were identified by GC/FTIR and comparison of IR spectra to those of known compounds kindly supplied by Dr. McHale.[9]

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Supplementary Material Available: Tables of complete composition vs time data for linalyl and geranyl acetate solvolysis under all conditions and structures of minor products (7 pages). Ordering information is given on any current masthead page.

1,3-Dialkyltriazenes: Tautomeric Equilibria and Rates and Products of Decomposition†

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Unsymmetrical 1,3-dialkyltriazenes, RN=NNHR′, exist as a tautomeric mixture because of rapid proton exchange between nitrogens 1 and 3. Hydronium ion catalyzed decomposition of these triazenes gives rise to a mixture of alkanediazonium ions, RN_2^+ and $R'N_2^+$, and the corresponding primary amines. The objective of this study was to determine the factors that influence partitioning between the two pathways originating from the two tautomers. A series of 1-alkyl-3-methyltriazenes, where the alkyl groups were ethyl, *n*-propyl, *n*-butyl, isopropyl, *tert*-butyl, and benzyl, were prepared. A new, and potentially less hazardous, preparation of low molecular weight alkyl azides was developed. The corresponding symmetrical 1,3-dialkyltriazenes were also prepared. The rates of decomposition in aqueous buffers were measured. The general kinetic behavior suggested that the overall mechanism was specific acid catalysis in glycine buffer, in keeping with previously published data on symmetrical dialkyltriazenes (*J. Am. Chem. Soc.* **1986**, *108*, 3726–3730). The products of the decomposition of unsymmetrical triazenes were determined quantitatively, with particular reference to the alcohols formed by hydrolysis of the diazonium ions, RN_2^+ and $R'N_2^+$. The tautomeric distributions of the unsymmetrical triazenes were determined by NMR in various solvents, and it was found that Lewis base solvents (methanol, THF, acetone) capable of forming a hydrogen bond to the triazene gave very similar distributions, which was markedly different from solvents such as dichloromethane or chloroform. For each triazene, the tautomer in which the larger alkyl group is located on nitrogen 1 was favored. It was assumed that the distribution in water was similar to that observed in methanol. The rates of tautomerization were measured by dynamic NMR methods. Quantitative analysis of the combined data indicated that the unsymmetrical triazenes obeyed the Curtin–Hammett principle. Both the rates of decomposition of the triazenes and the ratios of the products are a function of the rates of decomposition of the conjugate acids of the tautomers and the mole fraction and basicity of the individual tautomers. The analysis also provides a means of predicting the ratios of alkanediazonium ions derived from unsymmetrical triazenes.

Introduction

The synthesis[1,2] and kinetics of proteolytic decomposition of 1,3-dialkyltriazenes,[3] 1,3,3-trialkyltriazenes,[4,5] and 1,3-dialkyl-3-acyltriazenes[6] have been described. The preceding papers on dialkyltriazenes, however, dealt only with those compounds in which the alkyl substituents on N(1) and N(3) were the same (e.g., 1,3-dimethyltriazene (DMT), 1,3-diethyltriazene (DET), etc.). An additional complication arises when unsymmetrical 1,3-dialkyltriazenes are considered, because they exist as pairs of isomers in tautomeric equilibrium (see below).

We have shown previously[3] that the proteolytic decomposition of 1,3-dialkyltriazenes is initiated by a rapid and reversible proton transfer to N(3) and subsequent heterolysis of the protonated triazene to an alkanediazonium ion and an alkylamine. In the case of the unsymmetrical triazenes, the equilibrium distribution of the tautomeric forms may play a significant role in the determination of the rate of reaction and of the direction of heterolysis, which could lead to the formation of two diazonium ions, RN_2^+ and/or $R'N_2^+$ (and the primary amines $R'NH_2$ and RNH_2, respectively).

This paper seeks to study this problem. A series of unsymmetrical 1-alkyl-3-methyltriazenes were prepared together with the corresponding symmetrical 1,3-dialkyltriazenes. The rates of decomposition of these triazenes were determined in aqueous buffers; the yields of the alcohols, formed from the hydrolysis of the diazonium ions, were measured; and the tautomeric equilibria and the rates of proton transfers between N(1) and N(3) were measured

† This paper is dedicated with best wishes to Professor R. Preussmann, German Cancer Research Center, Heidelberg, on the occasion of his 60th birthday.

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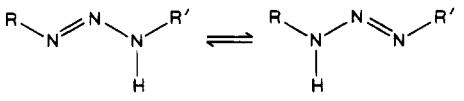
for the unsymmetrical triazenes by NMR spectroscopy.

The present work describes the decomposition of the following 1,3-dialkyltriazenes in aqueous buffers. For convenience of notation, unsymmetrically substituted 1,3-dialkyltriazenes will be referred to by a single name, although, as shown here and discussed later, these substances exist as a mixture of two tautomeric isomers, A and B.



A			B		
	R	R′		R	R′
DMT	Me	Me	MET	Me	Et
DET	Et	Et	MPT	Me	*n*-Pr
DPT	*n*-Pr	*n*-Pr	MBT	Me	*n*-Bu
DBT	*n*-Bu	*n*-Bu	MIT	Me	*i*-Pr
DIT	*i*-Pr	*i*-Pr	MTT	Me	*t*-Bu
DTT	*t*-Bu	*t*-Bu	MBzT	Me	benzyl

Experimental Section

Safety Note. Triazenes are potent biological alkylating agents and should be considered to be toxic and potentially carcinogenic. Efficient hoods and protective clothing should be used at all times. Alkyl azides are potentially explosive, and suitable precautions should be observed.

