DETSB has proved to be a useful force field for our current studies.

In Table VI of the supplementary material[20] we present the details of the four force fields used in the calculations described in Tables IIA, IIB (supplementary material), and IV. All constants have been converted to the same units so that intercomparisons are possible. ALL71 uses a displaced center for computing van der Waals interactions with hydrogen atoms; this is 0.9 the distance along the C–H bond. The listing for ALL71 omits the interaction terms; these are not used in the other three force fields.

Calculations. Molecular mechanics calculations were carried out with the program MOLMEC.[39] The data in the tables in this paper were processed with data base programs on microcomputers. Copies of MOLMEC and associated programs are available on request.

Acknowledgment. This work was supported in part by a grant from the National Science Foundation and in part by an NIH grant. This work was also supported in part by a grant of computing time by Florida State University.

Appendix: Example Calculation of Correction Terms for FSE

To obtain the *d* terms for eq 6 for the DETSB force field we set up eq A1 (eq 5). We then set up the five equations

$$\text{FSE} = 0 = \text{SE} - d(\text{CH}_3)n(\text{CH}_3) - d(\text{CH}_2)n(\text{CH}_2) \quad \text{(A1)}$$

A2. Solution gives $d(\text{CH}_3) = 0.121$ and $d(\text{CH}_2) = 0.785$.

$$\text{FSE} = 0 = 1.81 - d(\text{CH}_3) \times 2 - d(\text{CH}_2) \times 2 \quad \text{butane}$$

$$\text{FSE} = 0 = 2.60 - d(\text{CH}_3) \times 2 - d(\text{CH}_2) \times 3 \quad \text{pentane}$$

$$\text{FSE} = 0 = 3.38 - d(\text{CH}_3) \times 2 - d(\text{CH}_2) \times 4 \quad \text{hexane}$$

$$\text{FSE} = 0 = 4.17 - d(\text{CH}_3) \times 2 - d(\text{CH}_2) \times 5 \quad \text{heptane}$$

$$\text{FSE} = 0 = 4.95 - d(\text{CH}_3) \times 2 - d(\text{CH}_2) \times 6 \quad \text{octane} \quad \text{(A2)}$$

Substituting these values into eq A3 gives d(CH) = 2.237.

$$\text{FSE} = 0.70 = 4.05 - 0.121 \times 3 - 0.785 \times 1 - d(\text{CH}) \quad \text{2-methylbutane}$$

$$\text{FSE} = 0.70 = 4.88 - 0.121 \times 3 - 0.785 \times 2 - d(\text{CH}) \quad \text{2-methylpentane}$$

$$\text{FSE} = 0.70 = 5.67 - 0.121 \times 3 - 0.785 \times 3 - d(\text{CH}) \quad \text{2-methylhexane}$$

$$\text{FSE} = 0.70 = 6.45 - 0.121 \times 3 - 0.785 \times 4 - d(\text{CH}) \quad \text{2-methylheptane} \quad \text{(A3)}$$

Substitution into A4 gives d(C) = 4.803. These are the *d*

$$\text{FSE} = 1.40 = 7.42 - 0.121 \times 4 - 0.785 \times 1 - d(\text{C}) \quad \text{2,2-dimethylbutane}$$

$$\text{FSE} = 1.40 = 8.28 -0.121 \times 4 - 0.785 \times 2 - d(\text{C}) \quad \text{2,2-dimethylpentane}$$

$$\text{FSE} = 1.40 = 9.07 - 0.121 \times 4 - 0.785 \times 3 - d(\text{C}) \quad \text{2,2-dimethylhexane} \quad \text{(A4)}$$

values reported in Table I. The same procedure is to be used with any other force field.

We now illustrate the calculation of the FSE value of 2,2,3,4-tetramethylpentane based on SE = 17.91, eq A5.

$$\text{FSE} = 17.91 - 0.121 \times 6 - 2.237 \times 2 - 4.803 \times 1 = 7.91 \quad \text{(A5)}$$

These values may be compared with the entires in Table IIA.

