

Kinetics of the Reversible β -Scission of the Cyclopentyloxy Radical

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Abstract: The reaction of *N*-(cyclopentyloxy)pyridine-2-thione (**6**) with tributylstannane in benzene constitutes a clean experimental system for a kinetic study of the β -scission of the cyclopentyloxy radical (**1**). Product distributions are reported as a function of tributylstannane concentration over a temperature range of 6–80 °C. The results are consistent with a mechanism involving a reversible β -scission. Arrhenius parameters for the β -scission of the cyclopentyloxy radical (**1**) are $\log A$ (s⁻¹) = 12.55 ± 0.41 and E_a = 6.26 ± 0.54 kcal/mol, while those for the reverse reaction, the 1,5-exo cyclization of the 4-formylbutyl radical (**2**), are $\log A$ (s⁻¹) = 10.2 ± 0.3 and E_a = 6.88 ± 0.46 kcal/mol. The observed equilibrium constants and activation parameters are compared with theoretical calculations including group-additivity equilibrium constants and AM1-UHF activation parameters.

β -Scission of the cyclopentyloxy radical, **1**, to afford the 4-formylbutyl radical, **2**, is a well-documented reaction. It has been observed when **1** is generated under a variety of conditions including the photolysis of cyclopentyl nitrite (benzene, 18 °C),^{1,2} radical chain decomposition of cyclopentyl hypochlorite (CCl₄, 30–70 °C),³ photooxidation of cyclopentane (gas phase),⁴ thermolysis of dicyclopentyl peroxide (dodecane, 160 °C),⁵ and most recently, radical chain decomposition of *N*-(cyclopentyloxy)pyridine-2-thione (benzene, 80 °C).⁶ In all of these experiments, the products arose from cyclopentyloxy radical mainly via β -scission, thus indicating that this fragmentation occurs more rapidly than possible competing processes, i.e. disproportionation of **1** or hydrogen atom transfer. In a study of relative reaction rates, it was observed that the β -scission of cyclopentyloxy radical (**1**) proceeds at least 100 times more rapidly than does β -scission of the 2-butoxy radical.³ This rate difference was attributed to the greater relief of steric strain in the former reaction.^{3,7} Other factors which influence the rates of β -scission of alkoxy radicals include the stability of the leaving alkyl radical and the strength of the C–O π bond in the forming carbonyl group.^{3,7–9}

We became interested in this reaction as part of our continuing research in the area of free-radical cyclizations; the β -scission of **1** is the reverse of 1,5-exo ring closure of the 4-formylbutyl radical, **2**. While there has been no evidence for reversibility in prior studies of the β -scission of **1**,^{1–6} the reversible β -scission of substituted cyclopentyloxy radicals has been reported. During synthetic studies of α -caryophyllene^{10,11} and jervine¹² derivatives, it was noted that the photolysis of nitrite esters of substituted cyclopentyl alcohols gives rise to epimerization at the α -carbon, a process consistent with reversible β -scission of a cyclopentyloxy radical intermediate. The ability of substituted 4-formylbutyl radicals to undergo ring closure has also been demonstrated by

Tsang and Fraser-Reid.^{13,14} One of their examples,¹⁴ reproduced in Scheme I, allows an estimate of a rate constant for this type of reaction, because the radical involved is able to undergo intramolecular addition onto either the carbonyl group or the vinyl group. As these two cyclizations are in direct internal competition, the ratio of rate constants is related to the ratio of yields of cyclized products. If both reactions were irreversible, the ratio of rate constants would thus be 1:3. However, since cyclization onto the carbonyl group is likely to be reversible under the reaction conditions, this figure becomes the lower limit. To a good approximation, the rate constant for ring closure onto the vinyl group can be assigned the value of the rate constant for 1,5-exo cyclization of the 3-methyl-5-hexenyl radical, viz. 4.6×10^6 s⁻¹ at 80 °C.¹⁵ Hence the rate constant for ring closure onto the carbonyl group must be $\geq 1.5 \times 10^6$ s⁻¹ at 80 °C.

The rapidity of this cyclization suggests that the β -scission of cyclopentyloxy radical (**1**) may be reversible under normally encountered reaction conditions. Consequently, a study of the kinetics of the β -scission of **1** could also provide information concerning the reverse reaction. Herein, we show that this is so; we report results consistent with a reversible β -scission mechanism and present Arrhenius parameters for the β -scission of **1** and the 1,5-exo cyclization of 4-formylbutyl radical (**2**).