Materials. All chemicals were reagent grade (Aldrich), used as purchased without further purification. Buffers for kinetic measurements were prepared as described previously[5] with water distilled from $KMnO_4$. A Fisher Accumet Model 825MP digital pH meter and a Fisher (13-639-270) high ionic strength combination electrode (calomel reference) were used in pH measurements. IR spectra were obtained on a Perkin-Elmer Model 297 spectrophotometer. UV spectra were recorded on either a Hewlett-Packard Model 8450A double-beam diode-array processor or a Shimadzu Model UV-260 spectrophotometer. NMR spectra were obtained on a Varian XL-200 spectrometer.

Ethyl Azide. Sodium azide (13.0 g, 0.20 mol) was added at room temperature to a stirred suspension of iodoethane (15.6 g, 0.10 mol), tetrabutylammonium tetrafluoroborate (1.65 g, 0.005 mol), diethyl ether (40 mL), and water (15 mL). The reaction mixture was sealed with a neoprene stopper, shielded from light, and stirred vigorously at room temperature. After 7 days, IR analysis of the ether layer showed an intense azide band at approximately 2100 cm^{-1}. (This band did not appreciably increase upon further stirring.) The ether layer was separated, diluted with 100 mL of pentane, and dried two times over anhydrous sodium sulfate.

The resulting solution could be used directly in reactions with organometallic reagents to prepare 1,3-dialkyltriazenes (see following). Typical triazene yields in excess of 46% based on starting alkyl halide were obtained from using such solutions. Storage of the solution at −20 °C for several weeks before use caused no significant diminution in triazene yield; however, prolonged storage of these hazardous materials is not recommended.

Preparation of Triazenes. The synthesis of DMT[2] (λ_{max}230, log ϵ 3.90), DET[2] (λ_{max} 232, log ϵ 3.92), and DIT[3] (λ_{max} 237, log ϵ 3.86) have been described earlier. The unsymmetrical triazenes, MET (bp 48 °C, 40 mmHg; λ_{max} 231, log ϵ 3.89), MPT (bp 57 °C, 31 mmHg; λ_{max} 231, log ϵ 4.04), MIT (bp 44 °C, 30 mmHg; λ_{max} 231, log ϵ 3.89), MBT (bp 69 °C, 24 mmHg; λ_{max} 232, log ϵ 3.77), MTT (bp 29 °C, 10 mmHg; λ_{max} 230, log ϵ 3.99), and MBzT (bp 30 °C, 0.02 mmHg; λ_{max} 232, log ϵ 4.08) were prepared from the appropriate alkyl azides and methyllithium. DPT (bp 60 °C, 9 mmHg; λ_{max} 234.4, log ϵ 4.06) and DBT (bp 85 °C, 5 mmHg; λ_{max} 234, log ϵ 3.82) were prepared in an analogous manner from the appropriate alkyl azides and Grignard reagents. DTT (bp 40 °C, 9 mmHg; λ_{max} 241, log ϵ 3.95) was prepared by the method of Brand and Roberts[7] from *tert*-butyllithium and *tert*-butyl azide.[8]

Product Studies. The alcohol products of the decomposition of each of the 1,3-dialkyltriazenes were determined on 5.0×10^{-3} M solutions of the triazene in pH 9.5 aqueous buffers of either 0.1 M sodium phosphate or 0.1 M glycine at 25 °C. The ionic strength of each buffer was maintained at 0.3 M by the addition of appropriate amounts of sodium perchlorate. Buffer was added to a weighed amount of the triazene, and after careful mixing to assure solution, the reactions were allowed to stand sealed at 25 °C for a minimum of 24 h before analysis. A measured amount of a solution of an internal standard (generally some other low molecular weight alcohol) was added, and the product alcohols were separated on a 6 ft × 2 mm ID glass column packed with Super-Q (80–100 mesh). The column temperature varied somewhat with the alcohol to be analyzed, but was generally in the vicinity of 140 °C. These separations were carried out on a Perkin-Elmer Sigma III-B gas chromatograph equipped with an FID detector. The output was interfaced to an Apple II+(64K) computer equipped with an Interactive Microware Ada-AMP amplifier and Ada-Lab data acquisition board. Detector responses for each of the product alcohols versus the appropriate internal standard were determined prior to analysis.

The method of analysis for MBzT was different due to the low water solubility of benzyl alcohol. After MBzT had been decomposed in aqueous buffers as described for the other triazenes, a known amount of a solution of ethanol was added and the reaction solution analyzed for methanol, as described above. To determine the amount of benzyl alcohol in the samples, a known amount of an ether solution of 1-hexanol (internal standard) was added to the reaction mixture. The reaction solution was then extracted with 10 mL of ether and the ether solution separated on a 6 ft × 2 mm ID glass column packed with 10% OV-1 on Chromosorb G (100–120 mesh) and operated at 90 °C. The gas chromatograph and data acquisition system described above were used in these analyses. Replicate solutions containing weighed amounts of benzyl alcohol were treated in a similar manner to obtain detector response values for benzyl alcohol versus 1-hexanol and to verify that this method is reproducible within ±5%.