Registry No. Ethane, 74-84-0; propane, 74-98-6; butane, 106-97-8; pentane, 109-66-0; hexane, 110-54-3; heptane, 142-82-5; octane, 111-65-9; 2-methylpropane, 75-28-5; 2-methylbutane, 78-78-4; 2-methylpentane, 107-83-5; 2-methylhexane, 591-76-4; 2-methylheptane, 592-27-8; 2,4-dimethylpentane, 108-08-7; 2,5-dimethylhexane, 592-13-2; 2,2-dimethylpropane, 463-82-1; 2,2-dimethylbutane, 75-83-2; 2,2-dimethylpentane, 590-35-2; 2,2-dimethylhexane, 590-73-8; 3,3-dimethylpentane, 562-49-2; 3,3-dimethylhexane, 563-16-6; 2,2,3-trimethylbutane, 464-06-2; 2,2,3-trimethylpentane, 564-02-3; 2,2,4-trimethylpentane, 540-84-1; 2,3,3-trimethylpentane, 560-21-4; 2,2,3,3-tetramethylbutane, 594-82-1; 2,2,3,3-tetramethylpentane, 7154-79-2; 2,2,3,4-tetramethylpentane, 1186-53-4; 2,2,4,4-tetramethylpentane, 1070-87-7; 3,3,5,5-tetramethylheptane, 61868-61-9; 2,2,4,4,5-pentamethylhexane, 60302-23-0; tri-*tert*-butylmethane, 35660-96-9.

Supplementary Material Available: Formal steric enthalpies Tables IIB, IV, and VI (force fields), 2nd pictorial conformational data (33 pages). Ordering information is given on any current masthead page.

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(39) DeTar, D. F.; *Comput. Chem.* 1977, *1*, 141.

(40) In a personal communication, Prof. C. Rüchardt reports $\Delta H = -56.4$. This corresponds to FSE = 36.89.

Substituent Effects and Isokinetic Relations in the Homolysis of Hyponitrite Esters. The Question of Free-Radical Homoconjugation

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Received November 21, 1984

Activation parameters for first-order homolysis of 14 *trans*-hyponitrites (alkyl, benzylic, and benzhydryl) in *tert*-butylbenzene are reported. Activation energies varied from 25–30 kcal/mol and log A/s from 13.2–15.9. These and published activation parameters on hyponitrites could be represented by isokinetic relationships, with all the compounds appearing on a single line ($r = 0.99$) in a double-log plot of calculated rate constants at 70 and 43.7 °C. The effects of α-phenyl substitution and of aromatic ring substituents on the rate constants are discussed in light of possible homoconjugation in the developing alkoxy radicals.

Substituent effects on the rates of homolytic decomposition of azo alkanes[1] and peroxides[2] have been extensively studied. The rates of homolysis of ring-substituted benzyl hyponitrites (eq 1) were measured by DeSousa, who found

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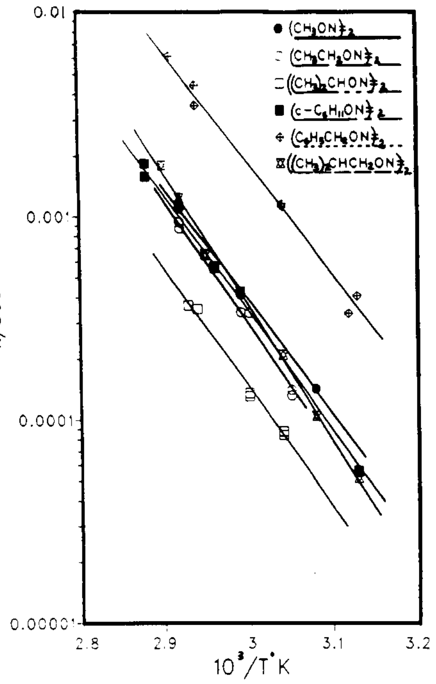

Figure 1. Arrhenius plots of the first-order rate of decomposition of alkyl hyponitrites.

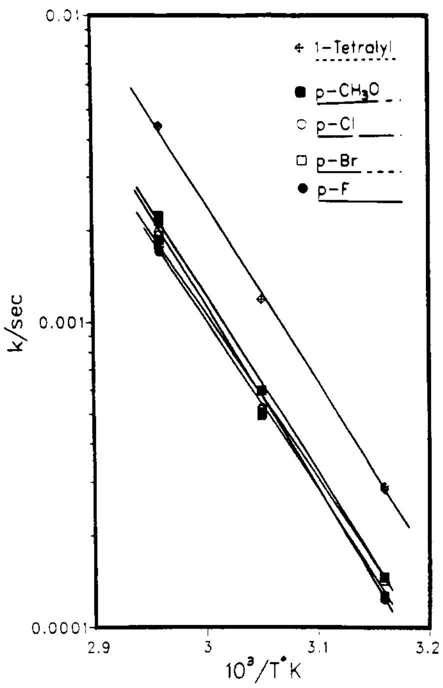

Figure 2. Arrhenius plots of the first-order rate decomposition of hyponitrites with aromatic rings. The lines fall at the left side of the figure in the same order as the captions.