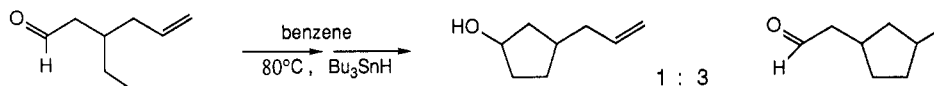
Methods and Results

In principle it should be possible to obtain reliable absolute kinetic data for alkoxy radical reactions by the competitive method. The requirements of a suitable experimental system are (i) that the reaction the rate constant of which is to be measured should compete directly with a bimolecular reaction of known rate constant and (ii) that both reactions should afford products capable of sustaining the radical chain. For intramolecular reactions of alkyl radicals, these conditions are met in the interaction of alkyl halides and tributylstannane.¹⁶ A similar system should be suitable for alkoxy radical reactions: the rate constant for the reaction of *tert*-butoxy radicals with tributylstannane is known,¹⁷ and since it is very large (2×10^8 s⁻¹ M⁻¹ at 25 °C), the values for other alkoxy radicals should be of similar magnitude. Unfortunately, the usual precursors for alkoxy radicals, viz. peroxides, peresters, hyponitrites, nitrites, nitrates, and hypohalites, do not interact with tributylstannane by clean chain processes involving alkoxy radicals as intermediates.^{18,19} Also, some of them, e.g.

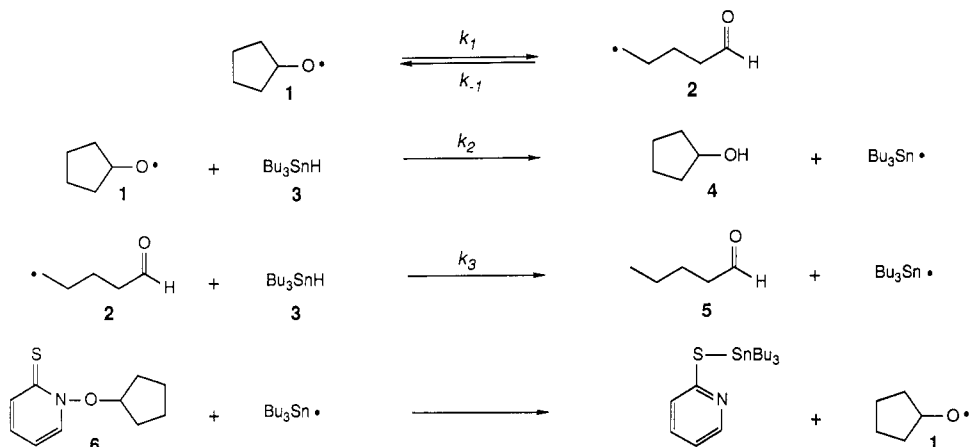
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Scheme I

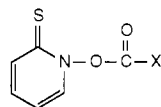


Scheme II



dialkyl peroxides, are difficult to prepare except in simple cases, while others, e.g. peroxyoxalates, are unstable. Our aim, therefore, was to devise procedures for the generation of alkoxy radicals which utilize readily prepared and relatively stable precursors and are suitable for kinetic experiments involving tributylstannane. We decided, therefore, to investigate the utility of Barton precursors²⁰ for this purpose.

Since carbamates of the general type **7** have proved to be suitable precursors of alkylamino radicals, $\text{RR}'\text{N}^\bullet$,²¹ via generation and decarboxylation of the corresponding carboxylate radicals, $\text{RR}'\text{NCO}_2^\bullet$, we expected that the analogous carbonates, **8**, would be similarly effective precursors for alkoxy radicals, RO^\bullet .



Treatment of the sodium salt of 2-mercaptopyridine *N*-oxide with cyclopentyl chloroformate in the usual way^{20,21} afforded the carbonate **8** (R = cyclopentyl) as a yellow solid stable in the dark. When heated in benzene with tributylstannane (0.030 M) and AIBN as initiator it underwent a rapid reaction to give cyclopentanol as the only product detected by GC. Since cyclopentyloxy radicals, when generated under these conditions, undergo ring opening, they cannot be intermediates in this reaction. We conclude that attack of tributylstannate radicals on **8** (R = cyclopentyl) proceeds as expected to give the carboxylate radical ROCO_2^\bullet , but that this does not undergo decarboxylation sufficiently rapidly to compete effectively with chain propagation by hydrogen atom transfer. The latter process affords the acid, ROCO_2H , which undergoes decarboxylation by a nonradical mechanism. Although quantitative data is not yet available, it seems clear that $\text{RR}'\text{NCO}_2^\bullet$ radicals undergo decarboxylation much more rapidly than ROCO_2^\bullet radicals, but the reasons for

(19) Separate experiments have shown that the photolysis of cyclopentyl nitrite in the presence of tributylstannane in low concentration does not yield β -scission products, i.e. does not result in the formation of free cyclopentyloxy radicals.

