Stanulonis, J. J. Am. Chem. Soc. 1976, 98, 4009. (b) Kwart, H.; Barnette, W. E. Ibid. 1977, 99, 614. (c) Kwart, H.; Streith, J.; Benko, D. A.; Schuppiser, J. L. Ibid. 1978, 100, 6502.

⁽⁹⁾ Schneider, M. E.; Stern, M. J. J. Am. Chem. Soc. 1972, 94, 1517.

⁽¹⁰⁾ Buncel, E.; Bourns, A. N. Can. J. Chem. 1960, 38, 2457.
(11) Smith, P. J.; Pollack, C. A.; Bowins, A. N. Can. J. Chem. 1975.

^{53, 1319.} (12) Pollack, C. A.; Smith, P. J. Can. J. Chem. 1971, 49, 3856.

⁽¹³⁾ Kwart, H.; Lilley, T. H. J. Org. Chem 1978, 43, 2374.

Experimental Section

Preparation of Benzyl- α -*d* **Alcohol.** Under mechanical stirring of a lithium aluminum deuteride (99.8% Aldrich) suspension in anhydrous ether (2.0 g, 0.48 mol) was added dropwise freshly distilled benzaldehyde (20.0 g, 1.90 mol). The reaction mixture was heated to reflux after all the benzaldehyde was added and maintained at reflux for 12 h. After the mixture cooled to ambient temperature, 5 mL of water was added dropwise, followed by 5 mL of 10% aqueous KOH. The precipitated salts were filtered with a sintered-glass funnel, and the filtrate was washed with saturated salt solution. After the mixture was dried over MgSO₄, the solvent was stripped off on a rotary evaporator. The residue consisting of nearly pure product was used directly in the following procedure.

Preparation of Benzyl- α -*d* **Chloride.** The crude alcohol from the preceding procedure was added to 100 mL of benzene. Pyridine (24.4 mL) was then added dropwise under stirring, following which the reaction flask was cooled in a water-ice mixture while thionyl chloride (21.9 mL) was added slowly under stirring. After all the reagents were in, the mixture was heated to reflux and maintained at reflux for 12 h. After cooling, the mixture was diluted with water and extracted with ether. The combined ether extracts were washed with 10% aqueous NaOH and then 6 N HCl, followed by distilled water washing to neutrality. The neutral ether solution was then dried over MgSO₄ and the solvent stripped off on a rotary evaporator. The crude residue was shown to be almost pure product and was used as such in the following procedure.

Preparation of Benzyl- α **-***d* **Nitrate.** A solution of the crude product (from the procedure above) was made with 50 mL of acetonitrile. This was added dropwise to a stirred solution of AgNO₃ (40.0 g, 0.236 mol) in 150 mL of acetonitrile. After all the reagents were mixed, the resulting solution was allowed to stand for 5 days at ambient temperature. The precipitated AgCl was filtered off on a sintered-glass filter, and the filtrate was poured into an ice-water mixture. The product was then extracted with methylene chloride, the combined extracts were dried over MgSO₄, and the solvent, was stripped off on a rotary evaporator. The residue was carefully vacuum distilled through a short packed column, with good product¹⁰ collected in a narrow range around 115 °C (10 mm). Analysis of the product by GLC showed only a single peak on two different columns. Analysis by NMR showed complete monodeuteration within the usual precision of the 60-MHz instrument $\pm 5\%$). The yield of this product resulting from the sequence of steps starting with 2 g of lithium aluminum deuteride was 8.25 g.

Preparation and Thermolysis of Octyl Nitrate and α -Phenethyl Nitrate. *n*-Octyl bromide (1.61 g, 0.0078 mol) and α -phenethyl chloride (2.32 g, 0.0166 mol) were converted to their respective nitrates in the same manner as benzyl chloride (see above) was converted to benzyl nitrate by using silver nitrate (5 g, 0.029 mol, and 10 g, 0.059 mol, respectively).