a weak acceleration by electron-withdrawing substituents with $\rho = 0.06$ in the Hammett equation with σ parameters.[3] Dulog and Klein[4] later studied substituted cumyl hyponitrites and found a similar influence of substitutents but a better correlation with values of σ^+ rather than σ, even though the N–O bond was isolated from the ring by a quaternary carbon.

$$(XC_6H_4CR_2ON)_2 \rightarrow N_2 + 2XC_6H_4CR_2O\cdot \quad (1)$$

$$R = H \text{ or } Me$$

$$X = \text{ring substituent}$$

As part of a study of quantum yields of excited states from hyponitrites, we measured activation parameters for substituted 1-phenylethyl esters, which represent an intermediate case, along with a number of other esters. A linear plot of E_a vs. log A in the aliphatic series was presented recently in connection with the thermochemistry of these compounds.[5] In this paper we present an analysis of the available kinetic data on both aliphatic and benzylic hyponitrites in terms of isokinetic and Hammett-type relations.

Experimental Section

Most of the synthetic reagents were purchased from commercial sources and used as received. *tert*-Butylbenzene (Aldrich) was washed with sulfuric acid and aqueous EDTA, and redistilled from sodium before use. The 1-phenylethyl halides and derivatives were purchased (1-phenylethyl bromide, bromodiphenylmethane), prepared from the alcohol (1-tetralol), or otherwise prepared from the substituted acetophenone by reduction with alcoholic $NaBH_4$ followed by reaction with gaseous HCl.[4] *p*-Methoxy-1-phenylethyl alcohol was synthesized from *p*-methoxyacetophenone by Joseph A. Affholter. Alkyl halides were generally passed through silica gel before reaction with silver hyponitrite as described.[4,6] The yields and physical properties of the new compounds prepared in this study are given in Table I.

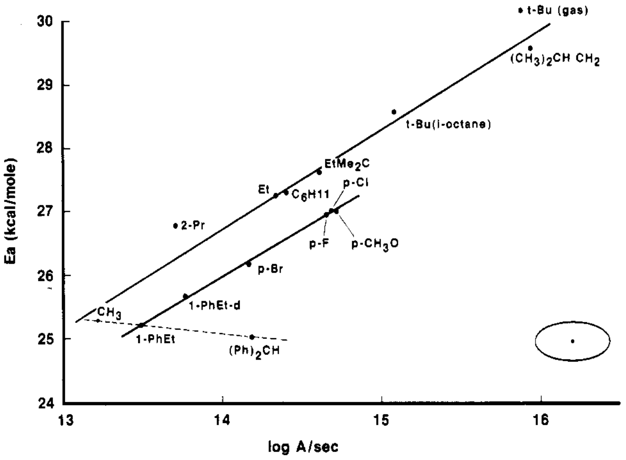

Figure 3. Plot of E_a vs. log A for the decomposition of hyponitrite esters. The axes of the oval represent the average errors of each data point.

Melting points were taken on a Mel-Temp hot stage and are uncorrected. IR spectra were recorded on a Perkin-Elmer Model 283, and NMR spectra with a Varian EMI360 or XL-200FT spectrometer. The kinetic studies were carried out by the chemiluminescence method as described earlier.[6]

Results

The decay of chemiluminescence from solutions of 10^{-3} M primary and secondary hyponitrites in the presence of 0.01 M 4-methyl-2,6-di-*tert*-butylphenol and (2–4) × 10^{-3} M 9,10-dibromoanthracene showed good adherence to first-order kinetics (Table II), and from earlier work[6] we

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(1) Engel, P. S. *Chem. Rev.* **1980**, *80*, 99–150.

(2) Swern, D., Ed. "Organic Peroxides"; John Wiley & Sons, Inc.: New York, 1972; Vol. I–III.

(3) DeSousa, J. B. *Nature (London)* **1963**, *199*, 64–65. In this paper both aromatic substituents were assumed to act on the transition state in an equivalent manner. This will not be the case if the thermolysis is a stepwise process.[5]

(4) Dulog, L.; Klein, P. *Chem. Ber.* **1971**, *104*, 902–908.

(5) Chen, H.-T. E.; Mendenhall, G. D. *J. Am. Chem. Soc.* **1984**, *106*, 6375–6378. Due to an unrecognized plotting error, the isokinetic relationship was described in that paper as a weak one.

(6) Ogle, C. A.; Martin, S. W.; Dziobak, M. P.; Urban, M. S.; Mendenhall, G. D. *J. Org. Chem.* **1983**, *48*, 3728–3733.