Kinetic Studies. Rates of triazene decomposition in aqueous solution were followed spectrophotometrically with a Shimadzu model UV-260 UV spectrophotometer. The analog output of absorbance versus time was recorded on an Apple IIe computer equipped with an Interactive Microwave Ada-Lab data acquisition board. The reaction solutions were contained in thermostated 1-cm cells, the temperature being held constant to within ±0.1 °C. The disappearance of each triazene was followed by monitoring the change in absorbance at its respective λ_{max} (recorded in triazene preparation section). In a typical kinetic run, the reaction cuvette was charged with buffer (1.341 mL) and the reaction was initiated by the addition of 9 μL of a 4.5×10^{-3} M solution of the triazene in acetonitrile; the final triazene concentration was 3.0×10^{-5} M. The reference cuvette contained 1.341 mL of buffer and 9 μL of acetonitrile. A minimum of 100 absorbance vs time points were measured over 3.5 half-lives. The first-order rate constants were calculated from these data by means of a computer program based on the Guggenheim approximation least-squares method.[9]

Results and Discussion

Synthesis of Triazenes. The preparation followed the methods that were described previously.[1,2] One item, however, deserves note. The synthesis of 1,3-dimethyltriazene, 1-ethyl-3-methyltriazene, and 1,3-diethyltriazene involves the preparation of the highly unpredictable methyl and ethyl azides. We have found that these azides can be prepared readily, and with minimum handling, by a phase-transfer reaction of methyl iodide or ethyl iodide in pentane with sodium azide, catalyzed by tetra-*n*-butylammonium hydrogen sulfate. These reactions proceed smoothly, and the alkyl azides do not need to be isolated from the organic layer before use in the next step. The detailed procedure is described in the Experimental Section.

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Table I. Rate of Hydrolysis of 1,3-Dialkyltriazenes[a] in 0.1 M Aqueous Buffer,[b] pH 9.50, 25 °C

R	R′	glycine buffer: k_{obsd} ± SD s^{-1} × 10^4	calcd from eq 4: k × 10^4	phosphate buffer: k_{obsd} ± SD s^{-1} × 10^4
Me	Me	1.10 ± 0.005		12.0 ± 0.2
Et	Et	4.46 ± 0.01		19.6 ± 0.2
Pr	Pr	6.38 ± 0.06		
Bu	Bu	7.38 ± 0.02		15.5 ± 0.06
i-Pr	*i*-Pr	15.5 ± 0.02		27.5 ± 0.2
t-Bu	*t*-Bu	24.7 ± 0.2		
Me	Et	3.16 ± 0.04	3.64	15.6 ± 0.1
Me	Pr	4.09 ± 0.05	5.30	
Me	Bu	4.55 ± 0.002	6.10[c]	15.4 ± 0.06
Me	*i*-Pr	13.5 ± 0.03	13.50	25.3 ± 0.04
Me	*t*-Bu	275.4 ± 3.1	22.98	
Me	Bz	0.237 ± 0.008		1.17 ± 0.007

[a] Triazene concentration 3.0×10^{-5} M. [b] Ionic strength 0.3 M maintained with $NaClO_4$. [c] Tautomer distribution assumed to be the same as in MPT (see Table III).

Rates of Decomposition in Buffer. The rates of decomposition of all of the triazenes were measured at pH 9.5 in a 0.1 M glycine buffer. The first-order rate constants are listed in Table I. The kinetics of some of the triazenes were also determined in phosphate buffer at the same pH; these rates constants are also presented in Table I. As was found earlier[3] with symmetrical 1,3-dialkyltriazenes, the decomposition in phosphate buffer was significantly faster than in amino acid buffers, such as glycine. We ascribed that difference in rate to the involvement of the phosphate buffer components in the rate-determining step (specific acid catalysis followed by a general base).

The rates of decomposition of the symmetrical 1,3-dialkyltriazenes in glycine buffer increased with the increasing complexity of the alkyl groups, $CH_3 < CH_3CH_2 < n\text{-}C_3H_7 \sim n\text{-}C_4H_9 < i\text{-}C_3H_7 < t\text{-}C_4H_9$. The increases, however, were not large, since the greatest difference, between methyl and *tert*-butyl, was only by a factor of 20. The observed order of reactivity is consistent with corresponding carbonium ion or diazonium ion stabilities, and consequently, the order does not provide information on the actual species formed in the rate-determining step.

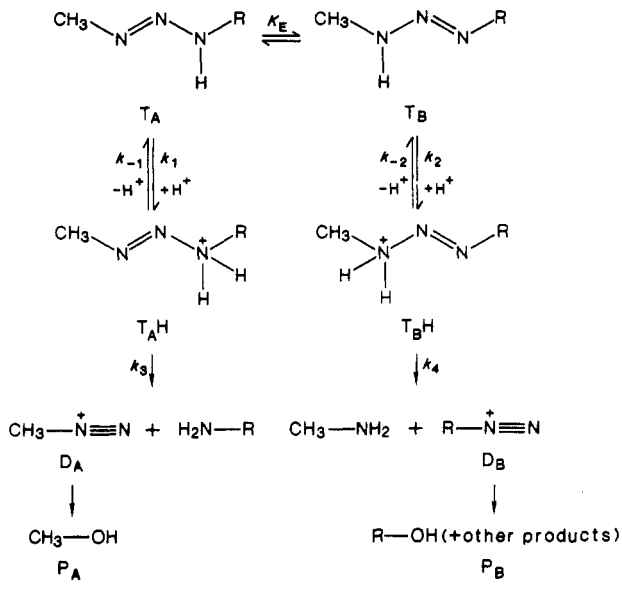
The unsymmetrical triazenes involve an additional level of complexity. The rates of decomposition of 1-ethyl-3-methyl-, 1-propyl-3-methyl-, and 1-butyl-3-methyltriazenes were virtually the same. The rate of decomposition of 1-isopropyl-3-methyltriazene was 3-fold faster than for the triazenes derived from the primary alkyl groups. The rate of 1-*tert*-butylmethyltriazene was 20 times faster than that of the isopropyltriazene. These kinetics were cleanly first-order, which suggests that the tautomeric equilibrium is established rapidly (see below). The observed rate constants, however, must be a composite of at least two rate constants, as indicated in Scheme I.