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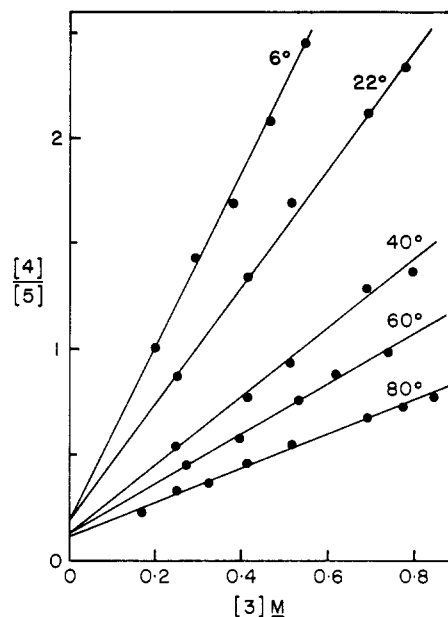


Figure 1. Plots of $[\text{4}]/[\text{5}]$ vs $[\text{3}]$ for the reaction of 0.03 M **6** in benzene under an argon atmosphere.

this difference in reactivity have not yet been identified.²²

We turned next to an examination of the behavior of simple *N*-alkoxy-pyridine-2-thiones and found that they undergo clean chain decomposition in the presence of tributylstannane. Thus, as previously reported,⁶ *N*-(cyclopentyloxy)pyridine-2-thione (**6**) reacts with 1 molar equiv of tributylstannane (**3**) at 80 °C in benzene to yield products consistent with the intermediacy of cyclopentyloxy radical, i.e. cyclopentanol (**4**) and 1-pentanal (**5**). The reaction of **6** with **3** in benzene has now been examined further at pseudo-first-order concentrations of **3**. When pyridinethione **6** was heated with 10 molar equiv or more of stannane **3**, the products, cyclopentanol (**4**) and pentanal (**5**), accounted for 90–95% of the starting material. Other possible products such as cyclopentanone (disproportionation), 1-pentanol (direct reduction of **5** by **3**), tetrahydropyran (1,6-endo cyclization of **2**), and (cyclopentyloxy)tributylstannane (radical–radical coupling)

(22) The relatively slow rate of decarboxylation of alkoxy-carbonyl radicals has been noted previously; see for example, Komai, T.; Matsuyama, K. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 2207. Van Sickle, D. E.; Mayo, F. R.; Arluck, R. M. *J. Org. Chem.* **1967**, *32*, 3680.

Table I. Relative Rate Constant Data^a

temp, °C	k_2/k_1 , M	k_2k_{-1}/k_1k_3	k_1/k_2 , \bar{M}	k_{-1}/k_3 , \bar{M}
6	4.18 ± 0.17	0.171 ± 0.067	0.24 ± 0.01	0.041 ± 0.016
22	2.79 ± 0.05	0.188 ± 0.030	0.36 ± 0.01	0.067 ± 0.014
40	1.64 ± 0.07	0.119 ± 0.041	0.61 ± 0.03	0.073 ± 0.029
60	1.18 ± 0.06	0.125 ± 0.033	0.84 ± 0.04	0.105 ± 0.033
80	0.79 ± 0.04	0.118 ± 0.022	1.28 ± 0.07	0.150 ± 0.033

^a Values of k_2/k_1 and k_2k_{-1}/k_1k_3 are the values of the slopes and intercepts calculated from the points in the plots of [4]/[5] against [3] (Figure 1) by linear regression. Values of k_1/k_2 and k_{-1}/k_3 were calculated from the plots by means of eq 1. All uncertainties reflect 1 SD.

were not detected. Relative amounts of **4** and **5** were measured as a function of [3] at 6, 22, 40, 60, and 80 °C. The results are given in Figure 1 as plots of [4]/[5] versus [3].

