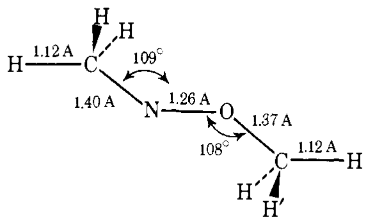

above would suggest a lower value than calculated for the 2p orbital.

Preliminary evidence suggests the formation of *N-tert*-butoxy-*N*-arylamino radicals in the decomposition of *tert*-butyl *N*-arylperoxycarbamates. Studies are continuing in this area.

Acknowledgment. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society (Grant No. PRF 5579-AC4), and the Kansas State University Bureau of General Research for support of this work.

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Primary Kinetic Isotope Effects and the Nature of Hydrogen-Transfer Transition States. The Reaction of a Series of Free Radicals with Thiols

Sir:

The magnitude of the primary isotope effect in a hydrogen-transfer reaction varies with the symmetry of the transition state and is a maximum when the hydrogen is symmetrically bonded to the atoms between which it is being transferred.[1–7] The first indication that such a maximum could be experimentally observed was reported by Kresge[3] and by Bell,[4] who compiled data on proton exchange reactions. In addition, calculations of isotope effects for simplified models of proton transfer reactions are consistent with the conclusion that the isotope effect should pass through a maximum for a symmetrical transition state.[6] Nevertheless, some reservations have been expressed to this hypothesis.[2]

We here wish to report a maximum in the isotope effect for a homologous series of hydrogen-atom transfer reactions. The reactions we have studied involve the abstraction of a hydrogen atom from the S–H position of an isotopically labeled thiol, as shown in eq 1 and 2

$$\mathrm{Q\cdot + RSH^* \longrightarrow QH^* + RS\cdot} \qquad (1)$$

$$\mathrm{Q\cdot + PhSH^* \longrightarrow QH^* + PhS\cdot} \qquad (2)$$

where Q· is any organic free radical, RSH* is an isotopically labeled aliphatic thiol (usually *tert*-butyl mercaptan), and PhSH* is labeled thiophenol.[8] The postulate, which was first formalized by Hammond,[9,10] suggests that the most symmetrical transition state in such a series of reactions should occur for that case in which the heat of reaction is most nearly zero; exothermic and endothermic reactions would be predicted to have relatively unsymmetrical transition states resembling either reactants or products, respectively. Table I gives the observed isotope effect for a number of organic radicals, the preexponential ratios, and activation energy differences calculated from measurements of the isotope effect as a function of temperature, and a tabulation of the ΔH for each reaction as calculated from bond dissociation energies. Figure 1 shows the relation between the isotope effect and heat of reaction for eq 1 and 2; the curve shows a clear maximum.

Most of the data were obtained using *tert*-butyl mercaptan as RSH* in eq 1. With the exception of the points for the cyclohexyl and 1-adamantyl radicals, all of the data for this mercaptan fall near the curve in Figure 1. Both the cyclohexyl and 1-adamantyl radicals appear to be more reactive than would be predicted from the curve; this greater reactivity is consistent with the notion of some degree of geometrical destabilization for radical centers that may not achieve a planar conformation.[11]

Figure 1 also shows the data for thiophenol as the hydrogen donor, and the data appear to be correlated reasonably well by the same curve that fits the data for the aliphatic thiol. This would be expected since, to a first approximation, the differences in the S–H vibrational frequencies between the thiol and transition state will not be affected by the alkyl or aryl substituent on the sulfur.[12]

The heat of reaction for any given radical is 13 kcal/mol more exothermic for reaction with thiophenol than with *tert*-butyl mercaptan. The isotope effect

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[1] The original postulate and theoretical background for this statement can be found in: (a) F. H. Westheimer, *Chem. Rev.*, **61**, 265 (1961); (b) J. Bigeleisen, *Pure Appl. Chem.*, **8**, 217 (1964); (c) L. Melander, "Isotope Effects on Reaction Rates," Ronald Press, New York, N. Y., 1960.

[2] Reservations to this postulate have been expressed by: (a) A. V. Willi and M. Wolfsberg, *Chem. Ind.* (*London*), 2097 (1964); (b) R. F. W. Bader, *Can. J. Chem.*, **42**, 1822 (1964); (c) W. H. Saunders, Jr., *J. Amer. Chem. Soc.*, **91**, 16 (1969); (d) F. G. Bordwell and W. J. Boyle, Jr., *ibid.*, **93**, 512 (1971).