The overall decomposition of the triazenes is governed by the Curtin–Hammett principle, namely, that the equilibrium distribution of tautomers T_A and T_B affects the rate of total triazene disappearance, but may or may not be the sole determinant of the product distribution.[10]

The tautomer distribution effect on the rate arises from the fact that the overall rate is the sum of the rates of decomposition of the individual tautomers.

$$\frac{dT}{dt} = \frac{dT_A}{dt} + \frac{dT_B}{dt}$$

Scheme I



This leads to the following expression for the observed rate constant:

$$k_{obsd} = \frac{k_3 N_A}{K_{a(T_AH)}} + \frac{k_4 N_B}{K_{a(T_BH)}} \quad (1)$$

where N_A and N_B are the mole fractions of T_A and T_B, respectively, and the K_a's are the respective dissociation constants of the protonated tautomers. Although the acid equilibrium constants for the triazenes are not available, we argue that the *order* of these constants should be similar to the *order* of the K_a's of the corresponding primary amines. Surprisingly, the pK_a's of all primary amines, methylamine through *tert*-butylamine, are remarkably similar (pK_a = 10.59 ± 0.04). The only exception is benzylamine, which is a significantly weaker base than the others, pK_a = 9.34.[11] Therefore, it seems unlikely that the K_a terms play a significant role in overall rate constants, with the possible exception of the benzyl case. Consequently, the differences in the observed rate constants for the symmetrical and unsymmetrical triazenes must be a function of the tautomer distribution and the specific rate constants for the decomposition of the individual protonated tautomers. This implies that an estimate of the rates of decomposition of the unsymmetrical triazenes can be made from the rates of the corresponding symmetrical triazenes, if the tautomer distribution is known.

Tautomer distribution information may be obtained by low-temperature NMR studies, which, unfortunately, prevent measurement in water. The NMR spectra of triazenes are complicated by several dynamic phenomena. Firstly, the slow rotation of the N(2)–N(3) bond contributes to line broadening at temperatures slightly below room temperature,[1] precluding the accurate use of the coalescence temperature for the tautomerization measurement. In order to suppress the rotation, the NMR measurements have to be carried out at low temperatures. Lower temperatures are also required to slow the rate of the proton interchange so that the individual tautomers can be observed. The tautomer distributions of two unsymmetrical triazenes, methylethyltriazene (MET) and

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Table II. Effect of Solvent on Tautomeric Distribution of Unsymmetrical 1,3-Dialkyltriazenes[a] at −66 °C

$CH_3N{=}N{-}NHR \rightleftharpoons (CH_3)HN{-}N{=}NR$
A B

solvent	% tautomer B[b] R = Et	% tautomer B[b] R = *i*-Pr
toluene-d_8	62	75
$CDCl_3$	62	83.8
CD_2Cl_2	62.8	83.9
THF-d_8	76	95.3
acetone-d_6	74.8	95.0
CD_3OD	75.7	95.5

[a] Concentration of triazene, 0.068 M. [b] Obtained from the ratio of CH_3 ^1H NMR signals; N(1) ca. δ 2.85, N(3) ca. δ 3.35.

Table III. Tautomeric Distribution of Unsymmetrical 1,3-Dialkyltriazenes[a] at −66 °C

$CH_3N{=}N{-}NHR \rightleftharpoons (CH_3)HN{-}N{=}NR$
A B

R	% tautomer B[b] CD_2Cl_2	% tautomer B[b] CD_3OD
Et	62.9	75.7
Pr	64.6	79.6
t-Bu	68.8	>92.7
Bz	72.9	86.2
i-Pr	83.9	95.5

[a] Concentration of triazene, 0.068 M. [b] Obtained from the ratio of CH_3 ^1H NMR signals; N(1) ca. δ 2.85, N(3) ca. δ 3.35.

methylisopropyltriazene (MIT), were measured in several solvents of varying polarity at −66 °C. These data are presented in Table II. It is clear that the nonpolar solvents (toluene, chloroform, and dichloromethane) favor a more equal distribution, while the solvents that contain a proton acceptor atom (THF, acetone, and methanol) favor the tautomer with the larger alkyl group on N(1). Moreover, there is very little change in the distribution between tautomers in the latter group of solvents. Consequently, we can assume that the distribution in aqueous buffers will be similar to that in methanol. Some variations in this tautomer distribution might be expected at 25 °C, but these are expected to be minor. Determinations nearer 25 °C, through the use of coalescence temperatures, were deemed less satisfactory due to the expected errors from the other dynamic phenomena mentioned above. Table III presents the tautomer distribution for several unsymmetrical triazenes in dichloromethane and in methanol. We elected to use the values in methanol.

The estimate of the rates of decomposition of the unsymmetrical triazenes can be made in the following manner, using MET as an example. Equation 1 can be modified by the assumption that the acid dissociation constants K_a for the triazene tautomers are linearly related to the dissociation constants for the corresponding primary amines ($MeNH_3^+$ and $EtNH_3^+$), with c being the propotionality constant. Therefore, we write

$$k_{MET} = \frac{k_3 N_{1\text{-Me}}}{cK_{a(EtNH_3^+)}} + \frac{k_4 N_{1\text{-Et}}}{cK_{a(MeNH_3^+)}} \quad (2)$$

where $N_{1\text{-Et}}$ and $N_{1\text{-Me}}$ are the mole fractions of 1-ethyl-3-methyltriazene and 3-ethyl-1-methyltriazene, respectively, and k_4 and k_3 are the specific rate constants for the decomposition of the respective protonated tautomers. We estimated k_3 (for MET) from eq 3, wherein k_3 is assumed