Table I. Physical Properties of Hyponitrite Esters

precursor[a]	yield, %	mp, °C	IR, cm^{-1}; ^{1}H NMR (δ from Me_4Si) maxima
$(CH_3)_2CHCH_2I$	20	<−15	2980 s, 2940 m, 2885 s, 1475 s, 1390 s, 1375 s, 1325 s, 1200 s, 1110 m, 1040 s, 965 s, 945 m, 925 m, 790 s; ($CDCl_3$) 3.15 (d, J = 7 Hz), 1.75 (septet, J = 7 Hz), 1.00 (d, J = 7 Hz)
p-$FC_6H_4CHClCH_3$	10	58–59 dec	2840–2980 s 1520 s, 1460 s, 1380 s, 1235 w, 1160 w, 1080 w, 1060 m, 1020 s, 985 s, 835 s, 720 w; ($CDCl_3$) 1.71 (q, 3 H, J = 7 Hz), 5.41 (q, 1 H, J = 7 Hz), 6.80–7.30 (aromatic)
p-$ClC_6H_4CHClCH_3$	21	79–80 dec	2860–2980 s, 1600 w, 1490 m, 1460 s, 1420 m, 1380 s, 1201 m, 1000 s, 980 s, 720 s, 630 s, 610 s, 530 m; ($CDCl_3$) 1.86 (d, 7 Hz), 6.85 (q, 7 Hz), 7.38 (aromatic)
p-$BrC_6H_4CHClCH_3$	13	73–74 dec	2840–2980 s, 1460 s, 1370 s, 1100 w, 1075 s, 1010 s, 1000 s, 985 s, 825 s, 610 s; ($CDCl_3$) 1.71 (d, 3 H, J = 7 Hz), 5.51 (q, 1 H, J = 7 Hz), 7.52 (aromatic)
p-$CH_3OC_6H_4CHClCH_3$	39	69 dec	2860–2980 s, 1610 m, 1510 m, 1460 s, 1380 s, 1250 m, 1180 m, 990 s, 720 m, 610 m; ($CDCl_3$) 1.69 (d, J = 7 Hz), 3.60 (s), 6.70 (q, J = 7 Hz), 7.35 (aromatic)
1-tetralyl-Cl	15	67–68 dec	2860–2980 s, 1455 s, 1380 s, 1150 w, 1010 s, 1000 s, 975 s, 765 s, 720 m; ($CDCl_3$) 5.45 (t, 1 H), 2.82 (q, 2 H), 1.81 (distorted quintet, 2 H), 2.27 (t, 2 H), 7.22 (aromatic)
Ph_2CHBr	12	72 dec	2840–2980 s, 1460 s, 1380 s, 1190 w, 1160 w, 1000 s, 955 m, 875 w, 740 w, 705 s, 650 s; ($CDCl_3$) 6.42 (s, 1 H), 7.20 (aromatic)

[a] Solvent for reaction with $Ag_2N_2O_2$ was hexane except for Ph_2CHBr (CH_2Cl_2).

Table II. Rate Constants for Alkyl Hyponitrite Thermolyses

R in RONNOR	T, °C	10^5 (rate const), s^{-1}
$C_6H_5CHCH_3$	43.7	12.1, 12.5
	55.5	49.5, 49.7
	66.1	173, 175
$C_6H_5CDCH_3$	43.7	10.9, 10.4
	54.7	44.3, 43.4
	65.1	141, 140
c-C_6H_{11}	46.2	5.64, 5.59
	64.4	57.3, 56.2
	73.8	159, 185
$C_6H_5CH_2$	46.5	33.6
	47.6	41.0
	55.7	113, 116
	66.5	355
	67.3	445
	70.2	614
CH_3	51.1	14.3, 14.3
	60.9	41.6, 43.1
	68.9	110, 113
CH_3CH_2	54.4	14.1, 13.2
	60.4	34.0, 33.8
	69.8	94.4, 87.8
$(CH_3)_2CH$	43.7	1.70, 1.75
	55.6	8.44
	55.7	8.78
	60.1	13.6, 13.1
	66.8	35.2
	68.4	36.7
p-$FC_6H_4CHCH_3$	43.7	12.5, 12.4
	54.7	50.0, 50.3
	64.3	171
	65.1	185
p-$ClC_6H_4CHCH_3$	43.7	12.7, 12.6
	54.7	51.7, 52.4
	65.1	199, 193
p-$BrC_6H_5CHCH_3$	43.7	13.4, 12.6
	54.7	49.8, 50.6
	65.1	178, 183
p-$CH_3OC_6H_5CHCH_3$	43.7	14.6, 14.6
	54.7	60.0, 59.9
	65.1	223, 216
1-tetralyl	43.7	29.0, 28.4
	54.7	119, 119
	65.1	444, 441
$(C_6H_5)_2CH$	29.5	16.6
	29.6	13.5
	43.7	104, 105
	55.2	387, 381
$(CH_3)_2CHCH_2$	52.1	12.7
	55.3	19.1
	61.2	43.1
	65.5	65.7, 65.3
	69.7	124
	71.4	186