The product distributions are consistent with the mechanism given in Scheme II, steady-state analysis of which shows that under pseudo-first-order concentrations of **3**, the ratio [4]/[5] is related to [3] by eq 1. This relationship correctly predicts the observed product distributions, i.e. graphs of [4]/[5] against [3] give linear plots with positive, nonzero intercepts (failure to include reversibility of the β -scission yields a rate law predicting zero intercepts). The slopes and intercepts of these plots provide the values of k_1/k_2 and k_{-1}/k_3 summarized in Table I. Linear regression analysis of $\ln(k_1/k_2)$ against $1/T$ and of $\ln(k_{-1}/k_3)$ against $1/T$ gives the relative temperature dependencies shown in eq 2 and 3 where θ represents 2.3RT kcal/mol.

$$[4]/[5] = (k_2/k_1)[3] + (k_2/k_1)(k_{-1}/k_3) \quad (1)$$

$$\log(k_1/k_2) \text{ (M)} = (2.85 \pm 0.11) - (4.43 \pm 0.16)/\theta \quad (2)$$

$$\log(k_{-1}/k_3) \text{ (M)} = (1.13 \pm 0.24) - (3.18 \pm 0.24)/\theta \quad (3)$$

In order to obtain Arrhenius parameters for the β -scission of **1**, values are required for the reference reaction, namely hydrogen atom abstraction from **3** by an alkoxy radical. These values can be accurately estimated from literature data. The Arrhenius parameters for H[•] abstraction from **3** have been measured for a variety of abstracting radicals.^{23,24} Values of $\log A$ ($M^{-1} s^{-1}$) for all the radicals studied fall within the narrow range of 8.4–10.0. The more reactive abstracting radicals exhibit the largest values of $\log A$, e.g. cyclopropyl (9.3 ± 0.5), 2,2-dimethylvinyl (9.7 ± 0.3), and benzoyloxy (10.0 ± 0.2). Alkoxy radicals belong in this category, and, therefore, we can confidently assign a value of 9.7 ± 0.4 to the $\log A$ term for H[•] abstraction from **3** by **1**.

Given values of $\log A$ and a rate constant, the activation energy E_a can be calculated. The rate constant for H[•] abstraction from tributylstannane (**3**) by the *tert*-butoxy radical was found to be $2.2 \times 10^8 M^{-1} s^{-1}$ at 22 °C.¹⁷ When combined with our estimate for $\log A$ this gives $E_a = 1.83 \pm 0.54$ kcal/mol. This result is consistent with the E_a values reported for the other reactive radicals cited above, e.g. 1.9 ± 0.6 , 1.6 ± 0.4 , and 1.7 ± 0.3 kcal/mol, respectively.²⁴

Thus, to a good approximation, the temperature dependence of k_2 (the rate constant for H[•] abstraction from **3** by **1**) is given by eq 4. Combination of eq 4 and 2 yields eq 5, which gives the temperature dependence of k_1 (the rate constant for the β -scission of **1**). Values of k_1 calculated from eq 5 are $9.1 \times 10^7 s^{-1}$ at 25 °C and 2.7×10^8 at 60 °C.

$$\log k_2 \text{ (M}^{-1} \text{ s}^{-1}\text{)} = (9.70 \pm 0.40) - (1.83 \pm 0.54)/\theta \quad (4)$$

$$\log k_1 \text{ (s}^{-1}\text{)} = (12.55 \pm 0.41) - (6.26 \pm 0.56)/\theta \quad (5)$$

A similar approach yields Arrhenius parameters for the 1,5-exo ring closure of the 4-formylbutyl radical (**2**). Here, the reference

Table II. Arrhenius Parameters for Selected 1,5-Exo Radical Cyclizations

radical	$\log A$, s^{-1}	E_a , kcal/mol	k , s^{-1} , at 25 °C	ref
$\cdot\text{CH}_2(\text{CH}_2)_3\text{CH}=\text{CH}_2$	10.42 ± 0.32	6.85 ± 0.42	2.5×10^5	16
$\cdot\text{CH}_2(\text{CH}_2)_3\text{CH}=\text{O}$	10.2 ± 0.3	6.88 ± 0.46	1.4×10^5	^a
$\cdot\text{CH}_2(\text{CH}_2)_3\text{C}=\text{CH}$	10.56 ± 0.20	8.32 ± 0.22	2.5×10^4	20
$\cdot\text{CH}_2(\text{CH}_2)_3\text{C}\equiv\text{N}$	9.9 ± 1.0	8.60 ± 1.0	3.9×10^3	21

^a This work.

Table III. Thermodynamic Properties at 25 °C and 1 atm (Gas Phase)

property	cyclopentyloxy radical, 1		4-formylbutyl radical, 2		transition state: AM1-UHF
	AM1-UHF	additivity	AM1-UHF	additivity	
ΔH_f° , kcal/mol	-25.12	-5.70	-28.28	-8.68	-10.66
C_p , cal/(mol·K)	22.05	22.20	27.48	30.22	22.88
S_{trans} , cal/(mol·K)	39.35		39.25		39.25
S_{rot} , cal/(mol·K)	26.31		27.04		26.38
S_{vib} , cal/(mol·K)	11.94		22.19		11.33
S_{elec} , cal/(mol·K)	1.37		1.37		1.37
S°_{total} , cal/(mol·K)	78.87	79.68	89.85	93.69	78.33