$$k_3 \cong k_{dis} = k_{DMT}(cK_{a(MeNH_3^+)}) \quad (3)$$

to be the same as the rate constant, k_{dis}, for the dissociation of protonated DMT, k_{DMT} being the observed rate constant for the decomposition of DMT. The constant k_4 can be estimated from an analogous equation for DET. The rate of decomposition of MET can now be estimated by substituting the expressions for k_3 and k_4 into eq 2 to obtain eq 4, recalling that the K_a's for methyl- and ethylamine

$$k_{MET} = k_{DMT}N_{1\text{-Me}} + k_{DET}N_{1\text{-Et}} \quad (4)$$

are essentially identical. The mole fractions $N_{1\text{-Et}}$ and $N_{1\text{-Me}}$ can be obtained from the data in Table III. The value calculated for k_{MET} by using eq 4 is 3.64×10^{-4} s^{-1}. The experimentally determined value (Table I) is 3.16×10^{-4} s^{-1}. The calculated values for the other triazenes are also presented in Table I. It is clear that this simple analysis is successful in predicting the rates of the unsymmetrical triazenes. Consequently, the underlying assumption that these rates are governed by the tautomeric equilibria and by the specific rates of decomposition of the protonated tautomers appears to be correct. It should be pointed out that the influence of the tautomer distribution plays a relatively minor role in determining the rate since the variation in mole fractions of the favored tautomer ranged only from 0.76 to near unity. A further point is the simplification arising from the near equivalence of the approximated tautomer basicities. Thus, the critical feature that determines the rate of decomposition of the unsymmetrical triazenes is the propensity of the protonated tautomers to undergo heterolysis.[12]

The calculated rate of decomposition of 1-*tert*-butylmethyltriazene, MTT, is off by 1 order of magnitude from the experimentally observed value. Its rate is actually closer to that which would have been predicted from comparison of solvolytic rates for various alkyl bromides.[13] This suggests that a rate prediction based on the rate of 1,3-di-*tert*-butyltriazene, DTT, is incorrect because the rate of DTT is unusually slow. It is difficult to understand the reason for the anomalous behavior of DTT. Several explanations are possible but unfortunately cannot be distinguished on the basis of the present data. Ab initio SCF calculations on the protonation of triazenes[14] have suggested that one possible pathway for their decomposition involves the acid-catalyzed isomerization via N(1) protonation of the normal *E* configuration to the *Z* and subsequent heterolysis of that isomer. The *Z* configuration of DTT would be impossibly crowded, and hence, the compound would have to decompose by a different path. Another possibility is that the protonation of DTT is difficult because the highly hydrophobic *tert*-butyl group would prevent the water of solvation from approaching the cationic center. A third, and perhaps the most likely,

(12) A referee correctly pointed out that the foregoing discussion omits consideration of N(1) protonation of each tautomer, a point that we have previously addressed (see ref 14). A more precise statement of eq 1, which takes N(1) protonation into account, would be

$$k_{obsd} = \frac{K_{a(T_AH_1)}k_3N_A}{K_{a(T_AH_3)}} + \frac{K_{a(T_BH_1)}k_4N_B}{K_{a(T_BH_3)}}$$

where the subscript, x, on T_AH_x and T_BH_x refers to site of protonation on the respective tautomers. This equation can be reduced to

$$k_{obsd} = \frac{[T_AH_3]k_3N_A}{[T_AH_1]} + \frac{[T_BH_3]k_4N_B}{[T_BH_1]}$$

However, it is expected that the N(3)/N(1) protonation ratios for the various symmetrical triazenes will be similar, and consequently the N(1) protonation terms as expressed in a modified form of eq 3 will cancel after substitution into eq 2. Thus, eq 4 will remain unchanged by inclusion of the N(1) protonation preequilibrium.

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(14) Schmiedekamp, A.; Smith, R. H.; Michejda, C. J. *J. Org. Chem.* **1988**, *53*, 3433–3436.

Table IV. Activation Parameters[a] for Hydrolysis of 1,3-Dialkyltriazenes[b] in 0.1 M Glycine Buffer,[c] pH 9.00

R	R′	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, cal/(mol K)
Me	Me	13.7	12.8
Me	Et	12.6	11.0
Me	*i*-Pr	11.6	10.7
Me	Bz	14.9	13.3

[a] Calculated by using values of $k_{obsd} \times [H_3O^+]^{-1}$; $[H_3O^+] = 1.0 \times 10^{-9}$ M. Duplicate runs at four temperatures spanning the range of 25–40 °C were used for each determination. Least-squares analysis of each of the lines gave a correlation coefficient of at least 0.999. [b] Triazene concentration 3.0×10^{-5} M. [c] Ionic strength 0.3 M, maintained with $NaClO_4$.

explanation is that, because of the various stereoelectronic peculiarities of this hindered molecule, DTT decomposes by an altogether different mechanism than that which appears to operate for the other triazenes, and therefore, predictions based on its rate of decomposition are inaccurate. Resolution of this point will have to await further experimentation.