Table III. Activation Parameters of Hyponitrites in *tert*-Butylbenzene

R in RON═NOR	E_a, kcal/mol	log A, s^{-1}	10^3k, s^{-1}
$C_6H_5CHCH_3$	25.24 ± 0.2	13.49 ± 0.1	0.015[a]
$C_6H_5CDCH_3$	25.69 ± 0.7	13.76 ± 0.2	0.013[a]
c-C_6H_{11}	27.26 ± 0.3	14.40 ± 0.2	5.22[b]
$C_6H_5CH_2$	26.06 ± 0.4	14.37 ± 0.2	0.029[a]
CH_3	25.35 ± 0.4	13.23 ± 0.2	5.20[b]
CH_3CH_2	27.22 ± 0.1	14.33 ± 0.6	4.70[b]
$(CH_3)_2CH$	26.77 ± 0.1	13.71 ± 0.7	2.12[b]
$(CH_3)_2CHCH_2$	29.55 ± 1.0	15.94 ± 0.6	7.18[b]
p-$FC_6H_4CHCH_3$	26.91 ± 0.2	14.65 ± 0.1	0.013[a]
p-$ClC_6H_4CHCH_3$	27.25 ± 0.4	14.90 ± 0.3	0.013[a]
p-$BrC_6H_4CHCH_3$	26.16 ± 0.2	14.16 ± 0.2	0.015[a]
p-$CH_3OC_6H_4CHCH_3$	26.96 ± 0.1	14.76 ± 0.1	0.015[a]
1-tetralyl	27.21 ± 0.1	15.22 ± 0.1	0.030[a]
$(C_6H_5)_2CH$	25.04 ± 0.5	14.27 ± 0.3	

[a] k extrapolated to the isokinetic temperature, 28 °C. [b] k extrapolated to the isokinetic temperature, 84 °C.

equate the luminescence intensity, arising principally from low yields of ketone triplet states,[7] to the relative rate of hyponitrite decomposition. Arrhenius plots of the data appear in Figures 1 and 2, and the derived parameters are given in Table III.[8]

Isokinetic Relations. The data of Table III are plotted in Figure 3 to reveal relationships between the Arrhenius parameters. The aliphatic and monophenyl-substituted hyponitrites follow two nearly parallel lines, with the point for diphenylmethyl hyponitrite removed from the lower line by approximately the distance separating both lines. The dotted line in the figure connects the points for activation parameters for the series in which the H atoms of methyl hyponitrite are successively replaced by phenyls. A similar relation is not obtained, however, on successive substitution of methyl for hydrogen. The "isokinetic" temperatures for the phenyl and aliphatic lines in Figure 3 are 28 and 84 °C, respectively.

The statistical significance of plots such as Figure 3, regardless of their obvious predictive ability, has been questioned.[9] A double-log plot of rate constants calculated with the Arrhenius parameters in Table III at two temperatures that were close to the experimentally limiting ones appears in Figure 4. The resulting plot shows good linearity in addition to heeding statistical propriety. The

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(7) Quinga, E. M. Y.; Mendenhall, G. D. *J. Am. Chem. Soc.* **1983**, *105*, 6520–6521.

(8) The values in Table III have not been rounded off because the rate constants calculated from them would then differ significantly. For instance, the experimental half-lives of benzhydryl hyponitrite at 43.7 °C are 11.1 and 11.0 min. The parameters in Table III gave $t_{1/2}$ = 11.6 min but rounding them to the nearest tenth leads to a predicted $t_{1/2}$ of only 10.1 min at this temperature.

(9) Exner, O. In "Progress in Physical Organic Chemistry"; Streitwieser, A. S., Jr., Taft, R. W., Eds.; Wiley-Interscience: New York, 1973; Vol. 10, p 511 and references therein.

Table IV. Rate Constants and Analysis of Benzylic Hyponitrites according to Hammett Equations with σ and σ^+

		substituent						
R in RON=NOR	T, °C	H	p-F	p-Cl	p-Br	p-CH$_3$O	m-CH$_3$	m-Cl
σ/σ^+			0.06/−0.25	0.23/0.04	0.23/0.03	−0.27/−0.65	−0.07/0.07	0.37/0.40
$C_6H_5CH_2$[a] (10^4k, s^{-1})	35.4	6.60		6.80	6.93		6.22	7.11
$\rho = 0.12 \pm 0.02/\rho^+ = 0.13 \pm 0.02$								
$C_6H_5C(CH_3)_2$[b] (10^4k, s^{-1})	40.0	1.15		1.28	1.28	0.67	1.21	
$\rho = 0.50 \pm 0.11/\rho^+ = 0.42 \pm 0.03$								
$C_6H_5CHCH_3$[c] (10^4k, s^{-1})	43.7	1.20	1.25	1.27	1.30	1.46		
$\rho = -0.11 \pm 0.05/\rho^+ = -0.08 \pm 0.03$								

[a] Data from ref 3. [b] Data from ref 4. [c] This work. Rate constants given as 10^4k, s^{-1}.