reaction is H[•] abstraction from **3** by the primary alkyl radical **2**, for which the Arrhenius parameters are assumed to be the same as those previously determined for ethyl or butyl radicals [$\log A = 9.1 M^{-1} s^{-1}$, $E_a = 3.7$ kcal/mol].^{23,24} Combination of these data with eq 3 yields eq 6, which gives the temperature dependence of k_{-1} , the rate constant for the 1,5-exo cyclization of the 4-formylbutyl radical (**2**). Typical values of k_{-1} calculated from eq 6 are $1.4 \times 10^5 s^{-1}$ at 25 °C and $4.8 \times 10^5 s^{-1}$ at 60 °C.

$$\log k_{-1} \text{ (s}^{-1}\text{)} = (10.2 \pm 0.3) - (6.88 \pm 0.46)/\theta \quad (6)$$

Discussion

The assignment of the slope and intercept data to k_1/k_2 and k_{-1}/k_3 ratios (Table I) is based upon the mechanism given in Scheme II. In addition to the literature precedent cited in the introduction and the quantitative agreement observed in plots of [4]/[5] against [3] (Figure 1), further support for Scheme II is provided by comparison of the kinetic results with available literature experimental data and with the results of theoretical calculations.

Comparison with Literature Experimental Data. Walling and Clark³ have reported values of k_1/k_H for the β -scission of **1**, where k_H is the rate constant for H[•] abstraction from cyclohexane by **1**. Relative Arrhenius parameters calculated from their data (three points, 30–70 °C, CCl₄) are given in eq 7. If it is assumed that

$$\log(k_1/k_H) \text{ (M)} = (3.47 \pm 0.02) - (2.69 \pm 0.03) \quad (7)$$

the temperature dependence of k_H is similar to the measured values of $\log A$ ($M^{-1} s^{-1}$) = 8.5 ± 0.5 and $E_a = 3.47 \pm 0.6$ kcal/mol for H[•] abstraction from cyclohexane by the *tert*-butoxy radical,²⁵ it follows that k_1 has $\log A$ ($M^{-1} s^{-1}$) = 12.0 ± 0.5 and $E_a = 6.2 \pm 0.6$ kcal/mol. These values are in excellent agreement with those obtained in this study for k_1 (eq 5), i.e. $\log A$ ($M^{-1} s^{-1}$) = 12.4 ± 0.4 and $E_a = 6.3 \pm 0.6$ kcal/mol.

In Table II, the Arrhenius parameters for the cyclization of **2** are seen to be comparable to those of other 1,5-exo cyclizations, e.g. the 5-hexenyl,²³ 5-hexynyl,²⁶ and 1-cyano-5-pentyl radicals.²⁷ The rate constants for these cyclizations span a range of 2 orders of magnitude ($\Delta\Delta G^\ddagger = 2.7$ kcal/mol) at 25 °C, thus demonstrating that the rate is not greatly dependent upon the identity of the unsaturated group. Over this small range, however, the order of decreasing rate, $\cdot\text{CH}_2(\text{CH}_2)_3\text{CH}=\text{CH}_2 > \cdot\text{CH}_2(\text{CH}_2)_3\text{CHO} > \cdot\text{CH}_2(\text{CH}_2)_3\text{C}=\text{CH} > \cdot\text{CH}_2(\text{CH}_2)_3\text{C}\equiv\text{N}$, does parallel the order of decreasing stability of the product radical as reflected by the order of increasing H bond dissociation energy

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(24) Johnston, L. J.; Luszyk, J.; Wayner, D. D. M.; Abeywickreya, A. N.; Beckwith, A. L. J.; Scaiano, J. C.; Ingold, K. U. *J. Am. Chem. Soc.* **1985**, *107*, 4594. (Because of the slow rate of decarboxylation, the data reported in this reference for the phenyl radical actually pertains to the benzoyloxy radical.)

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(27) Griller, D.; Schmid, P.; Ingold, K. U. *Can. J. Chem.* **1979**, *57*, 831.

Table IV. Theoretical vs Experimental Thermodynamics of the Equilibrium $1 \rightleftharpoons 2$

method	ΔH° , kcal/mol	ΔS° , cal/mol K	ΔG°_{25} , kcal/mol	K , s^{-1} , at 25 °C
AM1-UHF (gas phase, 25 °C)	-3.16	14.82 ^a	-7.58	2.8×10^6
group additivity (gas phase, 25 °C)	-2.98	14.01	-7.16	1.7×10^5
experimental (benzene, 6-80 °C)	-0.62 ± 0.72	10.7 ± 2.0	-3.8 ± 0.9	$(6 \pm 9) \times 10^3$

^aThe AM1-UHF ΔS° value was calculated with the group-additivity entropy for **2** (see text).