As noted earlier, the identity of the cationic species formed in the rate-determining step is uncertain. The behavior of 1-benzyl-3-methyltriazene (MBzT) may be instructive in this regard. From Table I, it can be seen that the rate of hydrolysis of MBzT is exceptionally slow compared with that of the other triazenes. Benzylamine is a significantly weaker base than the other amines considered (pK_a = 9.34 versus ~10.5 for the other amines), and so N(3) protonation in the 3-benzyl-1-methyl tautomer should be less favorable than in the 1-benzyl-3-methyl tautomer. Further, Table IV shows that the tautomer distribution of MBzT favors the 1-benzyl species ($N_{1\text{-Bz}}$ = 0.86). Therefore, the rate of decomposition of MBzT may be expected to proceed predominantly through the N(3) conjugate acid of the 1-benzyl tautomer. These observations can be used to obtain a comparison for the specific rate constants for the two competing rate-determining steps. Division of eq 2 for MBzT by eq 3 for DMT gives eq 5. Rearranging this expression gives eq 6, which, when

$$\frac{k_{MBzT}}{k_{DMT}} = \frac{K_{a(MeNH_3^+)}N_{1\text{-Me}}}{K_{a(BzNH_3^+)}} + \frac{k_4 N_{1\text{-Bz}}}{k_3} \qquad (5)$$

evaluated, results in the value $k_4/k_3 = 0.241$.

$$\frac{k_4}{k_3} = \left(\frac{k_{MBzT}}{k_{DMT}} - \frac{K_{a(MeNH_3^+)}N_{1\text{-Me}}}{K_{a(BzNH_3^+)}}\right)\frac{1}{N_{1\text{-Bz}}} \qquad (6)$$

Clearly, the rate constant for formation of a cationic species from a benzyl moiety is less favorable than that from a methyl group. Even allowing for the approximations made is this calculation, this result speaks strongly in favor of a rate-determining formation of an alkanediazonium ion, not an alkyl carbonium ion.

Further support for this conclusion is found from an activation-parameter analysis of the reaction, Table IV. The activation parameters for MBzT are remarkably similar to those for DMT; the slightly higher values for both the enthalpy and entropy of activation reflect the somewhat slower rate of MBzT as compared with DMT. If the decomposition of MBzT involved the synchronous formation of the benzyl cation, nitrogen, and methylamine, the activation parameters would be dramatically different. For example, depending on the location of the transition state on the reaction coordinate, the entropy term could be much more negative (transition state product-like) or more positive (transition state with a decreased number of degrees of freedom). Since the activation parameters for MBzT are close to the other entries in Table IV, particularly those for DMT, we favor decomposition to the phenylmethanediazonium ion rather than the benzyl cation.

Products of Decomposition of 1,3-Dialkyltriazenes. The yields of alcohols from the decomposition of the symmetrical and unsymmetrical 1,3-dialkyltriazenes were examined in the same buffers as were used for the kinetic runs. The decision to analyze alcohol rather than amine products was based on the desire to observe the actual extent of alkylation resulting from the competitive formation of cationic intermediates. The alcohol data are presented in Table V (glycine buffer) and Table VI (phosphate buffer). In general for the unsymmetrical triazenes, the yields in the glycine buffer tended to favor the more substituted alcohols, as opposed to methanol, but the total yields were very similar in both buffer systems. Some of the alkanediazonium ions, particularly those derived from the branched alkyl groups, decomposed to alkenes in addition to alcohols. These were not quantified, but their amounts could be estimated from the alcohol yields of the symmetrical triazenes.[5] The yields of the alcohols were determined to provide some information on the influence of tautomer distribution on product yields. According to the Curtin–Hammett principle, the yields from tautomers in rapid equilibrium should not be dependent solely on the tautomeric equilibrium constant.[10] The unsymmetrical 1,3-dialkyltriazenes should provide a

Table V. Product Yields from Hydrolysis of 1,3-Dialkyltriazenes[a] in 0.1 M Glycine Buffer,[b] pH 9.50, 25 °C

R	R′	R–OH (1-ROH, 2-ROH)	Me–OH	R–OH/Me–OH	k_4/k_3[c]	k_4/k_3[d]
Me	Me		93.8 ± 2.2			
Et	Et	78.0 ± 2.1				
Pr	Pr	46.2 ± 0.3				
		(30.2 ± 0.8, 16.0 ± 0.1)				
Bu	Bu	76.4 ± 1.9				
		(49.6 ± 1.5, 26.8 ± 0.4)				
i-Pr	*i*-Pr	53.6 ± 1.1				
t-Bu	*t*-Bu	36.2 ± 1.8				
Me	Et	63.4 ± 0.5	14.3 ± 1.6	4.43	1.42	3.47
Me	Pr	34.1 ± 0.5	3.79 ± 0.06	9.00	2.30	4.41
		(21.8 ± 0.4, 12.3 ± 0.1)				
Me	Bu	73.5 ± 2.2	8.4 ± 0.3	8.75	2.24	4.94
		(45.6 ± 1.5, 27.9 ± 0.7)				
Me	*i*-Pr	59.4 ± 0.9	2.5 ± 0.3	23.8	1.12	12.8
Me	*t*-Bu	32.1 ± 0.2	≪0.2	≥160	≥12.6	270
Me	Bz	49.7 ± 2.0	43.1 ± 0.7	1.15	0.01	0.242

[a] Triazene concentration 5.0×10^{-3} M. [b] Ionic strength 0.3 M maintained with $NaClO_4$. [c] Calculated from product data by using eq 7 and again assuming proportionality between primary amine and triazene basicities. [d] Calculated from the rate data in Table I by using an equation analogous to eq 6.