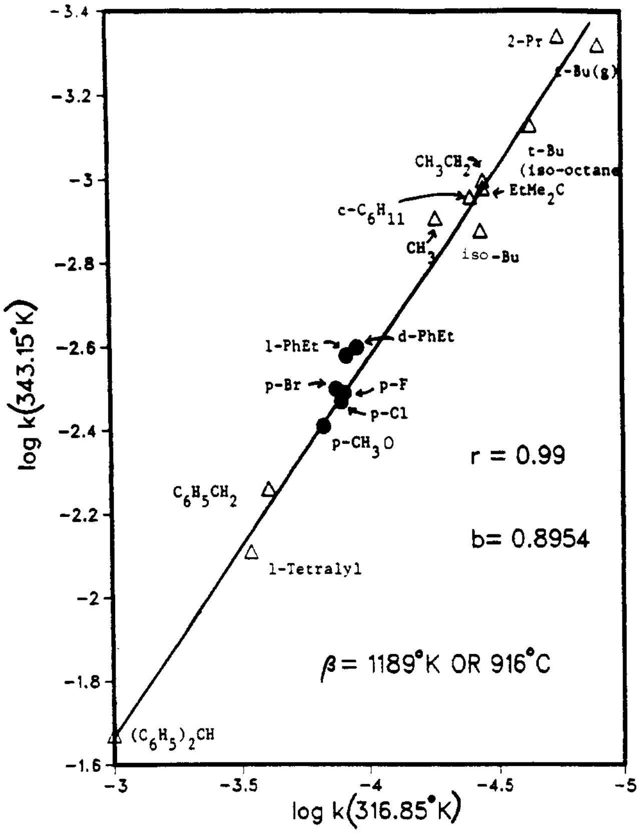

Figure 4. Isokinetic relationship of organic hyponitrites. Kinetic data from this paper and from ref 5 and 6 are included. The para-substituted 1-phenylethyl series appears as filled circles.

slope b of Figure 4 is related to the isokinetic temperature by $\beta = T_1T_2(1 - b)/(T_1 - bT_2)$, which gives β = 1189 K (916 °C). The Arrhenius plots (Figure 1 and 2) do not uniformly intersect at the isokinetic temperatures predicted from the slopes of the lines in either Figure 3 or 4.

Hammett-Type Relations. We have analyzed our data on phenylethyl hyponitrites, the data of Ho and DeSousa on benzyl hyponitrite, and of Dulog and Klein[4] on cumyl hyponitrite with σ and σ^+ parameters. The results with the published data and with the phenylethyl series at the lower temperatures are listed in Table IV.

With more recent[10] values of σ and σ^+ neither relation was uniformly successful in accounting for substituent effects, and the ρ values for the phenylethyl series differed in sign from the others. The correlation with σ^+ in the cumyl series rests largely on the decrease in rate constant by about 40% with p-methoxy substitution, whereas in the phenylethyl series this substituent results in about a 20% increase (Table IV). The changes in rate constants in three benzylic series are extremely small, and the variety of substituents is rather limited. Unfortunately we were not able to prepare benzylic hyponitrites by conventional procedures with several other substituents.

The Swain–Lupton equation[10] was also applied to the rate constants for the aromatic compounds in our study and from earlier ones. The least-squares fits to rate constants at several temperatures resulted in widely varying estimates of the r and f parameters, with generally about equal contributions from the field and resonance terms.

Discussion

The continuity implied by the isokinetic plot in Figure 4 is entirely reasonable, since the substituents are remote from the N–O bond that undergoes homolysis and in the absence of electron transfer would be expected to have a small influence on the mechanism. The reduction of the lines and point in Figure 3 to a single line on replotting in Figure 4 with unique isokinetic temperatures derived from the slopes in each case, and the lack of a true isokinetic temperature, are all classic patterns that have been described in other systems.[9,11]

The linear relationship in Figure 4 represents compounds with activation energies of 25–30 kcal/mol, and rate constants differing by about two orders of magnitude. By contrast, the very small substituent effects in the benzylic series in Table IV are inconsistent and cannot be interpreted in a straightforward way.[4] Whereas phenyl-for-H substitution lowers E_a and raises log A, it can be seen in Table III that the effect of substitution on phenyl in the phenylethyl series is to raise both E_a and log A. As a consequence the unsubstituted shows a greater deviation than the substituted phenylethyl hyponitrites from the line in Figure 4. Another factor, however, may be differences in the stereochemistries of the phenylethyl derivatives we isolated (racemate or meso), which we have not yet determined.