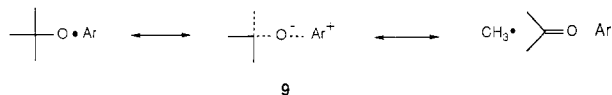
Table V. Geometry of the AM1-UHF Transition Structure for $1 \rightleftharpoons 2$ (See Figure 2)

	bond length, Å		bond angle, deg		dihedral angle, deg	
1-2	1.4867	1-2-3	109.4	1-2-3-4	35.4	
2-3	1.5206	2-3-4	108.1	2-3-4-5	-37.9	
3-4	1.5155	3-4-5	108.9	3-4-5-6	130.8	
4-5	1.5125	4-5-6	120.2	2-1-5-6	-126.2	
5-6	1.2762	1-5-6	99.9			
1-5	1.9224	1-5-4	99.3			

(kcal/mol):²⁸ $\text{CH}_2(\text{CH}_2)_3\text{CHCH}_2\text{—H}$ (98) < $\text{CH}_2(\text{CH}_2)_3\text{CH—O—H}$ (104) < $\text{CH}_2(\text{CH}_2)_3\text{C=CH—H}$ (108) < $\text{CH}_2(\text{CH}_2)_3\text{C=N—H}$ (≥ 110).

Comparison with Theoretical Calculations. The thermodynamic properties of the cyclopentyloxy (**1**) and 4-formylbutyl (**2**) radicals were calculated in two ways; by Benson's group-additivity method²⁹ and by the use of a standard AM1-UHF program.³⁰ The results are given in Table III. The ΔH_f° values obtained by the AM1-UHF method are in poor agreement with the group additivity values. This is not unexpected, as AM1-UHF calculations are known to underestimate heats of formation for neutral radicals.³⁰ The AM1-UHF values for C_p and S are in better agreement with group additivity results. For **1**, which contains no internal rotations, AM1-UHF and group additivity yield essentially the same values. However, the AM1-UHF values for C_p and S are lower than the group-additivity values for **2**, which contains four internal rotors. This is an expected result as AM1-UHF treats internal rotations as low-frequency vibrations and underestimates internal entropy contributions. Therefore, the group additivity S° value for **2** is used in all subsequent calculations.

The data given in Table III can be used to calculate the thermodynamics of the equilibrium $1 \rightleftharpoons 2$. The results of these theoretical calculations are compared to experimentally determined values in Table IV. The theoretical gas phase ΔG° values are ~ 3 kcal/mol more negative than the experimental value in benzene. The discrepancy can be attributed to enthalpic solvent effects. It has been noted that the activation enthalpy for the β -scission of the *tert*-butoxy radical is stabilized by 2.1 kcal/mol over that for H^\bullet abstraction from cyclohexane upon going from the gas phase to benzene solvent.³¹ The relative activation entropy, in contrast, remains the same. This solvent effect has been rationalized in terms of a charge-transfer complex as represented in **9**.³¹

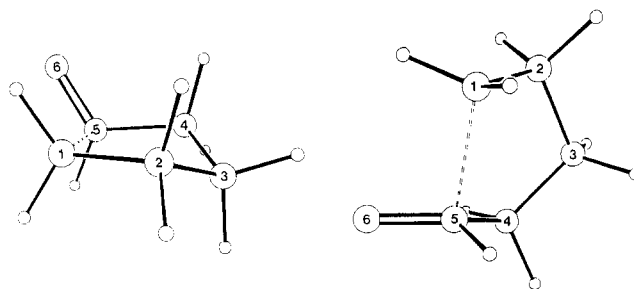


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**Figure 2.** Geometry of the transition structure for $1 \rightleftharpoons 2$ (see Table V).**Table VI.** Theoretical and Experimental Activation Parameters

	ΔH^\ddagger_1 , kcal/mol	ΔS^\ddagger_1 , cal/mol K	ΔH^\ddagger_{-1} , kcal/mol	ΔS^\ddagger_{-1} , cal/mol K
AM1-UHF ^a	14.46	-0.54	17.62	-15.4
experimental	5.67 ± 0.56	-1.2 ± 1.9	6.29 ± 0.91	-12.0 ± 1.4

^aAll values were calculated with 25 °C AM1-UHF data with the exception of ΔS^\ddagger_{-1} where the group-additivity value for the entropy of **2** was used (see text).