Table VI. Product Yield from Hydrolysis of 1,3-Dialkyltriazenes[a] in 0.1 M Phosphate Buffer,[b] pH 9.50, 25 °C

R	R′	R–OH (1-ROH, 2-ROH)	Me–OH	R–OH/ Me–OH
Me	Me		73.8 ± 1.4	
Et	Et	80.5 ± 2.1		
Pr	Pr	51.0 ± 1.1		
		(34.6 ± 0.8, 16.4 ± 0.3)		
Bu	Bu	70.6 ± 2.7		
		(46.8 ± 1.5, 23.8 ± 1.2)		
i-Pr	*i*-Pr	47.0 ± 1.1		
t-Bu	*t*-Bu	36.9 ± 2.0		
Me	Et	46.9 ± 2.3	24.8 ± 1.4	1.89
Me	Pr	29.7 ± 0.4	7.97 ± 0.22	3.73
		(19.7 ± 0.2, 10.0 ± 0.1)		
Me	Bu	60.1 ± 2.1	19.7 ± 1.6	3.05
		(39.4 ± 1.7, 20.7 ± 0.4)		
Me	*i*-Pr	43.9 ± 2.5	11.7 ± 0.6	3.75
Me	*t*-Bu	35.3 ± 1.4	0.9 ± 0.01	39.2
Me	Bz	27.1 ± 1.2	45.9 ± 1.0	0.59

[a] Triazene concentration 5.0×10^{-3} M. [b] Ionic strength 0.3 M maintained with $NaClO_4$.

Table VII. Rate of Tautomerization of 1,3-Dialkyltriazenes[a] in CD_3OD at 22 °C

R	R′	k, s^{-1}	h,[b] Hz	$\delta\nu$ N(3)–N(1), Hz
Me	Et	2040	8.7	106
Me	Pr	1750	9.04	100
Me	*i*-Pr	1650	10.44	104.2
Me	*t*-Bu	8.5	20.85	102
Me	Bz	4360	4.21	108

[a] Triazene concentration 0.068 M. [b] Width of CH_3 at half-height.

very good test of the principle, since it is also possible to estimate the rate of interconversion of the tautomers, because the rate is slow on the NMR time scale. We used the line broadening of the methyl group of the alkylmethyltriazenes in methanol-d_4 at 22 °C to calculate the rate of interconversion of the tautomers. At that temperature, the rate of rotation around the N(2)–N(3) bond in the triazenes is rapid and does not contribute to the line width.[1] The rate of tautomerization was calculated from the equation[15]

$$k = (\pi/2)\delta\nu[(\delta\nu/h)^2 - (h/\delta\nu)^2 + 2]$$

where $\delta\nu$ is the difference in frequency (in Hz) between the 1-methyl and the 3-methyl, and h is the width of the methyl resonance at half-height, given in Hz. The rate constants calculated in this manner, together with the relevant parameters, are presented in Table VII. It is clear that the rate of tautomer interconversion is at least 3 orders of magnitude faster than the rate of decomposition. This suggests that the tautomer distribution is not the only factor that determines the product distribution.

The product distribution can be analyzed by reference to Scheme I. It can be assumed that the formation of the alkanediazonium ions $CH_3N_2^+$ (D_A) and RN_2^+ (D_B) is not reversible and that the rate of formation of the alcohols CH_3OH (P_A) and ROH (P_B) is equivalent to the rate of formation of the diazonium ions, i.e.,

$$\frac{dD_A}{dt} = \frac{dP_A}{dt} \text{ and } \frac{dD_B}{dt} = \frac{dP_B}{dt}$$

Assuming a steady state for the protonated tautomers T_AH and T_BH ($k_{-1} \gg k_3$ and $k_{-2} \gg k_4$), the following expression for the ratio of alcohols can be derived, where K_E is the

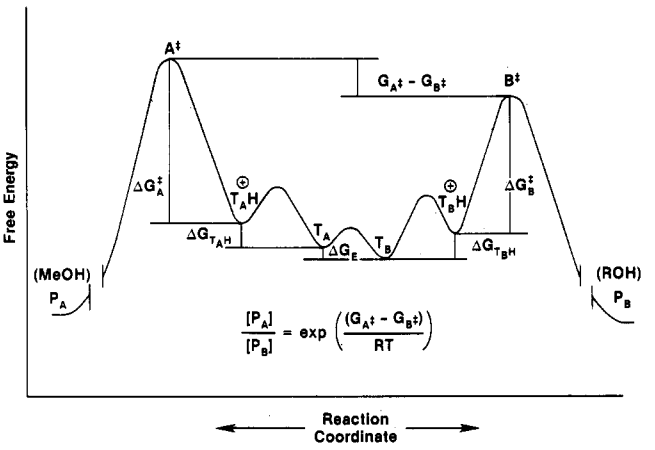

Figure 1. Qualitative free-energy diagram for conversion of unsymmetrical 1,3-dialkyltriazenes to alcohol products. Designations of intermediates are as in Scheme I, with A‡ and B‡ as transition states. The breaks preceding products indicate omission of steps following the rate-determining steps.

tautomeric equilibrium constant for the conversion of T_A to T_B, that is, T_B/T_A.

$$\frac{P_B}{P_A} = \frac{k_4 K_{b(T_B)} K_E}{k_3 K_{b(T_A)}} \quad (7)$$

Substitution of the appropriate free-energy values in a manner similar to that used by Eliel[16] yields eq 8. The

$$\frac{P_B}{P_A} = \exp[(\Delta G_A^{\ddagger} + \Delta G_{T_AH} - \Delta G_E - \Delta G_{T_BH} - \Delta G_B^{\ddagger})/RT] \quad (8)$$

relationship of the free-energy changes can be visualized from Figure 1, where it can be seen that

$$\Delta G_A^{\ddagger} + \Delta G_{T_AH} - \Delta G_E - \Delta G_{T_BH} - \Delta G_B^{\ddagger} = \Delta G_A^{\ddagger} - \Delta G_B^{\ddagger}$$

and thus

$$\frac{P_B}{P_A} = \exp[(\Delta G_A^{\ddagger} - \Delta G_B^{\ddagger})/RT] \quad (9)$$

The final equation (9) indicates that the ratio of the product alcohols is a function only of the difference in transition-state energies. It should be emphasized, however, that this does *not* mean that the product ratios are independent of the tautomeric distribution and the pK_a of the individual tautomers. Thus eq 7 and 9 are not mutually contradictory. This issue is discussed in detail by Seeman.[10] Measurement of the alcohol yields provides an independent method of calculating the k_4/k_3 ratio previously determined from kinetic results, provided that the tautomeric distribution and the relative basicities are known. For convenience, the last column in Table V presents k_4/k_3 values calculated (eq 6) from observed rate constants for comparison with product yield ratios. There is reasonable agreement between these two sets of independently determined ratios, considering that a number of assumptions were made to calculate these values. For MBzT, k_4/k_3 is less than 1, further supporting the rate-determining formation of the alkanediazonium ion.