Since phenyl as a substituent is electron-withdrawing, the decreased E_a in the benzylic hyponitrites may be due to an incremental decrease in the attractive force between the N and O atoms in the hyponitrite, which on the basis of atomic electronegativities would be polarized as $[R{-}O^{\delta-}{-}N^{\delta+}{=}]_2$. An alternative explanation in terms of homobenzylic delocalization of the electrons in the developing benzyloxy radicals onto the aromatic ring would be consistent with the tentative evidence for resonance contributions from aromatic ring substituents.[4] On the other hand, interactions of this kind are usually associated with strong geometric requirements,[12] in this case a particular orientation (decreased entropy) of the aromatic ring with the breaking N–O bond in the transition state. This model is not consistent with the *increase* in log A with substi-

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(10) (a) Swain, C. G.; Lupton, E. C., Jr. *J. Am. Chem. Soc.* **1968**, *90*, 4328–4337. (b) Swain, C. G.; Swain, M. S.; Powell, A. L.; Alunni, S. *J. Am. Chem. Soc.* **1983**, *105*, 502–513.

(11) Petersen, R. C. *J. Org. Chem.* **1964**, *29*, 3133.

(12) Lowry, T. H.; Richardson, K. S. "Mechanism and Theory in Organic Chemistry", 2nd ed.; Harper and Row: New York, 1981; pp 397–403.

tution of phenyl for H Figure 3, dotted line), nor is it supported by the lack of analogous effects of phenyl-for-methyl substitution in dioxetanes.[13] The latter case however is complicated by postulated reverse reactions, and the symmetry of alkoxy radicals may lessen the geometrical demands for homoconjugation with the aromatic ring. More definitive evidence on this matter would come from electron detachment studies of substituted benzyl alcoholate ions, but these do not appear to have been carried out.

Acknowledgment. This work has been supported by a fellowship to E.M.Q. from the 3M Company.

Registry No. $(CH_3)_2CHCH_2I$, 513-38-2; *p*-$FC_6H_4CHClCH_3$, 456-16-6; *p*-$ClC_6H_4CHClCH_3$, 20001-65-4; *p*-$BrC_6H_4CHClCH_3$, 20488-10-2; *p*-$CH_3OC_6H_4CHClCH_3$, 1538-89-2; Ph_2CHBr, 776-74-9; *trans*-$C_6H_5CH(CH_3)ON{=}NOCH(CH_3)C_6H_5$, 97012-02-7; *trans*-$C_6H_5CD(CH_3)ON{=}NOCD(CH_3)C_6H_5$, 97012-03-8; *trans*-*c*-$C_6H_{11}ON{=}NOC_6H_{11}$-*c*, 86886-18-2; *trans*-$C_6H_5CH_2ON{=}NOCH_2C_6H_5$, 86886-20-6; *trans*-$CH_3ON{=}NOCH_3$, 86886-15-9; *trans*-$CH_3CH_2ON{=}NOCH_2CH_3$, 91606-80-3; *trans*-$(CH_3)_2CHON{=}NOCH(CH_3)_2$, 86886-16-0; *trans*-$(CH_3)_2CHCH_2ON{=}NOCH_2CH(CH_3)_2$, 97012-04-9; *trans*-*p*-$FC_6H_4CH(CH_3)ON{=}NOCH(CH_3)C_6H_4$-*p*-F, 97012-05-0; *trans*-*p*-$ClC_6H_4CH(CH_3)ON{=}NOCH(CH_3)C_6H_4$-*p*-Cl, 97012-06-1; *trans*-*p*-$BrC_6H_4CH(CH_3)ON{=}NOCH(CH_3)C_6H_4$-*p*-Br, 97012-07-2; *trans*-*p*-$CH_3OC_6H_4CH(CH_3)ON{=}NOCH(CH_3)C_6H_4$-*p*-$OCH_3$, 97012-08-3; *trans*-$(C_6H_5)_2CHON{=}NOCH(C_6H_5)_2$, 97012-10-7; *p*-$FC_6H_4COCH_3$, 403-42-9; *p*-$ClC_6H_4COCH_3$, 99-91-2; *p*-$BrC_6H_4COCH_3$, 99-90-1; *p*-$CH_3OC_6H_4COCH_3$, 100-06-1; *p*-$CH_3OC_6H_4CH(OH)CH_3$, 3319-15-1; 1-tetralol, 529-33-9; 1-tetralyl chloride, 58485-68-0; *trans*-bis(1-tetralyl)hyponitrite, 97012-09-4.