The transition-state geometry and thermodynamic properties for $1 \rightleftharpoons 2$ were calculated by AM1-UHF. The presence of exactly one negative eigenvalue in the molecular force constant matrix was proof of a transition state.³² Geometric features of the transition structure are given in Figure 2 and Table V. At the transition state for $1 \rightleftharpoons 2$, the C-C bond undergoing cleavage has stretched to 1.92 Å. This is significantly shorter than the values of 2.20 Å (MINDO/3),³³ 2.20 Å (MNDO),³⁴ and 2.34 Å (STO-3G)³⁵ obtained for the corresponding C-C bond in the transition structure for the ring opening of cyclopentylmethyl radical (**10**) to give hex-5-enyl radical (**11**). This result reveals



that $1 \rightleftharpoons 2$ has an earlier transition state than $10 \rightleftharpoons 11$, an observation consistent with the fact that the former reaction is exoergic ($\Delta G^\circ = -7$ kcal/mol, gas phase), while the latter reaction is endoergic ($\Delta G^\circ = 12$ kcal/mol, gas phase).³⁶

The thermodynamic properties of the transition structure for $1 \rightleftharpoons 2$ are given in Table III. The data in Table III, which also includes data for **1** and **2**, can be used to calculate activation parameters for $1 \rightarrow 2$ and $2 \rightarrow 1$. The results are compared with the experimental activation parameters in Table VI. The AM1-UHF values of ΔH^\ddagger_1 and ΔH^\ddagger_{-1} are far too large. While some of this difference could be due to solvent effects (vide supra), it has been noted that the AM1-UHF method overestimates activation enthalpies.³⁰ The theoretical values for ΔS^\ddagger_1 and ΔS^\ddagger_{-1} , on the other hand, are in reasonable agreement with the experimental activation entropies.

Previous calculations, based upon an early transition-state model, predict that $\Delta S^\ddagger = 1.7 - 2.6$ cal/(mol·K) for the β -scission of $\text{R}_1\text{R}_2\text{R}_3\text{CO}^\bullet$ (R = H, CH_3 , C_2H_5 , isopropyl) with the exception of cases where there are changes in rotational symmetry.⁸ The main contributions to these activation entropies arise from changes in vibrational frequencies, decreases in the potential barriers for internal rotations, and increasing moments of inertia. For the β -scission of **1**, only the changes in vibrational frequencies are significant as there are no internal rotors and the small change in the moments of inertia results in an external rotational contribution of only 0.07 cal/(mol·K) (see Table III). Therefore, one would expect the value of ΔS^\ddagger_1 to be lower than the ΔS^\ddagger range

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(36) The value of ΔG° for $10 \rightleftharpoons 11$ was estimated by using the group-additivity method:²⁹ 10 , $\Delta H_f^\circ = 20.4$ kcal/mol, $S^\circ = 84.6$ cal/mol K; 11 , $\Delta H_f^\circ = 36.0$ kcal/mol, $S^\circ = 95.9$ cal/mol K.

for the alkoxy radicals given above.

1,5-Exo cyclizations for radicals, including **2**, exhibit activation entropies in the range of -12 to -15 cal/(mol·K) (calculated from the data in Table II). The major contribution to this entropy change arises from the "freezing" of hindered rotations present in the open chain radical. The difference in the entropies of cyclopentane and pentene, 14.5 cal/(mol·K),²⁹ provides an estimate of the maximum expected contribution of 3.6 cal/(mol·K) per "frozen" rotation. As with the β -scission of **1**, the external rotational contribution is small, amounting to -0.66 cal/(mol·K) for the cyclization of **2** (see Table III).

Conclusions

The results presented above show that the β -scission of **1** is a reversible process in solution at temperatures from 6 to 80 °C.³⁷ They also provide absolute rate constants for the β -scission of **1** and the 1,5-exo cyclization of **2**. The reaction of *N*-alkoxy-pyridine-2-thiones with tributylstannane (**3**) has been shown to be a suitable system for the measurement of the rates of alkoxy radical reactions. With H[•] abstraction from **3** as a kinetic reference, the methods used in this study should allow the measurement of rate constants for a variety of alkoxy radical reactions within the range 10^6 – 10^9 s⁻¹ for unimolecular processes and 10^4 – 10^9 M⁻¹ s⁻¹ for bimolecular processes.