It thus appears clear that, for the decomposition of unsymmetrical 1,3-dialkyltriazenes in aqueous buffers, the overall rate is a function of triazene tautomer distribution and basicity as well as the stability of a cationic species

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(16) Eliel, E. L. *Stereochemistry of Carbon Compounds*; McGraw-Hill: New York, 1962; pp 234–239.

formed in the rate-determining step. In keeping with the Curtin-Hammett principle, the distribution of product alcohols also is a function of the triazene tautomer distribution and basicity and the relative rates of the competing rate-determining steps. We must conclude from our results that the cationic species is most probably an alkanediazonium ion, rather than an alkyl carbonium ion.

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Structural and Energetic Analysis of Gas-Phase Hydrated Ammonium Ions with Relevance to the "Anomalous" Order in Amine Basicities

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The underlying cause for the anomalous basicity of the methylamine series in aqueous solution is investigated. The proton affinity of the amines in the gas phase follows the order ($NMe_3 > NMe_2H > NMeH_2 > NH_3$) due in large part to the inductive effect of the methyl group. The aqueous-phase basicity order from protonation enthalpies is $NH_2Me > NH_3 > NHMe_2 > NMe_3$. An *E*, *C*, and *W* analysis of the gas-phase data for reaction of these amines with $(H_2O)_nH^+(g)$ was used to incorporate these acid–base interactions into the correlation. One of the key factors leading to the observed basicity order in aqueous solution is the increased fractional importance of the electrostatic interaction as *n* increases in the gas-phase $(H_2O)_nH^+$ species. The species with $n = 6$ undergoes an essential electrostatic interaction with the small covalent contribution giving an order that differs slightly in magnitude from the pure electrostatic order of the E_B numbers. The gas-phase proton affinities follow the trend of the amine C_B numbers though an appreciable electrostatic contribution occurs. In view of these differences, the gas-phase proton is concluded to be a poor model for predicting the chemistry of $H(H_2O)_n^+$ in aqueous solution. The *E*, *C*, and *W* analysis clearly shows that the addition of four and possibly up to as many as six water molecules to the ammonium ions leads to water clusters as opposed to water acting as a Lewis base toward the other NH protons of ammonia or methyl- or dimethylamine. Semiempirical intermediate neglect of differential overlap calculations were carried out in conjuction with the *E*, *C*, and *W* analysis. Both the *E*, *C*, and *W* and MO analyses conclude that hydrogen bonding of water (as a Lewis base) molecules up to $n = 6$ to the additional amine protons in ammonia, primary and secondary amines is disfavored in relation to binding this water to protons on oxygen forming a water chain in the gas-phase systems.

Introduction

The advent of ICR and related techniques for studying gas-phase ion equilibria has led to many interesting comparisons of gas phase to solution chemistry[1] with differences often attributed to solvation and no attempt made to discuss the fundamental interactions involved. The acceptance of such statements as "explanations" has served to cloud a basic understanding of the molecular interactions involving the solvent. In protonic solvents the term solvation is as difficult to define as is the chemical bond. In the extremes, the coordination (Lewis acid–base interactions) that hold clusters of solvent bound to the solute can be distinguished from a bulk dielectric effect (Born charging) that solvates these clusters. Variation in cluster size and the dynamics of these processes add to the complexity. We shall use the term nonspecific solvation for gross dielectric effects caused by the solvent and the term acid–base for specific, directional interactions involving localized sites that hold clusters of molecules together.

In this article, we explore solvation effects in aqueous protonation and gain further insight about the often analyzed "anomalous order" of amine basicities.[2] Gas phase data indicate that increased methyl substitution increases amine basicity toward H^+ as evidenced by more positive proton affinities.[1] This trend follows the inductive effect

Table I. Amine Proton Affinities and Aqueous Enthalpies of Protonation

base, B (*C*, *E*)	$-\Delta H$ $BH(g)^+$ or PA[a]	$-\Delta H$ $BH^+(aq)$[b]	$-\Delta H$ B(aq)[c]
NH_3 (3.32, 1.48)	204.0	12.5	8.5
NH_2Me (5.63, 1.50)	214.1	13.2	11.1
$NHMe_2$ (8.47, 1.33)	220.6	12.0	13.2
NMe_3 (11.20, 1.19)	225.1	8.8	13.2
H_2NEt (5.91, 1.51)	217.0	13.7	13.0
$HNEt_2$ (8.59, 1.11)	225.6	12.8	15.3
NEt_3 (10.83, 1.29)	232.3	10.3	16.7

[a] Equation 1, ref 5b. [b] $B(aq) + H^+(aq) \rightarrow BH^+(aq)$, ref 3. [c] $B(g) + H_2O(aq) \rightarrow BH_2O(aq)$, ref 5b.

(1) See for example: Aue, D. H.; Bowers, M. J. *Gas Phase Ion Chemistry*; Bowers, M. J., Ed.; Academic Press: New York, 1979 (and references therein).

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