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Reactions of the Chlorine Complex of Tetrahydrothiophene

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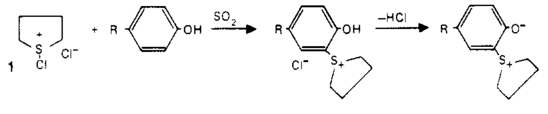
Received May 24, 1984

The chlorine complex of tetrahydrothiophene (THT) undergoes the Pummerer reaction to yield not only the expected 2-chloro- and 2,3-dichlorotetrahydrothiophene products but also 1-(2-chlorotetrahydro-3-thienyl)-tetrahydrothiophenium chloride (**10**), which upon hydrolysis yields 1-(tetrahydro-2-hydroxy-3-thienyl)tetrahydrothiophenium chloride **3** and upon elimination of HCl produces 1-(4,5-dihydro-3-thienyl)tetrahydrothiophenium chloride (**2**). The sulfonium **10** was formed by the addition of the chlorine–THT complex to the Pummerer-derived 2,3-dihydrothiophene. The sulfonium formation was monitored in CCl_4, CH_2Cl_2, and liquid SO_2 by proton NMR, and the addition of the complex to cyclohexene, dihydrofuran, styrene, and thiophene was studied. There was a dramatic increase in reactivity of the complex in sulfur dioxide both to addition and substitution type reactions.

Aryl cyclic sulfonium zwitterions are polymerizable monomers[1-3] that are prepared[4] by the reaction of a phenol with the 1:1 complex of chlorine and tetrahydrothiophene **1**. The electrophilic substitution to yield sulfonium goes exclusively para to the phenolic hydroxy. If the para position is blocked, then ortho substitution occurs at a much lower rate. It is interesting that liquid SO_2 is the only solvent that gives a practical reaction rate for ortho substitution to phenols.[4]



zwitterion monomer

The chlorosulfonium salt **1** may be formed by chlorination of tetrahydrothiophene (THT) with chlorine or sulfuryl chloride or from tetrahydrothiophene 1-oxide (THTO) in cold, saturated HCl solutions of methanol[2] or water–methanol.[5]

In the course of preparing large quantities of the zwitterion, we observed that excess **1** and elevated reaction temperatures produced toxic solutions. The toxicity was not related to the THT substitution reaction to phenols but was a result of the unexpected addition of **1** to the Pummerer-derived 2,3-dihydrothiophene to yield bioactive sulfoniums. We report here a subsequent study of the Pummerer rearrangements of **1** and a previously unreported reaction of **1** with alkenes.

Isolation of Sulfoniums. The zwitterion solutions containing the toxic substances were analyzed by high-performance liquid chromatography (HPLC) using a cationic exchange column for separation of the unknown species. Because neuromuscular blockade was the pharmacological property related to toxicity, a bioassay technique reported by Kordaš[6] was used to monitor the HPLC. This method proved both sensitive and semiquantitative. Sufficient material was isolated from the most bioactive HPLC peak for partial characterization. A sample of crystalline material was isolated by picrate precipitation from a solution of zwitterion containing the toxic substance. The chloride salt of this material was identical by bioassay and proton NMR with samples isolated by HPLC.

On the bases of NMR, IR, elemental, and mass spectral analyses this bioactive compound was tentatively assigned structure **2**. Later, chemical considerations confirmed $\beta(3)$

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[4] Klingler, T. C.; Schmidt, D. L.; Jensen, W., Jr.; Urchick, D. U.S. Patent 4 089 877, 1978.

[5] Schmidt, D. L., unpublished results.

[6] Kordaš, M. *Int. J. Neuropharmacol.* **1964**, *3*, 77. The bioassay depended upon the percent depression of an isolated perfused rat phrenic nerve–diaphram (IPD) as described by Kordaš. The toxicity was due to neuromuscular blockage and the potency was quantitated by the percent depression in the contraction of the nerve–diaphragm. After the compounds had been isolated, the potency was compared by the quantity needed for a 25% depression. The LD_{50} in mice was determined by intraperitoneal administration and the measured LD_{50} values were **2a**, 0.83 mg/kg; **3a**, 3.16 mg/kg; and **4a**, 6.81 mg/kg.

0022-3263/85/1950-2840$01.50/0