

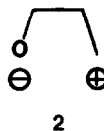
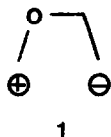
THE EFFECTS OF MEDIUM ON THE RATE AND REGIOCHEMISTRY
OF THERMALLY INDUCED OXETANE CYCLOREVERSIONS

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(Received in USA 28 February 1974; received in UK for publication 7 May 1974)

The work of numerous groups has indicated a free radical course for the decomposition of most cyclic and acyclic ethers,¹ and from stereochemical results a mechanism involving diradicals has been tentatively suggested for the homogeneous fragmentation of oxetanes.² On the other hand, it seems reasonable that some charge separation should be manifest in fragmentation transition states involving oxygen,³ and for the small ring oxirane decompositions, the formation of discrete dipoles has been confirmed by chemical trapping for some ring substituent patterns⁴ and remains a distinct possibility for others.⁵

In our program to probe mechanistic and synthetic aspects of oxetane decomposition, we have examined the effects of medium on the course of oxetane cleavage with reference to the possible intervention of dipoles 1 (a homocarbonyl ylide) and 2.

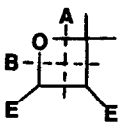
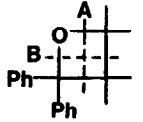
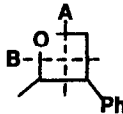


An examination of homopolar vs. heteropolar bond dissociation energies⁶ indicates that significant substituent and/or solvent stabilization should be required for

dipole formation. In fact solvent effects vary widely for dipolar cycloadditions,⁷ but for some reaction systems in principle involving 1,3 or 1,4 dipoles an increase in solvent polarity brings about striking changes.⁸

Oxetanes 3 (trans), 4, and 5 (trans) were pyrolyzed either at 10 - 20% solutions in pyrex ampoules or in a packed flow system (contact time, 10-15 sec). Fragmentation products were compared with authentic samples.^{2,9} The results of a combination of glc and nmr analyses concerning the rates of oxetane decomposition and the modes of cleavage (A vs. B) are shown in the Table. A heterogeneous component in the

Table. Regioselectivity and Rates of Oxetane Cycloreversion.

Starting oxetane	Solvent	Temperature(°C)	k(sec ⁻¹)	Regioselectivity (A/B)
 $E = CO_2Me$	DPE	290.5	$2.69 \pm .07 \times 10^{-4}$	> 13
	90% diglyme	290.5	$< 4.5 \times 10^{-4}$ ^a	> 13
	flow	390-410	---	> 13
	DPE	310.0	$1.36 \pm 0.13 \times 10^{-4}$	4.9 ± 0.7
	DMF	310.0	$1.40 \pm 0.14 \times 10^{-4}$	15.0 ± 2.0
	flow	420-435	---	12.9 ± 4.8
	DPE	352.0	$2.0 \pm 0.1 \times 10^{-4}$	2.6 ± 0.4 ^b
	DMF	352.0	$2.0 \pm 0.5 \times 10^{-4}$	3.4 ± 0.4
	flow	440-470	---	2.6 ± 0.3 ^b

^a Side products observed but cracking still largely unchanged.

^b 95 ± 2% retention of configuration in product olefin.

fragmentation of 4 was apparent. In most purified solvents (diphenylmethane, methyl benzoate, and HMPA), cleavage mode B predominated (as previously reported⁹), and the overall decomposition rate was accelerated slightly. However, in carefully base-treated diphenyl ether (DPE) and DMF slower rates and high regioselectivity (favoring A) were observed (see Table). As expected acid-catalyzed (e.g., CCl₄, H₂SO₄) cracking of 4 and 5 proceeded near room temperature and gave

exclusively products of fragmentation B.

The data clearly indicate little if any response to change in medium from the gas phase to solvent of low polarity (DPE, $\epsilon = 3.65$, 30°) to solvent of high polarity (DMF, $\epsilon = 36.71$, 25°). Notwithstanding the diminution of dielectric constant for organic liquids at high temperature,¹⁰ one must conclude that there is no significant charge separation at the rate determining transition state for cycloreversion of these oxetanes. The medium response of these reactions parallels that of the least polar of potentially dipolar cycloadditions.⁷ The charge stabilizing ability of substituents in 3-5 is moderate, but it appears that the substituent requirement is not excessive for dipolar ring opening in the model oxirane systems.^{4,5} Moreover, regiochemistry (especially for 5) provides a sensitive fingerprint of reactivity, since it might depend on the formation of 1 or 2 in competition with a concerted or diradical path and therefore respond to solvent polarity dramatically. That a dipolar intermediate is not involved in either fragmentation mode is also supported by the failure of a good dipolarophile, dimethyl maleate (1.0 M in DPE), to alter the rate ($0.96 \pm .08 \times 10^{-4} \text{ sec}^{-1}$) or regioselectivity (A/B >15) of decomposition of 4 at 310.0° .

The temperature dependence of cycloreversion of 5 was examined by a least squares treatment of first order rate data in the range $339-366^\circ$. For overall decomposition, $\Delta H = 51.5 \pm 2.5 \text{ kcal/mol}$ and $\Delta S = 5.6 \pm 4.1 \text{ eu}$. From an Arrhenius plot of $\log A/B$ vs. $1/T$ ($352-470^\circ\text{C}$, data from static and flow pyrolysis) and incorporating generously probable errors in product ratio and temperature, $\Delta E_a = 1.3 \pm 2.1 \text{ kcal/mol}$ and $\Delta \log A = 0.0 \pm 0.7$, consistent with the notion that the cracking modes follow similar mechanisms.

Regioselectivity in cracking for 3-5 appears to be predictable on the basis of formation in each case of the more stable diradical.¹¹ With the defineable loss of stereochemistry,² the absence of a solvent effect, and with the activation parameters reported here and elsewhere¹³ for simple oxetane cleavages, the diradical path

presently is the mechanism of choice. However, caution is in order since a comparison of activation data for 2 ($E_a = 54 \pm 2$ kcal/mol) and for oxetane itself ($E_a = 60 \pm 1$ kcal/mol¹³) reveals a combined diradical stabilizing effect for methyl and phenyl of only 3-9 kcal/mol.¹⁴ Thus, 5 is perhaps the most stable phenylated small ring yet studied.

In fulfillment of synthetic objectives a combination of acid catalyzed (for 4 and 5) and homogeneous pyrolytic (for 3) cleavages gives 'carbonyl-olefin metathesis' (from photocycloaddends).⁹ We will soon report several synthetically non-trivial examples of use of this synthon involving bicyclic oxetanes.

ACKNOWLEDGEMENTS

We thank Research Corporation, the donors of the Petroleum Research Fund, and Sigma Xi, The Scientific Research Society of America for generous financial support.

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