[3] A. J. Kresge, *Discuss. Faraday Soc.*, **39**, 49 (1965).

[4] R. P. Bell has published experimental and theoretical arguments supporting this statement: (a) R. P. Bell, *ibid.*, **39**, 49 (1965); (b) R. P. Bell *ibid.*, **39**, 16 (1965); (c) R. P. Bell and J. E. Crooks, *Proc. Roy. Soc., Ser. A*, **286**, 285 (1965); (d) R. P. Bell and D. M. Goodall, *ibid., Ser. A*, **294**, 273 (1966); (e) D. J. Barnes and R. P. Bell, *ibid., Ser. A*, **318**, 441 (1970); (f) R. P. Bell and B. G. Cox, *J. Chem. Soc. B*, 194 (1970).

[5] For additional experimental work and reviews on this topic see: (a) E. R. Thornton, *J. Org. Chem.*, **27**, 1943 (1962); (b) J. L. Longridge and F. A. Long, *J. Amer. Chem. Soc.*, **89**, 1292 (1967); (c) L. C. Gruen and F. A. Long, *ibid.*, **89**, 1287 (1967); (d) Y. Pocker and J. H. Exner, *ibid.*, 90, 6764 (1968); (e) A. J. Kresge, D. S. Sagatys, and H. L. Chen, *ibid.*, 90, 4174 (1968); also, see ref 3; (f) J. E. Dixon and T. C. Bruice, *J. Amer. Chem. Soc.*, **92**, 905 (1970); (g) T. Yokota and R. B. Timmons, *Int. J. Chem. Kinet.*, **2**, 325 (1970); (h) J. R. Jones, *Trans. Faraday Soc.*, **65**, 2138 (1969); (i) J. R. Jones, *ibid.*, **65**, 2430 (1969); (j) J. F. Bunnett, *Surv. Progr. Chem.*, **5**, 53 (1969).

[6] Calculations supporting this postulate are given by: R. A. M. O'Ferrall and J. Kouba, *J. Chem. Soc. B*, 985 (1967).

[7] Since the submission of this paper, several important communications have appeared on this subject: (a) R. P. Bell and B. G. Cox, *J. Chem. Soc. B*, 783 (1971); (b) H. Kwart and M. C. Latimore, *J. Amer. Chem. Soc.*, **93**, 3770 (1971); (c) E. S. Lewis and M. M. Butler, *Chem. Commun.*, submitted for publication, and private communication.

[8] The asterisks in eq 1 and 2 indicate isotopic substitution. Both deuterium and tritium have been used. When tritium is used, the isotope is present in tracer amounts; when deuterium is used, either competition in a mixture of RSH–RSD was used, or parallel experiments were done with normal thiol and then with completely labeled thiol-*S*-d_1.

[9] G. S. Hammond, *J. Amer. Chem. Soc.*, **77**, 334 (1955).

[10] For the application to free-radical reactions, see W. A. Pryor, "Free Radicals," McGraw-Hill, New York, N. Y., 1966, p 156.

[11] (a) F. D. Greene, C. Chu, and J. Walia, *J. Amer. Chem. Soc.*, **84**, 2463 (1962); (b) J. P. Lorand, S. D. Chodroff, and R. W. Wallace, *ibid.*, 90, 5266 (1968).

[12] Most thiols have an S–H stretching vibration between 2600 and 2500 cm^{-1}; for example, L. J. Bellamy in "Organic Sulfur Compounds," Vol. I, N. Kharasch, Ed., Pergamon Press, New York, N. Y., 1961, p 51.

Table I. Kinetic Isotope Effects on Hydrogen Atom Abstraction by Organic Radicals in Solution