The thermolyses of the crude nitrates were carried out exactly as described in the kinetic procedure at 180 °C. The crude product remaining after evaporation of the pentane solvent was converted to the DNPH derivative, the yields of which exceeded 80% of theory on the basis of the octyl bromide and α -phenethyl chloride starting materials: acetophenone DNPH derivative, mp 105 °C (lit.¹⁴ mp 106 °C); octanal DNPH derivative, mp 235 °C (lit.¹⁴ mp 238 °C).

Kinetic Procedure. A Pyrex pressure bottle was charged with 50 mL of dry (distilled over CaH₂) Me₂SO and sealed with an inert elastomer stopple. The bottle was allowed to equilibrate with the thermostat at the chosen temperature (± 0.05 °C). When thermal equilibrium was attained, a sample of ~ 300 mg of benzyl- α -d nitrate was rapidly injected under vigorous agitation of the contents of the bottle in the bath, while the evolving gases were vented through a fine needle inserted in the stopple and connected to an indicating bubbler tube. When gas evolution had completely subsided and the reaction was completed, the bottle was withdrawn from the bath. After cooling, the resulting Me₂SO solution of the product was diluted with 100 mL of water and extracted with three 30-mL portions of pentane. The combined extracts were dried, and the solvent was carefully stripped to leave a nearly quantitative yield (>95%) of benzaldehyde (as determined gravimetrically via the DNPH derivative).

In each case, the benzaldehyde residue after removal of most of the pentane was immediately converted to the 2,4-dinitrophenylhydrazone derivative. Mass ratio analysis via the highprecision mass spectrometric technique previously described⁸ was performed directly on the DNPH derivative;¹⁵ (see Table I).

Registry No. Benzyl-2-d alcohol, 4546-45-6; benzaldehyde, 100-52-7; benzyl-2-d chloride, 79449-94-8; benzyl-2-d nitrate, 76946-77-5; octyl nitrate, 629-39-0; α -phenethyl nitrate, 7214-65-5; octyl bromide, 111-83-1; α -phenethyl chloride, 672-65-1; acetophenone DNPH, 1677-87-8; octanal DNPH, 1726-77-8; dimethyl sulfoxide, 67-68-5; benzaldehyde DNPH, 1157-84-2.

New Approach to the Mechanism of the Reaction between Benzyl Grignard Reagents and Carbonyl Compounds

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The reaction of the [(1-naphthyl)methyl]magnesium chloride with ketones can lead to the formation of ortho alcohols 4, normal alcohols 3, or enolates. We propose a mechanism for the reaction whose first step, as in the case of aldehydes, is a reversible attack of the ketone at the ortho position of the benzylic Grignard reagent, which can then lead to the formation of the normal alcohol and/or enolate. The fact that benzylmagnesium chloride reacts with cyclobutanone to give a diol analogous to that obtained in reactions with aldehydes, while its reaction with 1,1,1-trifluoro-2-propanone does not give a diol, leads us to propose an interpretation involving steric effects in the rearrangement alkoxide. In the case of ketones, these steric interactions generally prevent the Prins-type reaction leading to diols.

In a previous study of the reaction of [(1-naphthyl)methyl]magnesium chloride with monomeric formaldehyde¹ we proposed a mechanism to explain the formation of diols in the reaction of this benzyl Grignard

⁽¹⁴⁾ Shriner, R. L.; Fuson, R. C.; Curtin, D. Y.; Morrill, T. C. "The Systematic Identification of Organic Compounds", 6th Ed.; Wiley: New York, 1980.

⁽¹⁵⁾ The likelihood of biasing the isotope ratio measurements by partial recovery of the labeled reaction product was deemed to be very remote for two reasons: (a) the >95% recovery of the DNPH derivative (by gravimetric determination) and (b) calibration experiments where the known isotope ratio in a benzaldehyde sample was determined by an independent (mass spectral) method.