Experimental Section

Materials and Analyses. All solvents were distilled prior to use. The purity of tributylstannane (**3**) was determined by H₂ evolution from its reaction with dichloroacetic acid. If the purity was below 95%, **3** was purified by vacuum distillation. Sodium pyridine-2-thione *N*-oxide was purified by precipitation from methanol/ethyl acetate and dried in vacuo to a constant weight (mp 276 – 279 °C, lit.³⁸ mp 285 – 290 °C). ¹H NMR

spectra (200 MHz) were measured on a Varian XL-200 spectrometer. Analysis by gas chromatography was performed on a Varian 3400 with a 25-m phenyl methyl silicone capillary column; the response of the flame-ionization detector was calibrated with authentic compounds.

Preparation of *N*-(Cyclopentylloxy)pyridine-2-thione (6**).** The following manipulations were carried out with minimal exposure to light. Dry DMF (15 mL), sodium pyridine-2-thione *N*-oxide (1.5 g, 10 mmol), and cyclopentyl bromide (1.5 g, 10 mmol) were placed in a 50-mL round-bottom flask fitted with a reflux condenser. The contents were placed under argon and heated at 80 °C for 16 h. The dark yellow reaction mixture was diluted with 200 mL of 0.1 M aqueous NaOH and extracted with 5×50 mL aliquots of ether. The combined ether extracts were washed with 2×25 mL of H₂O and 25 mL of saturated NaCl and dried over MgSO₄. Removal of the solvent yielded an amber oil, which was further purified by column chromatography (ether, silica gel) to give **6** (0.6–0.8 g, 30–40%) as a yellow oil which eventually crystallized upon standing at -5 °C: mp 42 – 44 °C; MS, *m/z* 195.1; ¹H NMR (CDCl₃) δ 1.77 (m, 8 H), 5.62 (m, 1 H), 6.58 (dt, 1 H), 7.14 (dt, 1 H), 7.66 (m, 2 H). Anal. Calcd for C₁₀H₁₃NOS: C, 61.51; H, 6.71; N, 7.17. Found: C, 61.14; H, 7.04; N, 7.08.

Reactions of **6 with **3**.** Reactions were performed in Pyrex vials sealed with Teflon-surfaced rubber septa. In a typical experiment, a vial was wrapped in alumina foil and charged with 0.5 mL of a 0.030 M benzene solution at **6**. The vial was sealed, frozen in liquid nitrogen, evacuated, and filled with argon via a needle through the septum. The vial was then placed in a thermostated bath (± 1 °C). After 15 min, **3** was injected through the septum to start the reaction. At temperatures ≥ 40 °C, the reactions were self-initiating and had gone to completion (yellow solutions became clear) within 1 h at 40 °C, 10 min at 60 °C, and 5 min at 80 °C. At temperatures < 40 °C, the aluminum foil was removed after the addition of **3** and the reactions were initiated by exposure to a 250-W tungsten lamp and were complete within 5 min.

Registry No. **1**, 53578-06-6; **2**, 78939-50-1; **6**, 114720-44-4; sodium pyridine-2-thione *N*-oxide, 15922-78-8; cyclopentyl bromide, 137-43-9; 5-bromo-1-pentanal, 1191-30-6.

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Diffusion–Reaction Kinetics Related to Grignard Reagent Formation. Analytic Steady-State Solution of a Simplified D Model, a Mechanism with First-Order Surface and First- and Second-Order Solution Steps¹

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Abstract: An analytic steady-state solution is obtained for a simplified "D model", a mechanism that may describe Grignard reagent formation. The reactive intermediate R is created at flux v at a planar solid surface. R and other intermediates Q and S diffuse freely in solution. R isomerizes to intermediate Q and reacts with the solvent SH, giving product RH and intermediate S. Q also reacts with solvent, giving QH and S. R, Q, and S react among themselves, giving products RR, RQ, RS, QQ, QS, and SS. At the surface, R, Q, and S react to form products RZ, QZ, and SZ. The transport of R, Q, and S is described by diffusion equations with the same coefficient D . The reactivities of R, Q, and S at the surface, with the solvent, and with one another are independent of the identity of the intermediate. Product yields vary with v and the parameters governing surface and solution reactivities of R, Q, and S. There is more isomerization in solution products than in those formed at the surface. Although a homogeneous reaction in either two or three dimensions would give a value of 2.0 for the yield ratio $Y_{RQ}/(Y_{RR}Y_{QQ})^{1/2}$, it is typically near 1.0 in the D model.

Kinetic treatments of the competitions that determine product distributions are essential tools for mechanistic investigations of reactions in homogeneous solutions. Similar studies have not been

brought to bear on nonelectrochemical reactions that occur at liquid–solid interfaces, such as Grignard reagent formation. This may be for good reason; among the possible complications are the following. (1) Reaction conditions may be ill-defined or uncontrollable. (2) Reactants, intermediates, and products may adsorb on the surface of the solid. (3) Surfaces, concentrations,

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