Radical, Q·	Heat of reaction (ΔH), kcal mol^{-1} Q· + RSH* → QH* + RS·	Thiol	k_H/k_D[a]	A_H/A_D	$-(E_H - E_D)$, kcal mol^{-1}
Phenyl[b]	−24[e,f]	*tert*-BuSH	1.88	0.42	0.90
p-Nitrophenyl[b]	−20[d]	*tert*-BuSH	2.49	1.11	0.46
Hydrogen atom[c]	−16[g]	*tert*-BuSH	1.60	1.07	0.15
Trifluoromethyl[c,h]	−16[g]	H_2S	2.8	0.8	0.7
Methyl[c]	−16[e,g]	*tert*-BuSH	2.71	0.59	0.90
Methyl[c,i]	−14[e,g]	H_2S	3.8	0.75	1.15
1-Nonyl[b]	−10[g]	*tert*-BuSH	3.40	0.99	0.73
3-Heptyl[b]	−7[g]	*tert*-BuSH	4.40	0.87	0.96
Cyclohexyl[b]	−6[e,g]	*tert*-BuSH	2.96	0.21	1.56
1-Adamantyl[b]	−6[d]	*tert*-BuSH	1.89	0.53	0.75
Triethylmethyl[b]	−3[g]	*tert*-BuSH	5.35	1.14	0.81
Benzyl[b]	+3[e,g]	*tert*-BuSH	6.35	0.89	1.17
Diphenylmethyl[b]	+4[d]	*tert*-BuSH	6.59	1.92	0.73
Trityl[b]	+5[d]	*tert*-BuSH	6.65	1.12	1.03
DPPH[c]	+5[d]	PhSH	5.40		
Benzyl[b]	−10[e,g]	PhSH	3.90	0.61	1.10
DPPH[c]	+18[d]	*tert*-BuSH	4.34	0.53	1.25

[a] Extrapolated to 25° using the measured Arrhenius parameters. [b] Measured as k_H/k_T and corrected using the Swain (C. G. Swain, E. C. Stivers, J. F. Reuwer, Jr., and L. J. Schaad, *J. Amer. Chem. Soc.*, **80**, 5885 (1958)) equation. [c] Measured directly as k_H/k_D. [d] Estimated bond dissociation energy for Q–H. [e] S. W. Benson, "Thermochemical Kinetics," Wiley, New York, N. Y., 1968, p 215. [f] A. S. Rodgers, D. M. Golden, and S. W. Benson, *J. Amer. Chem. Soc.*, **89**, 4578 (1967). [g] J. A. Kerr, *Chem. Rev.*, **66**, 465 (1966). [h] N. L. Arthur and P. Gray, *Trans. Faraday Soc.*, **65**, 434 (1969). [i] N. Imai, T. Dohmaru, and O. Toyama, *Bull. Chem. Soc. Jap.*, **38**, 639 (1965).

for reaction with thiophenol is observed to become *either* larger *or* smaller, relative to that for *tert*-butyl mercaptan, depending on whether this change in ΔH leads to a *more* or *less* symmetrical transition state. This is demonstrated by the changes in the isotope effects for the reactions of the DPPH and $PhCH_2\cdot$ radicals in Figure 1.

The two points shown as triangles in Figure 1 are for isotope effects for the reaction of either $CH_3\cdot$ or $CF_3\cdot$ with H_2S. These data, taken from gas-phase studies, also appear to lie reasonably near to the same curve.

In some cases the isotope effects were measured at temperatures other than 25°, but all of the data have been recalculated to that temperature using known Arrhenius parameters. As coded in Table I, some of the isotope effects were measured with deuterium and some with tritium, depending on which was the more experimentally precise and convenient; the deuterium isotope effect was calculated from that due to tritium using the Swain equation.[13]

It is evident from Figure 1 that the largest isotope effect is the one in which hydrogen transfer is approximately half-complete at the transition state. For example, in the reaction with *tert*-butyl mercaptan, the transfer is more than half-complete at the transition state for DPPH but less than half-way along the reaction coordinate for the methyl radical. In reaction with thiophenol, the transfer is roughly half-complete at the transition state for reaction with DPPH, the transition state is very nearly symmetrical, and the isotope effect is near the maximum. The terms "half-complete" or "half-way" are defined in terms of equality of the vibrational force constants for the Q–H* and RS–H* partial bonds in the transition state $[Q{-}{-}{-}H^*{-}{-}{-}SR]^{\ddagger}$.[1–7] The results of the present system are consistent with recent suggestions and observations of isotope effect maxima in other series of closely related transfer processes.[4–7]

Kresge[3] has suggested that the difficulty in experimentally observing an isotope effect maximum in some systems may be due to the inability to examine a homologous reaction series over a wide enough range of reactivities. A number of absolute rate constants[14] for the reaction of radicals with thiols are known, and they vary from $4 \times 10^8\ M^{-1}\ \mathrm{sec}^{-1}$ for H· + CH_3SH to $4 \times 10^{-4}\ M^{-1}\ \mathrm{sec}^{-1}$ for DPPH + *tert*-C_4H_9SH. Apparently this spectrum of reactivities is sufficient to allow the detection of the maximum in the isotope

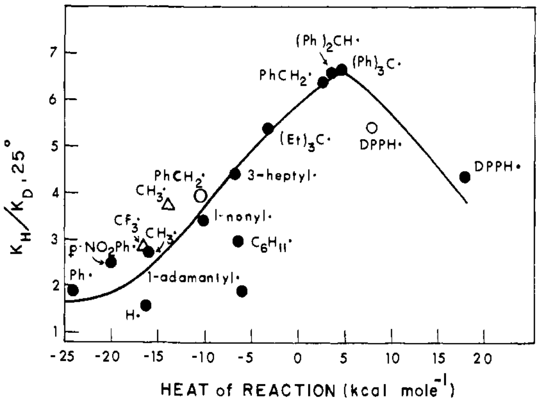

Figure 1. A plot of the heat of reactions 1 or 2 *vs.* the isotope effect at 25°. The formula by each point indicates the structure of the radical Q· in eq 1 or 2. The symbols are coded to show the nature of the thiol: ○, thiophenol; ●, *tert*-butyl mercaptan; △, H_2S.

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(13) (a) C. G. Swain, E. C. Stivers, J. F. Reuwer, and L. J. Schaad, *J. Amer. Chem. Soc.*, **80**, 5885 (1958); (b) J. Bigeleisen, "Tritium in the Physical and Biological Sciences," Vol. 1, International Atomic Energy Agency, Vienna, 1962.

(14) (a) H· + CH_3SH: T. Inabe and B. Darwent, *J. Phys. Chem.*, **64**, 1431 (1960); (b) DPPH + *tert*-C_4H_9SH: our data and K. E. Russell, *ibid.*, **58**, 437 (1954); (c) also see: N. Imai and O. Toyama, *Bull. Chem. Soc. Jap.*, **33**, 652 (1960); J. A. Kerr and A. F. Trotman-Dickenson, *J. Chem. Soc.*, 3322 (1957); N. L. Arthur and P. Gray, *Trans. Faraday Soc.*, **65**, 434 (1969); R. D. Burkhart, *J. Phys. Chem.*, **73**, 2703 (1969).

effect. A more detailed discussion will be presented in the full paper.

[15] John Simon Guggenheim Fellow, 1970–1971; National Institutes of Health Special Postdoctoral Fellow, Summer 1971.

[16] National Institutes of Health Predoctoral Research Assistant, 1968–1971. This work was partially supported by Grant No. GM 11908 from NIH.

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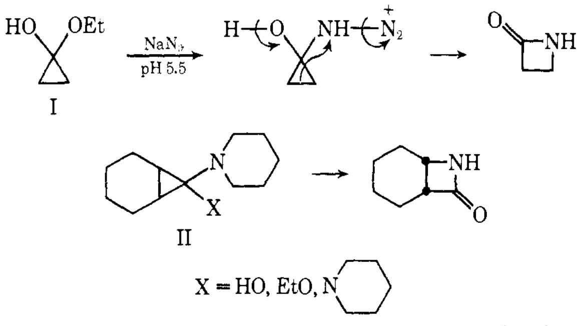
The Chemistry of Cyclopropanones. VI. A New Synthesis of β-Lactams[1]

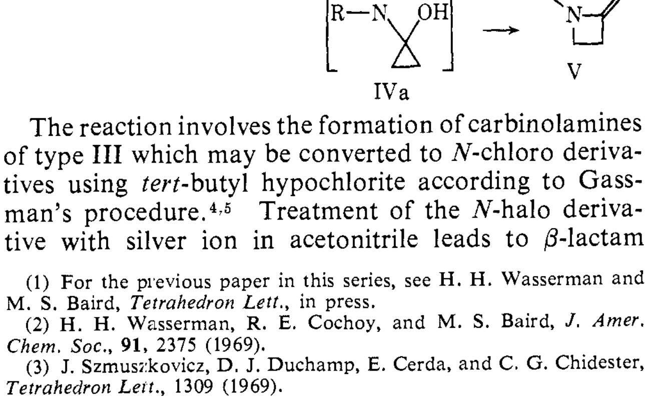
Sir:

We have previously reported[2] that the ethyl hemiketal (I) of cyclopropanone reacts with sodium azide in buffered solution to form β-lactam, and we have recently[1] extended this reaction to the preparation of fused-ring β-lactams from 1,1-disubstituted cyclopropanones in the bicyclo[4.1.0] series (II).[3]



We now wish to report a more general application of this ring enlargement sequence taking place through the electron-deficient (nitrenium ion) species IVa analogous to the cyclopropylcarbinyl cation, or by the concerted process (IV → V) outlined in Scheme I.

Scheme I



The reaction involves the formation of carbinolamines of type III which may be converted to N-chloro derivatives using *tert*-butyl hypochlorite according to Gassman's procedure.[4,5] Treatment of the N-halo derivative with silver ion in acetonitrile leads to β-lactam formation. Table I summarizes the results of our initial studies.

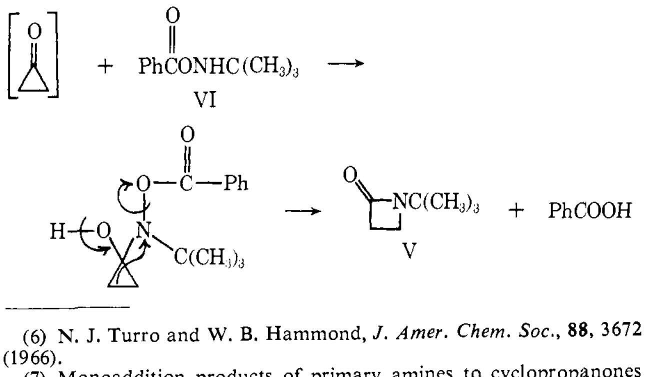
Table I[a]

Amine	Yield of β-lactam (V), %
c-$C_6H_{11}NH_2$	61
$CH_3(CH_2)_3NH_2$	43
$CH_3CH_2CH(\text{-}CH_3)NH_2$	38
$(CH_3)_3CNH_2$	52
$CH_3CH(\text{-}COOEt)NH_2$	65

[a] All new products gave satisfactory carbon, hydrogen, and nitrogen analyses and the expected parent peaks in the mass spectra.

The intermediates III were formed by treatment of ketene with diazomethane in ether at −78°[6] followed by the addition of 1 mol of primary amine to the reaction mixture. Evaporation of solvent below 30°, followed by repeated washing with cold petroleum ether, yielded the crude carbinolamines, which could be characterized by nmr and mass spectra. Because of the instability of the addition products of primary amines to cyclopropanone[7] we chose not to attempt isolation of the intermediates III, but found it advantageous to perform the halogenation directly on the crude carbinolamines after replacement of ether with acetonitrile. Thus, addition of 1 equiv of *tert*-butyl hypochlorite in the dark at 0° and stirring of the reaction mixture for 1 hr were followed by treatment with a threefold excess of silver nitrate and stirring for an additional 3 hr. After removal of silver chloride and evaporation of solvent, a residue was obtained which was treated with 6 N aqueous ammonia and extracted with ether. Evaporation of solvent yielded the crude β-lactam purified by column chromatography on silica gel. By this procedure, pure N-substituted β-lactams could be obtained in yields of *ca.* 50% based on the diazomethane employed.

In a further extension of this general method, we have investigated leaving groups other than Cl^- or N_2 in the ring enlargement. Thus, the O-benzoyl derivative of N-*tert*-butylhydroxylamine (VI)[8] reacts directly with cyclopropanone in ether at −78° to form the β-lactam V, R = *tert*-butyl (40%). To isolate the product, the ether solution was washed with bicarbonate and dried, the solvent was removed, and the residual liquid was purified by glc. The rearrangement is presumed to take place by the sequence shown below.



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[1] For the previous paper in this series, see H. H. Wasserman and M. S. Baird, *Tetrahedron Lett.*, in press.

[2] H. H. Wasserman, R. E. Cochoy, and M. S. Baird, *J. Amer. Chem. Soc.*, **91**, 2375 (1969).

[3] J. Szmuszkovicz, D. J. Duchamp, E. Cerda, and C. G. Chidester, *Tetrahedron Lett.*, 1309 (1969).

[4] P. G. Gassman, *Accounts Chem. Res.*, **3**, 26 (1970).

[5] P. G. Gassman and A. Carrasquillo, *Tetrahedron Lett.*, 109 (1971).

[6] N. J. Turro and W. B. Hammond, *J. Amer. Chem. Soc.*, **88**, 3672 (1966).

[7] Monoaddition products of primary amines to cyclopropanones have been reported to be too unstable for isolation: W. T. M. Tilburg, S. E. Schaafsma, H. Steinberg, and T. J. de Boer, *Recl. Trav. Chem. Pays-Bas*, **86**, 417 (1967).

[8] The O-acyl derivatives of the substituted hydroxylamines were prepared by treatment of the primary amine with benzoyl peroxide according to the method of G. Zinner, *Arch. Pharm.*, **296**, 57 (1963).